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REVIEW

Phytochemistry and Pharmacology of Genus *Artocarpus*: A Review on Current Status of Knowledge

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Abstract—*Artocarpus* (Moraceae) species have been widely studied for phytochemical components and pharmacological activity. This review aims to highlight key findings on the discovery, biosynthesis, and biological properties of *Artocarpus* metabolites. One hundred papers over the past 50 years were critically analysed. Current trends in the research of the genus are also discussed. The ethno-medicinal benefits of *Artocarpus* species, mainly for inflammation, malaria, diarrhoea, diabetes, and tapeworm infection, have a strong bond between traditional and modern sources. *Artocarpus* crude extract, especially those from the leaves, bark, stem, and fruit, contain numerous beneficial active molecules, including flavonoids, stilbenoids, aryl benzofurans, and the lectin jacalin. To understand the flavonoid and triterpenoid mechanisms as antimalarial agents, more research on *Artocarpus* is required. Highly collaborative programs that integrate conventional and modern techniques will be crucial for the future applications of *Artocarpus* as a possible source of medicinal natural products.

Keywords: *Artocarpus*, phytochemistry, pharmacology, *Artocarpus lakoocha*, traditional medicine, antimalarial

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Abbreviations: AL, *Artocarpus lakoocha* Roxb.; AH, *Artocarpus heterophyllus* Lam.; AA, *Artocarpus altilis*; Ah, *Artocarpus hirsutus*; AC, *Artocarpus camansi*; AK, *Artocarpus kemando* Miq; AI, *Artocarpus integer*; AE, *Artocarpus elasticus*; AR, *Artocarpus* rigidus; AS, *Artocarpus sericicarpus*; Pf, *Plasmodium falciparum*; Pb, *Plasmodium berghei*; ALL, *Artocarpus lingnanensis* lectin; NAD, *N*-acetyl-*D*-galactosaminide; DAAs, direct-acting antiviral; SVR, sustained virologic response; HCV, *Hepatitis* C virus; DCM, dichloromethane; IMC, isothermal microcalorimetry; AN, *Aspergillus niger*; XRD, X-ray diffraction; LPS, lipopolysaccharide; NF-B, factor-kappa B; MAPK, mitogen-activated protein kinase; NO, nitric oxide; PGE2, prostaglandin E2; Gg, *Glycyrrhiza glabra*; TYR, tyrosinase; MITF, microphthalmia-associated transcription factor; TRP-2, tyrosinase-related protein-2; ACS, alginate/chitosan; AI, *Artocarpus incises*; Ar, Artocarpin; At, *Artocarpus tonkinensis*; CIA, collagen-induced arthritis; PSE, plant sterol esters; LDL-C, LDL-cholesterol; TC, total cholesterol; TGF-β, transforming growth factor-beta; PDGF-BB, platelet-derived growth factor; TLC, thin layer chromatography; UV-Vis, ultraviolet-visible; FT-IR, fourier transform infrared; ^{1}H, hydrogen-1; ^{13}C-NMR, carbon-13 nuclear magnetic resonance; EA, *Enterobacter aerogenes*; MIC, minimum inhibitory concentration; *E. coli*, *Escherichia coli*; ATCC, american typre culture collection; IMC, isothermal microcalorimetry; cAMP, cyclic adenosine monophosphate; MAP, mitogen-activated protein; LDH, lactate dehydrogenase; HPTLC, high-performance thin layer chromatography; CMC, carboxymethyl cellulose; IC_{50}, inhibition concentrations; ED_{50}, effective dosage values; MABA, microplate alamar blue assay; HRMS, high resolution mass spectroscopy; HOMA-β, homeostasis model assessment, TFE, trifluoroethanol extracts; GC-MS, gas chromatography mass spectroscopy; DLS, dynamic light scattering; Ag_2O-NPs, silver oxide nanoparticles; COX-2, cyclooxygenase 2; DPPH, 2,2-diphenylpicrylhydrazyl; TPC, total phenolic content; PFBp, protein fraction of breadfruit pulp; OxLDL, oxidised LDL; PSE, plant sterol esters; LDL-C, LDL-cholesterol; TGF-β, transforming growth factor-beta; PDGF-BB, platelet-derived growth factor; TRAP, tartrate- resistant acid phosphatase; *Rf*, retention factor.

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INTRODUCTION

Plant-based medications are widely utilized in traditional systems of medicine and are growing increasingly popular. According to the World Health Organization, more than 85% of the world's population in developing countries rely on plant-based pharmaceuticals for their basic medical needs [1].

In many under developed nations, including India, conventional medicine is the cornerstone of health care, and most treatments are extracted from plants. *Artocarpus* contains a significant number of nutritional components. Among the most iconic species are *Artocarpus lakoocha* Roxb. (AL), *Artocarpus heterophyllus* Lam. (AH), *Artocarpus altilis* (AA), *Artocarpus hirsutus* (Ah), and *Artocarpus camansi* (AC) [2].

Artocarpus lakoocha, commonly known as "dahu", monkey fruit, jackfruit, is a tropical plant spp. of the Moraceae family. The jackfruit is a perennial plant with a long history of use as a food and medical supplies and a growing list of health benefits. In addition to fruits and seeds, extracts from the aerial parts and beneath components have been used to control diabetes, mosquito-borne fever, asthma, eczema, tapeworm infection, anaemia, and other diseases which are depicted in (Fig. 1) [3].

This review aims to evaluate the Artocarpus species medicinal and nutritional characteristics depending on its traditional uses [4–130]. The pharmacological effects of the bioactive phytochemicals identified in these species have already been confirmed.

BOTANICAL DESCRIPTION

The biodiversity of threatened species and knowledge of *Artocarpus* (Moraceae) is not equal worldwide. They are usually found below 1000 m in altitude.

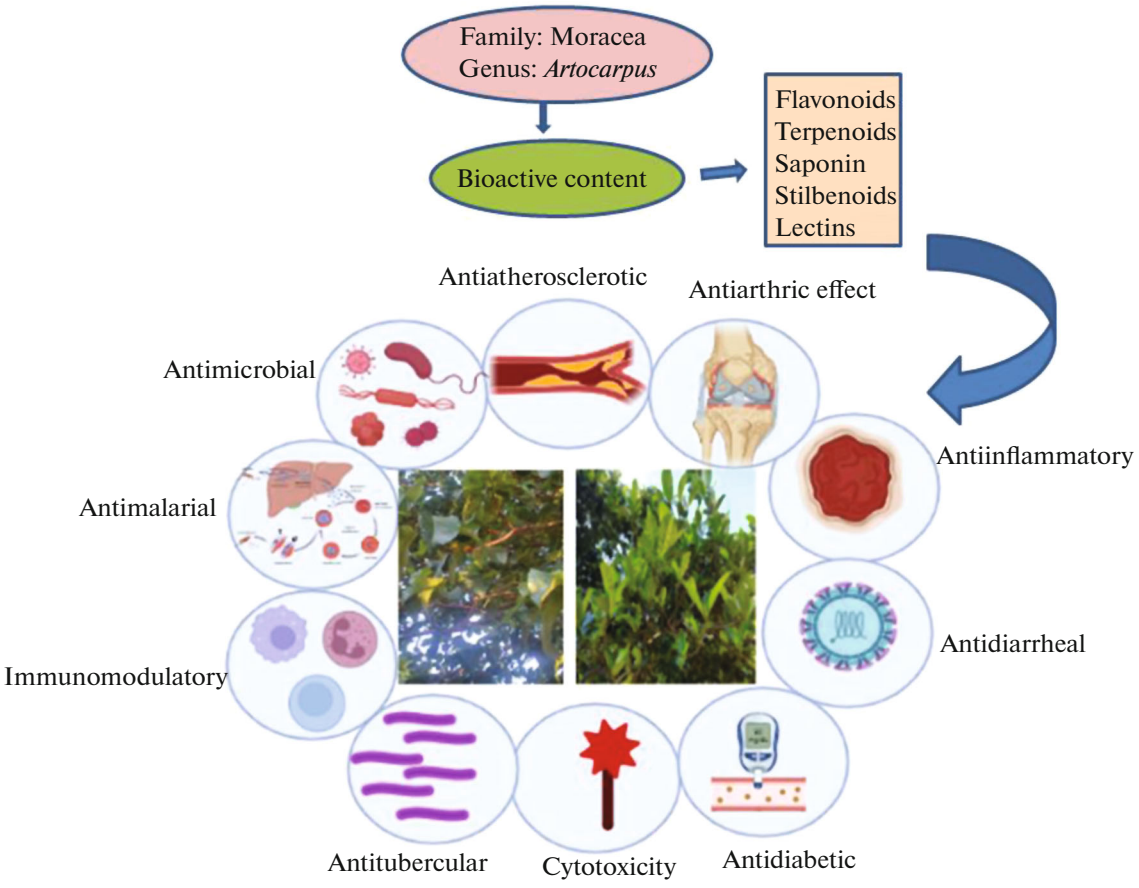


Fig. 1. Schematic representation of biological activities of *Artocarpus* species.

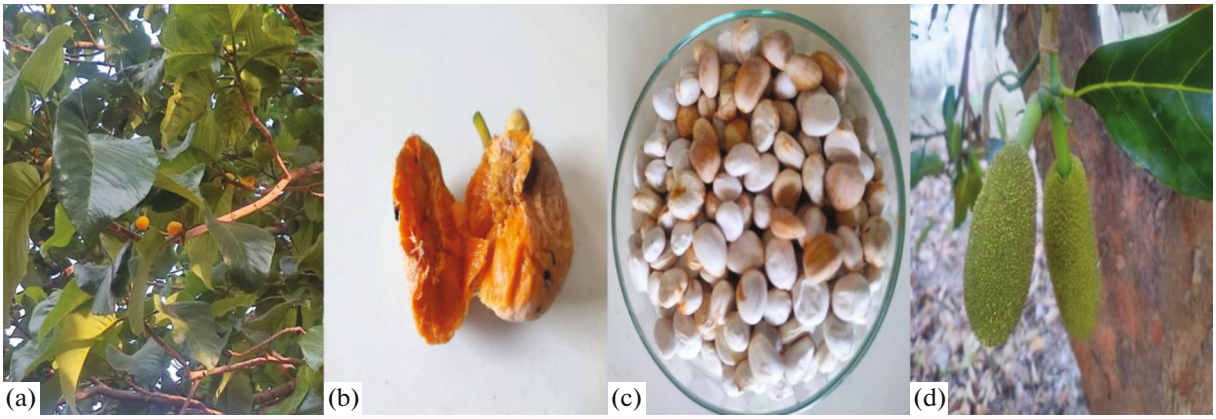


Fig. 2. (a) AL flowers; (b) AL fruit; (c) AL seeds; (d) AH fruits.

There are around 1000 species and 60 genera in the *Artocarpus* species cultivated in Asian nations. India, Sri Lanka, China, Myanmar, Malaysia, Indonesia, Bhutan, Vietnam, and Cambodia are among the countries that have embraced jackfruit Table 1 [2].

Artocarpus species are monoecious trees that range in size from small to large, are evergreen or deciduous, and have white latex throughout. Simple, whole to pinnatifid or petiolate leaves are spirally organized or alternating and distichous, coriaceous, hairless to glabrous, and clustered or alternating and distichous. Flowers are numerous, unisexual, capitates, head globose to spherical, lonely, or partnered in axils of the leaves or alternative type, and the inflorescence is unisexual. Various parts of *Artocarpus* species are depicted in (Fig. 2).

TRADITIONAL USES OF *ARTOCARPUS*

The *Artocarpus* genus is used in a variety of traditional folk medicinal remedies. The leaf, fruit, seed, root, and barks of the jack fruit and monkey fruit have medicinal value and are used in Ayurveda medicines. The mature fruits are delicious, pleasant, laxative, and nutritious and used to prevent excessive bile production. An extract prepared from the seeds is used to treat dysentery and diarrhoea. Modified seeds are said to have aphrodisiac properties. The leaves are valuable for treating asthma, worm infection, diabetes, and gall stones. In women and domesticated animals, the leaves are used also for wound-healing, antisyphilitic, vermifuge, and milk production [3].

EXPERIMENTAL

Design

The approach adopted in this study is literature review. A literature review examines and compiles the existing knowledge on the subject under study in order to identify any research gaps. A literature review is a methodical and understandable way to assess and summarise the findings of research and critical thinking produced by researchers and practitioners.

Article Criteria

In this study, inclusion criteria were developed in order to focus the search for the review papers. The inclusion criteria included a focus on mobe (*Artocarpus* species), a connection to medicine, full texts, articles published between 1972 and 2022, original research articles, English language articles, and articles with full texts. The goal of this study was to determine how frequently the biological activity, active ingredients, and pharmacological effects of *Artocarpus* species are subjected to rigorous scientific testing. Using search engines like PubMed, Science Direct, and Google Scholar, a total of 369 articles were discovered. Based on the search engine results, 129 articles were discovered that satisfied the inclusion criteria; these included articles on the biological activity of *Artocarpus* species, its active compounds, nutritional value, nutritional content, and pharmacological activity. Then, the items that met the requirements were compressed (Fig. 3) depicts the selection procedure.

Article Search

In the search combinations of specific word, such as "*Artocarpus*", "*Artocarpus lakoocha*", "Phytochemical", and "Pharmacological" were used. This search includes from Science Direct, Google Scholar, Pub Med and Elsevier portal, etc.

PHYTOCHEMISTRY

Flavonoids, Stilbenoids, and arylbenzofurons are phenolic compounds common in *Artocarpus* species, and their chemical compositions have previously been investigated [4]. June and December are being the busiest months for jackfruit, where one can expect its high availability [5]. The 100 g of ripe edible jackfruit

Table 1. *Artocarpus* species and geographical distributions

Species	Family	Geographical locations	Commercial use
Artocarpus lakoocha Lam.	Moraceae	Tropical regions of South and Southeast Asia, primarily Nepal, Sri Lanka, India, Myanmar, Indonesia, Vietnam, and Thailand	• Antiinflammatory therapy • Antiaging agent • Its dried aqueous extract of heartwood has been used as a traditional Antihelminthic agent. • The edible fruit pulp is used as a liver tonic.
Artocarpus heterophyllus	Moraceae	It is originated in the rain forests of India. Nowadays, jack fruit trees are widely grown in Bangladesh, Burma, and Indonesia. China, Sri Lanka, Thailand, the Philippines, parts of Africa, Australia, Brazil, and Florida	• The nutritious seeds are eaten as boiled or roasted chestnuts, added to flour for baking, or cooked in dishes. • The discarded leaves and fruit provide valuable fodder for cattle, pigs, and goats. • Jackfruit wood chips yield a dye, which is used to give Buddhist priests' robes their famous orange-red colour; • Leaves are useful in fever, boils, wounds, and skin diseases;
Artocarpus altilis	Moraceae	Native to New Guinea, Indonesia, and the Philippines. Currently, they are grown in Central and South America, Africa, India, Southeast Asia, the Maldives, Indonesia, Sri Lanka, and northern Australia.	• It exhibits cytotoxic and apoptotic effects on human cancer cells • The fruits are great source of carbohydrate and it has low fat. • Since the fruit can be steamed, fried, baked, roasted and fried, they can be eaten at all stages of growth.
Artocarpus hirsutus	Moraceae	It is an endemic tree species of southern Western Ghats of peninsular India	• Roots and bark are supposedly used to make a decoction that can treat diarrhoea. • Curcuma root and white camphor combined with the leaves is thought to be effective for treating venereal bubenes. • Alternating periods of bleeding
Artocarpus camansi	Moraceae	Originally from New Guinea, possibly also from Indonesia and the Philippines, and the Caribbean	• Yellowing or deteriorating leaves are boiled and used to relieve hypertension and control diabetes. • Tree sap is used as plaster to help dislocated joints. • The trunk and branches of the tree are frequently used as lumber.

usually contains carbohydrates, protein, moisture, fibre, total inorganic material, calcium, phosphorus, iron, and other nutrients [6].

The phytochemical which were detected in abundance among the five *Artocarpus* species were flavonoids, glycosides, tannins, phenols, saponin, alkaloids, steroids, and triterpenoids Table 2.

The plant sources/parts from where phytochemicals were isolated Table 3.

Phytochemical Profile of Artocarpus heterophyllus

According to the published existing literature, AH trees are likely to provide tannin, flavonoid, phenol, volatile constituents (Fig. 4), amino acid, sterol, mineral, and carotenoids [7–9]. Saturated fatty acids were observed to be higher than that of unsaturated fatty acids in jackfruit seed oil. Fatty acid contents were determined from jackfruit seed oil, with linoleic, palmitic, linoleic, stearic, and oleic acid as the main components reported in earlier studies [10].

Some of the primary bioactive components were reported in a heartwood, which includes Artocarpin, Brosimone, albanin A, cudraflavone C, B, prenyl apigenin, apigenin, norartocarpin, cudraflavone C, Morin, oxyresveratrol, norartocapetin, and artocarpesin, etc. [11, 12]. The flower's phenolic content, evaluated in Gallic acid equivalent, is greater than the flavonoid content, measured in quercetin equivalent, and the carotenoids. Calcium, potassium, and phosphorus are among the minerals with higher percentages, while magnesium, copper, manganese, and zinc are among the minerals with lower ratios reported previously, mentioned in Table 4 [13].

The bark contains betulinic acid, flavonoids, cycloheterophyllin, triterpenes compounds, and tannin [14, 15]. Usually, fruit is reported for higher amounts for vitamin A, vitamin C, thiamine, riboflavin, niacin, minerals, and other nutrients. It has been reported for its low caloric density, with only 94 calories in 100 g of fruit [16]. Varying amounts of sugar (79.13%), protein (5.84%), uronic acid (15.6%), phenolic acid (0.5%), and fifteen distinct amino acids were discovered in fruit pulp by one of recent study [17].

Fruit flakes were represented with a substantially higher phenolic content (11.57 GAE/g) than the methanolic of a fruit peel (48.04 GAE/g). The greatest flavonoid content was found in fruit peels (2.79 mg QuE/g), accompanied by fruit pulp with powder extracts [7]. Phenolic compounds, lignans, flavonoid, flavonols, saponin, amino, and volatiles were commonly reported in seeds [18].

The seed generally contains 21% starch, 11.40% crude oil, 20.20% protein, 51.80% carbohydrate, and dietary fibre (3.20%). Potassium (2500 ppm) concentrations were observed in much higher concentrations with respect to sodium (399 ppm), magnesium (230 ppm), and calcium (200 ppm) [7]. In two different varieties of AH seeds, carbohydrates were discovered in larger amounts (76.1%), followed by protein (17.8–18.3%) and crude lipids (2.1–2.5%) [19]. Seed kernels were demonstrated to have carotenes, zeacarotene, carboxyl group carotene, 6-epoxide, carotene-5, and crocetin as per one report [20].

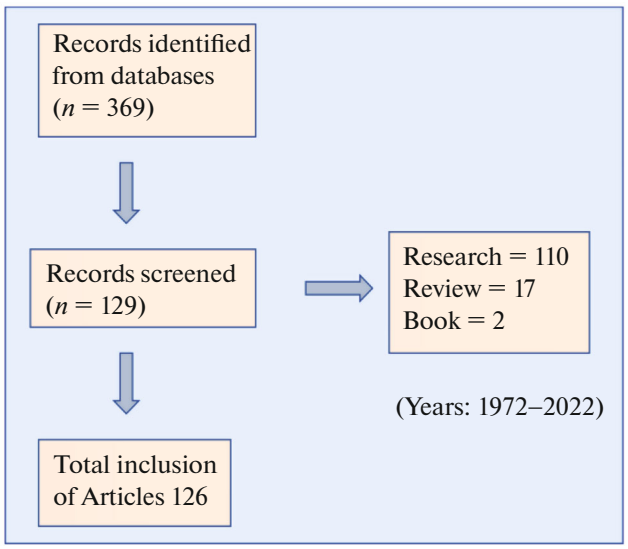


Fig. 3. Depicts the selection procedure of articles under considerations of this review.

The root contains flavonoids, ursolic acid, cycloartenone, β-sitosterol, and betulinic acid [21]. As per one research, 47 prenylated flavonoids were obtained in root ethanolic extract which were estimated with quadrupole time-of-flight mass spectrometry and linear trap quadrupole orbitrap mass spectrometry. During the investigation, 45 volatile compounds were also found in Malaysian AH fruit, 32 of which were uniquely identified. Esters, which are important for the fruit's associated aroma, were reported in high numbers (32%) from various studies [22, 23].

Phytochemical Profile of Artocarpus lakoocha

Various phytoconstituents like lakoochanosides, lakoochanone, Moracin C, integrin, cyclommunin, engeletin, isogemichalcone B, morachalcone A, heterophyllene B, albanin A, Moracin M, artocarpesin, norartocarpin, resveratrol, artocarpanone, and oxyresveratrol were reported in the bark, while flavones, phenols, tannins, eicosane, as well as diethyl phthalate are among the compounds found in the leaves [24–26].

The leaves of AH comprise of kaempferol and quercetin in noticeable amounts. Copper, zinc, manganese, and magnesium minerals were also described in abundance in the AL flower in previous studies. AL had been found with decreased levels of phosphorus, calcium, iron, and potassium [12]. The HPLC study also revealed that the fruit includes chromatotropic

Table 2. List of phytochemicals detected among varieties of *Artocarpus* species

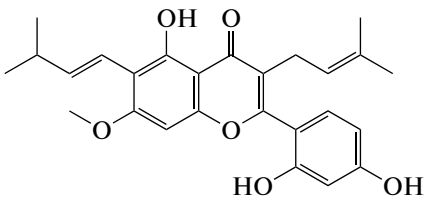
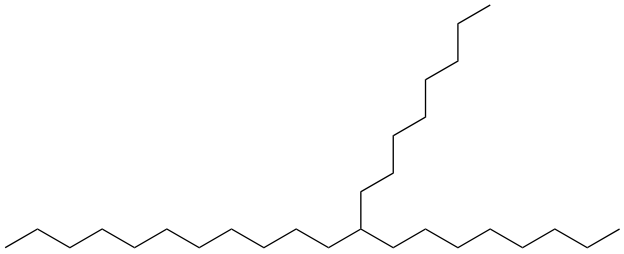
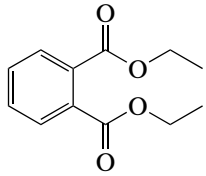
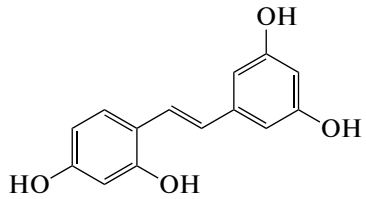
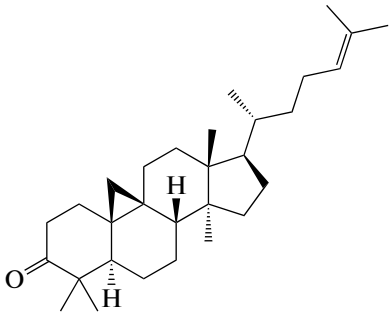
Name of the compound	Structure	Source	Activity
Artocarpin	 **IUPAC Name:** (*E*)-2-(2,4-dihydroxyphenyl)-5-hydroxy-7-methoxy-6-(3-methylbut-1-en-1-yl)-3-(3-methylbut-2-en-1-yl)-4*H*-chromen-4-one	*Artocarpus lakoocha*, *Artocarpus altalis*	Antimalarial Wound healing activity
Eicosane	 **IUPAC Name:** 9-octylicosane	*Artocarpus lakoocha*	Antifungal
Diethyl phthalate	 **IUPAC Name:** ethyl 2-(ethoxycarbonyl) benzoate	*Artocarpus lakoocha*	Antimicrobial Antioxidant
Oxyresveratrol	 **IUPAC Name:** 4-[(*E*)-2-(3,5-dihydroxyphenyl)ethen-1-yl]benzene-1,3-diol	*Artocarpus lakoocha*	Antioxidants, Antiinflammatory
Cycloartenone	 **UPAC Name:** (2*aR*,3*R*,5*aS*,5*bS*,7*aR*,11*aR*,12*aS*)-2*a*,5*a*,8,8-tetramethyl-3-((*R*)-6-methylhept-5-en-2-yl) tetradecahydro-9*H*,12*H*-cyclopenta [*a*]cyclopropa[*e*]phenanthren-9-one	*Artocarpus lakoocha*	Antioxidant

Table 2. (Contd.)

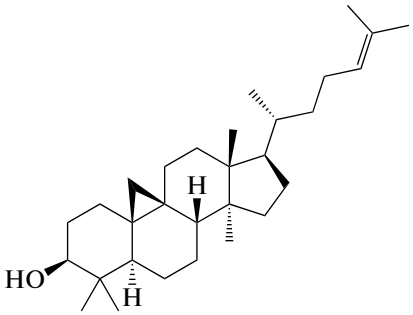
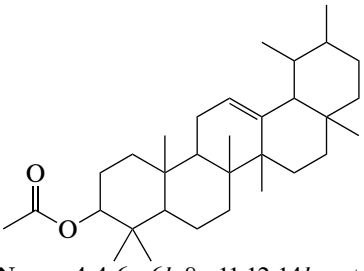
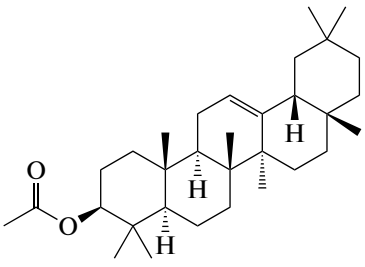
Name of the compound	Structure	Source	Activity
Cycloartenol	 **IUPAC Name:** (2*aR*,3*R*,5*aS*,5*bS*,7*aR*,9*S*,11*aR*,12*aS*)-2*a*,5*a*,8,8-tetramethyl-3-((*R*)-6-methylhept-5-en-2-yl)tetradecahydro-1*H*,12*H*-cyclopenta[*a*]cyclopropa[*e*]phenanthren-9-ol	*Artocarpus camansi*, *Artocarpus heterophyllus*	Antimicrobial activity
α-Amyrin acetate	 **IUPAC Name:** 4,4,6*a*,6*b*,8*a*,11,12,14*b*-octamethyl-1,2,3,4,4*a*,5,6,6*a*,6*b*,7,8,8*a*,9,10,11,12,12*a*,14,14*a*,14*b*-icosahydropicen-3-yl acetate	*Artocarpus lakoocha*	Antioxidant
β-Amyrin acetate	 **IUPAC Name:** (3*S*,4*aR*,6*aR*,6*bS*,8*aR*,12*aR*,14*aR*,14*bR*)-4,4,6*a*,6*b*,8*a*,11,11,14*b*-octamethyl-1,2,3,4,4*a*,5,6,6*a*,6*b*,7,8,8*a*,9,10,11,12,12*a*,14,14*a*,14*b*-icosahydropicen-3-yl acetate	*Artocarpus lakoocha*	antioxidant

Table 2. (Contd.)

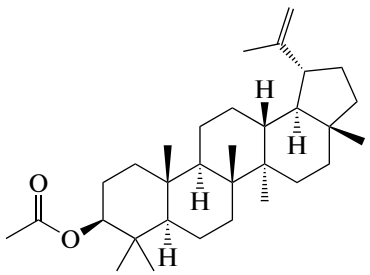
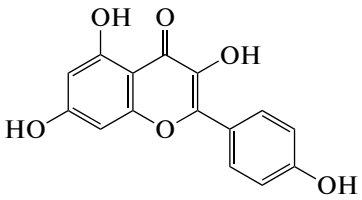
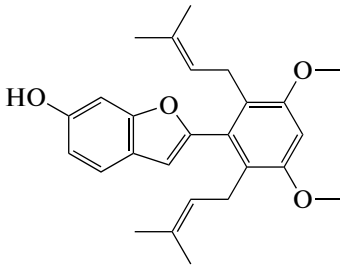
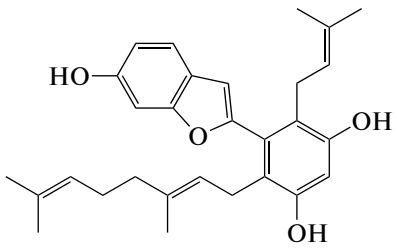
Name of the compound	Structure	Source	Activity
Leupeol acetate	 **IUPAC Name:** [(1*R*,3*aR*,5*aR*,5*bR*,7*aR*,9*S*,11*aR*,11*bR*,13*aR*,13*bR*)-3*a*,5*a*,5*b*,8,8,11*a*-hexamethyl-1-prop-1-en-2-yl-1,2,3,4,5,6,7,7*a*,9,10,11,11*b*,12,13,13*a*,13*b*-hexadecahydrocyclopenta[*a*] chrysen-9-yl] acetate	*Artocarpus camansi*, *Artocarpus lakoocha*, *Artocarpus heterophyllus*	Antioxidant
Kaempferol	 **IUPAC Name:** 3,5,7-trihydroxy-2-(4-hydroxyphenyl)-4*H*-1-benzopyran-4-one	*Artocarpus lakoocha*	Antioxidant, Hepatoprotective agents
Lakoochin A	 **IUPAC Name:** 2-[3,5-dimethoxy-2,6-bis(3-methylbut-2-enyl)phenyl]-1-benzofuran-6-ol	*Artocarpus lakoocha*, *Artocarpus xanthocarpus*	Antimicrobial activity
Lakoochin B	 **IUPAC Name:** 4-[(2*E*)-3,7-dimethylocta-2,6-dienyl]-5-(6-hydroxy-1-benzofuran-2-yl)-6-(3-methylbut-2-enyl)benzene-1,3-diol	*Artocarpus lakoocha*, *Artocarpus xanthocarpus*	Antimicrobial activity

Table 2. (Contd.)

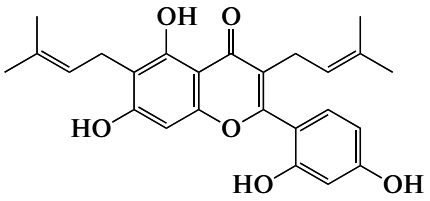
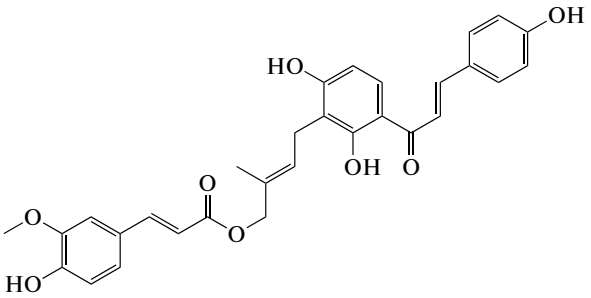
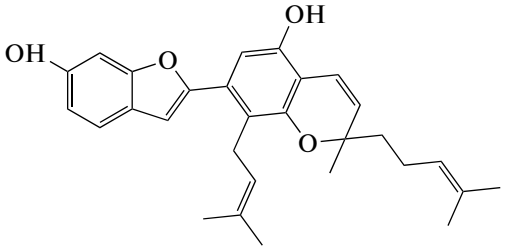
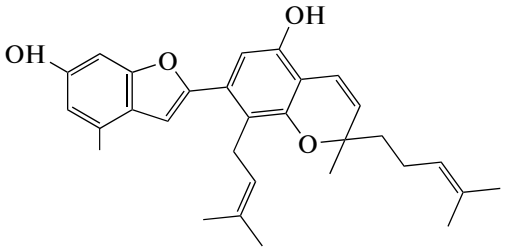
Name of the compound	Structure	Source	Activity
Cudraflavone C	 **IUPAC Name:** 2-(2,4-dihydroxyphenyl)-5,7-dihydroxy-3,6-bis(3-methylbut-2-enyl)chromen-4-one	*Artocarpus lakoocha*, *Artocarpus heterophyllus*, *Artocarpus champeden*	Cytotoxic, Antitubercular
Artocarmitin B	 **IUPAC Name:** (*E*)-4-(2,6-dihydroxy-3-((*E*)-3-(4-hydroxyphenyl)acryloyl)phenyl)-2-methylbut-2-en-1-yl (*E*)-3-(4-hydroxy-3-methoxyphenyl) acrylate	*Artocarpus heterophyllus*	Antioxidant activity
Artolakoochol	 **IUPAC Name:** 7-(6-hydroxybenzofuran-2-yl)-2-methyl-8-(3-methylbut-2-en-1-yl)-2-(4-methylpent-3-en-1-yl)-2*H*-chromen-5-ol	*Artocarpus heterophyllus*	Antiherpetic activity
4-Hydroxyartol-akoochol	 **IUPAC Name:** 2-(5-hydroxy-2-methyl-8-(3-methylbut-2-en-1-yl)-2-(4-methylpent-3-en-1-yl)-2*H*-chromen-7-yl)benzofuran-4,6-diol	*Artocarpus lakoocha*	Antiherpetic activity

Table 2. (Contd.)

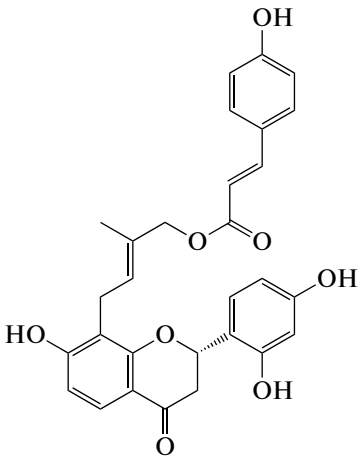
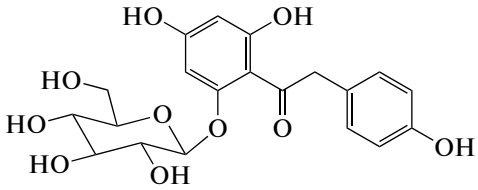
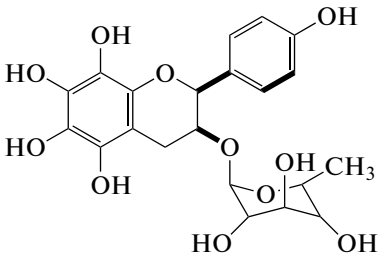
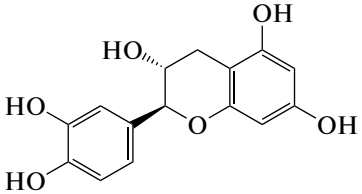
Name of the compound	Structure	Source	Activity
Lakoochanone	 **IUPAC Name:** (*E*)-4-((S)-2-(2,4-dihydroxyphenyl)-7-hydroxy-4-oxochroman-8-yl)-2-methylbut-2-en-1-yl (*E*)-3-(4-hydroxyphenyl)acrylate	*Artocarpus heterophyllus*, *Artocarpus lakoocha*	Antiplasmodium activity, Antitubercular activity
Lakoochanoside A	 **IUPAC Name:** 1-(2,4-dihydroxy-6-(((2*S*,3*R*,5*S*,6*R*)-3,4,5-trihydroxy-6-(hydroxymethyl)tetrahydro-2*H*-pyran-2-yl)oxy)phenyl)-2-(4-hydroxyphenyl)ethan-1-one	*Artocarpus lakoocha*	Antiplasmodial activity
Lakoochanoside B	 **IUPAC Name:** (2*S*,3*S*)-2-(4-hydroxyphenyl)-3-(((2*R*,3*S*,4*R*,6*S*)-3,4,5-trihydroxy-6-methyltetrahydro-2*H*-pyran-2-yl)oxy)chromane-5,6,7,8-tetraol	*Artocarpus lakoocha*	Antiplasmodial activity
Catechin	 **IUPAC Name:** (2*S*,3*R*)-2-(3,4-dihydroxyphenyl)chromane-3,5,7-triol	*Artocarpus lakoocha, Artocarpus heterophyllus*	Antimalarial Antioxidant Antibacterial

Table 2. (Contd.)

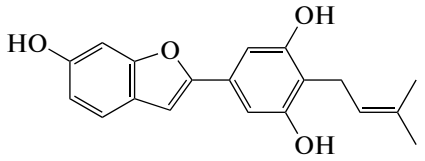
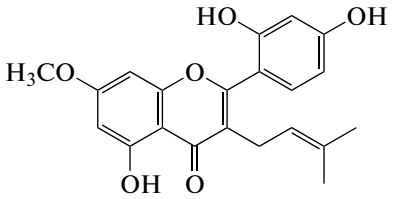
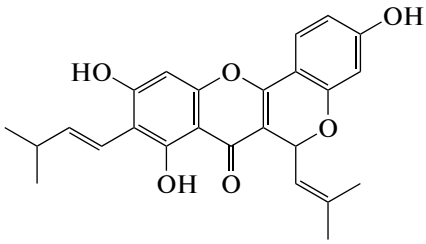
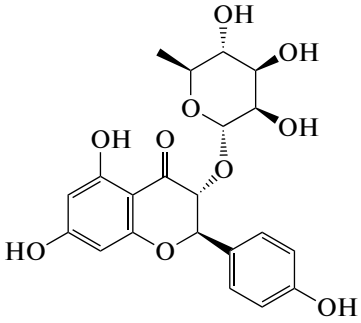
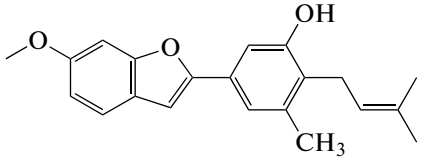
Name of the compound	Structure	Source	Activity
Moracin C	 **IUPAC Name:** 5-(6-hydroxybenzofuran-2-yl)-2-(3-methylbut-2-en-1-yl)benzene-1,3-diol	*Artocarpus lakoocha*, *Artocarpus heterophyllus*	Antiinflammatory, Antiviral, Antimalarial
Integrin	 **IUPAC Name:** 2-(2,4-dihydroxyphenyl)-5-hydroxy-7-methoxy-3-(3-methylbut-2-en-1-yl)-4*H*-chromen-4-one	*Artocarpus integrifolia*	–
Cyclocommunin	 **IUPAC Name:** (*E*)-3,8,10-trihydroxy-9-(3-methylbut-1-en-1-yl)-6-(2-methylprop-1-en-1-yl)-6*H*,7*H*-chromeno[4,3-*b*]chromen-7-one	*Artocarpus champeden*, *Artocarpus lakoocha*	Antiinflammatory activity
Engeletin	 **IUPAC Name:** (2*R*,3*R*)-5,7-dihydroxy-2-(4-hydroxyphenyl)-3-(((2*S*,3*R*,4*R*,5*R*,6*S*)-3,4,5-trihydroxy-6-methyltetrahydro-2*H*-pyran-2-yl)oxy)chroman-4-one	*Artocarpus lakoocha*	antioxidants
Sanggenofuran B		*Artocarpus lakoocha*	Cytotoxic activity
	 **IUPAC Name:** (*E*)-2-methoxy-4,3',5'trihydroxystilbene	*Artocarpus lakoocha*	Antimalarial, Antioxidant

Table 2. (Contd.)

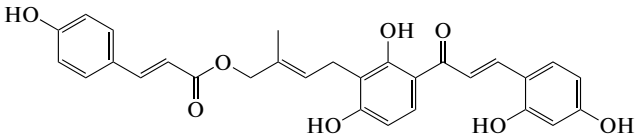
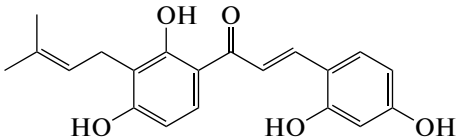
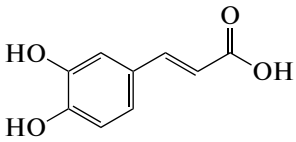
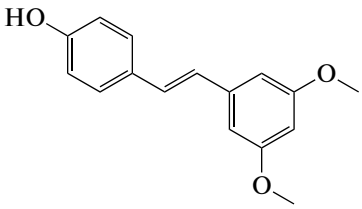
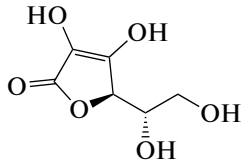
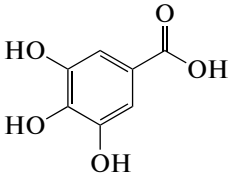
Name of the compound	Structure	Source	Activity
Isomigechalcone B	 **IUPAC Name:** (*E*)-4-(3-((E)-3-(2,4-dihydroxyphenyl)acryloyl)-2,6-dihydroxyphenyl)-2-methylbut-2-en-1-yl(*E*)-3-(4-hydroxyphenyl)acrylate	*Artocarpus lakoocha*	Antioxidant
Morachalcone A	 **IUPAC Name:** (*E*)-1-(2,4-dihydroxy-3-(3-methylbut-2-en-1-yl)phenyl)-3-(2,4dihydroxyphenyl) prop-2-en-1-one	*Artocarpus lakoocha*	Antiplatelets
Caffeic acid	 **IUPAC Name:** (*E*)-3-(3,4-dihydroxyphenyl)acrylic acid	*Artocarpus lakoocha, Artocarpus heterophyllus*	Antioxidants
Pterostilbene	 **IUPAC Name:** (*E*)-4-(3,5-dimethoxystyryl)phenol	*Artocarpus heterophyllus*	Antiglycation, Antioxidants
Ascorbic acid	 **IUPAC Name:** (*R*)-5-((*S*)-1,2-dihydroxyethyl)-3,4-dihydroxyfuran-2(5*H*)-one	*Artocarpus heterophyllus*, *Artocarpus lakoocha*	Antioxidants, Antifungal, Antibacterial, Antimalarial
Gallic acid	 **IUPAC Name:** 3,4,5-trihydroxybenzoic acid	*Artocarpus heterophyllus*, *Artocarpus lakoocha*	Antioxidant, Hepatoprotective agents, Antimalarial

Table 2. (Contd.)

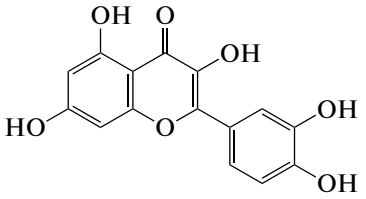
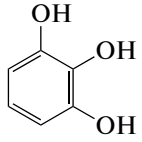
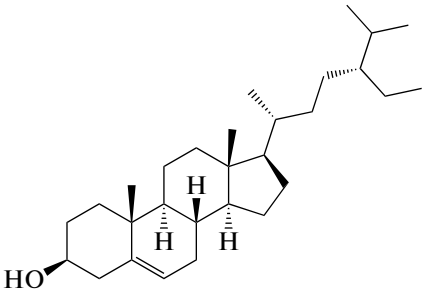
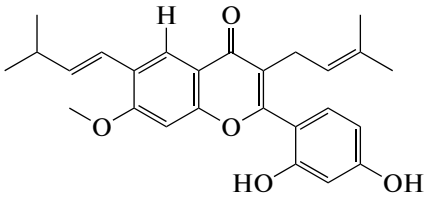
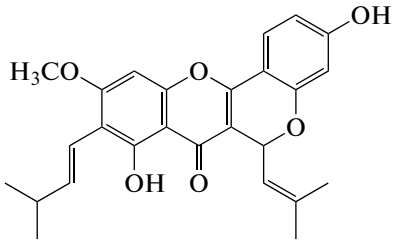
Name of the compound	Structure	Source	Activity
Quercetin	 **IUPAC Name:** 2-(3,4-dihydroxyphenyl)-3,5,7-trihydroxy-4*H*-chromen-4-one	*Artocarpus heterophyllus*, *Artocarpus lakoocha*	Antioxidant, Hepatoprotective agents, Antimalarial
Pyrogallol	 **IUPAC Name:** benzene-1,2,3-triol	*Artocarpus lakoocha*, *Artocarpus heterophyllus*	Antioxidants
β-Sitosterol	 **IUPAC Name:** (3*S*,8*S*,9*S*,10*R*,13*R*,14*S*,17*R*)-17-((2*R*,5*R*)-5-ethyl-6-methylheptan-2-yl)-10,13-dimethyl-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetrdecahydro-1*H*-cyclopenta[*a*]phenanthren-3-ol	*Artocarpus camansi*, *Artocarpus altilis*	Antiatherosclerotic
Norartocarpin	 **IUPAC Name:** (*E*)-2-(2,4-dihydroxyphenyl)-7-methoxy-6-(3-methylbut-1-en-1-yl)-3-(3-methylbut-2-en-1-yl)-4*H*-chromen-4-one	*Artocarpus heterophyllus*, *Artocarpus lakoocha*	Tyrosinase inhibitor
Cycloartocarpin	 **IUPAC Name**: (*E*)-3,8-dihydroxy-10-methoxy-9-(3-methylbut-1-en-1-yl)-6-(2-methylprop-1-en-1-yl)-6*H*,7*H*-chromeno[4,3-*b*]chromen-7-one	*Artocarpus altilis*	Antimalarial, Cytotoxic, Antitubercular

Table 2. (Contd.)

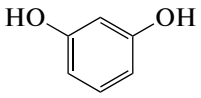
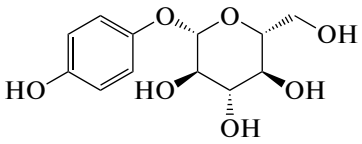
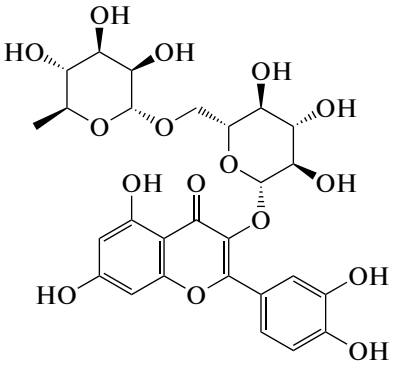
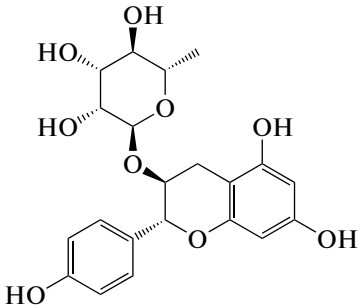
Name of the compound	Structure	Source	Activity
Resorcinol	 **IUPAC Name:** Benzene-1,3-diol	*Artocarpus heterophyllus*, *Artocarpus lakoocha*	Skin whitening
Arbutin	 **IUPAC Name:** (2*R*,3*S*,4*S*,5*R*,6*S*)-2-(hydroxymethyl)-6-(4-hydroxyphenoxy)tetrahydro-2*H*-pyran-3,4,5-triol	*Artocarpus heterophyllus*, *Artocarpus lakoocha*	Tyrosinase inhibitor
Rutin	 **IUPAC Name:** 2-(3,4-dihydroxyphenyl)-5,7-dihydroxy-3-(((2*S*,3*R*,4*S*,5*S*,6*R*)-3,4,5-trihydroxy-6-((((2*R*,3*R*,4*R*,5*R*,6*S*)-3,4,5-trihydroxy-6-methyltetrahydro-2*H*-pyran-2-yl)oxy)methyl)tetrahydro-2*H*-pyran-2-yl)oxy)-4*H*-chromen-4-one	*Artocarpus heterophyllus*, *Artocarpus lakoocha*, *Artocarpus altilis*	Antioxidants, Antimalarial, Antibacterial
(+)-Afzelechin 3-*O*-α-L-rhamnopyranoside	 **IUPAC Name:** (2*S*,3*R*,4*R*,5*R*,6*S*)-2-(((2*R*,3*S*)-5,7-dihydroxy-2-(4-hydroxyphenyl)chroman-3-yl)oxy)-6-methyltetrahydro-2*H*-pyran-3,4,5-triol	*Artocarpus lakoocha* Roxb.	Antimicrobial, Antimalarial

Table 2. (Contd.)

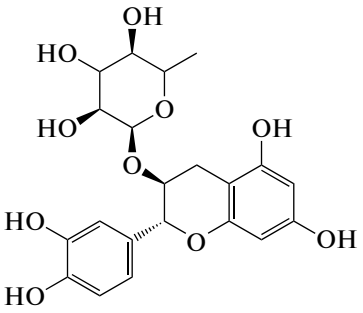
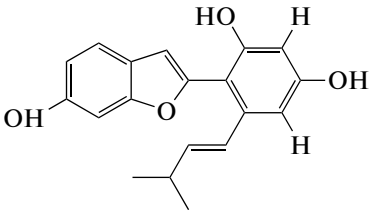
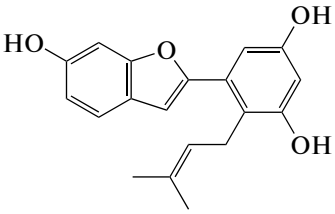
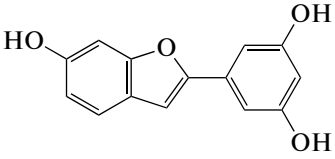
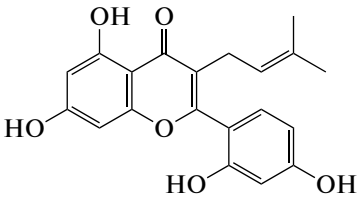
Name of the compound	Structure	Source	Activity
(+)-Catechin	 **IUPAC Name:** (2*S*,3*S*,5*R*)-2-(((2*R*,3*S*)-2-(3,4-dihydroxyphenyl)-5,7-dihydroxychroman-3-yl)oxy)-6-methyltetrahydro-2*H*-pyran-3,4,5-triol	*Artocarpus heterophyllus*	Antioxidant
Heterophyllene B	 **IUPAC Name:** (*E*)-4-(6-hydroxybenzofuran-2-yl)-5-(3-methylbut-1-en-1-yl)benzene-1,3-diol	*Artocarpus lakoocha*	Antioxidant, Antiplasmodial
Demethylmoracin I	 **IUPAC Name:** 5-(6-hydroxybenzofuran-2-yl)-4-(3-methylbut-2-en-1-yl)benzene-1,3-diol	*Artocarpus heterophyllus*	Tyrosinase inhibitory
Moracin M	 **IUPAC Name:** 5-(6-hydroxybenzofuran-2-yl)benzene-1,3-diol	*Artocarpus lakoocha*, *Artocarpus heterophyllus*	Tyrosinase inhibitory
Albanin A	 **IUPAC Name:** 2-(2,4-dihydroxyphenyl)-5,7-dihydroxy-3-(3-methylbut-2-en-1-yl)-4*H*-chromen-4-one	*Artocarpus heterophyllus*, *Artocarpus lakoocha*	Skin whitening agents

Table 2. (Contd.)

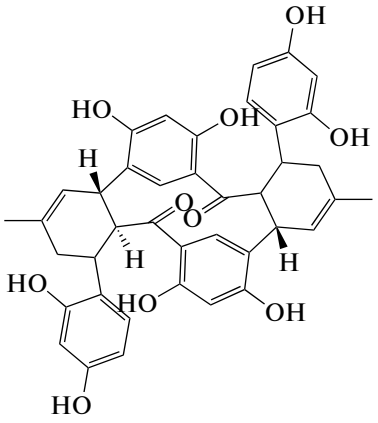
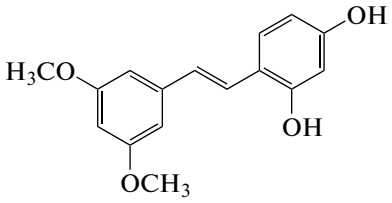
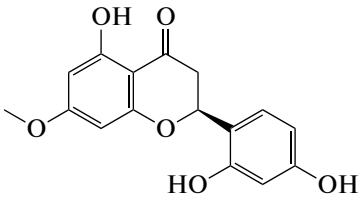
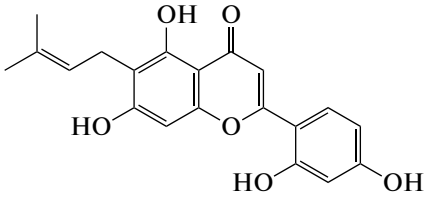
Name of the compound	Structure	Source	Activity
Brosimone	 **IUPAC Name:** (*E*)-4-(3,5-dimethoxystyryl)benzene-1,3-diol	*Artocarpus heterophyllus*, *Artocarpus lakoocha*	Antimalarial, Skin whitening agent
Heterophyllene D	 **IUPAC Name:**(*E*)-4-(3,5-dimethoxystyryl)benzene-1,3-diol	*Artocarpus lakoocha*	Antimalarial, Antimicrobial
Artocarpanone	 **IUPAC Name:** (*S*)-2-(2,4-dihydroxyphenyl)-5-hydroxy-7-methoxychroman-4-one	*Artocarpus lakoocha*, *Artocarpus communis*, *Artocarpus heterophyllus*	Antiinflammatory, Cytotoxic, Antidiarrheal
Artocarpesin	 **IUPAC Name:** 2-(2,4-dihydroxyphenyl)-5,7-dihydroxy-6-(3-methylbut-2-en-1-yl)-4*H*-chromen-4-one	*Artocarpus lakoocha*, *Artocarpus heterophyllus*	Antibacterial

Table 3. List of certain compounds from various plant parts of *Artocarpus* species*

Artocarpus species	Plant parts	Compound	Solvent
Artocarpus lakoocha	Flower	Carotenoids, flavonoids	Ethanol, methanol
	Bark	Lakoochanone, lakoochanosides, catechin, Moracin C, integrin, cyclocommunin, engeletin, isogemichalcone B, morachalcone A, heterophyllene B, albanin A, Moracin M, artocarpesin, norartocarpin, resveratrol, artocarpanone, oxyresveratrol	Acetone
	Fruits	Flavonoids, Tannins, terpenoids, saponin, glycosides, alkaloids, steroids, quercetin, Kaempferol	Methanol
	Heartwood	Oxyresveratrol	Ethanol
	Leaves	Flavonoids, phenols, tannins, eicosane, diethyl phthalate, 9-octyl eicosane	Pentane, *n*-hexane, ethyl acetate, acetone, methanol
Artocarpus heterophyllus Lam.	Flower	Carotenoids, flavonoids	Ethanol, methanol
	Leaves	Chromones, flavonoids, catechin, chlorogenic acid	Ethanol, methanol
	Roots	Flavonoids	Ethanol
	Stems	Chromones, flavonoids	Methanol
	Bark	Flavonoids, phenols, saponin, catechin, glycosides	Ethanol, methanol
	Peels		
	Pulps		
	Seeds	Flavonoids, tannins, saponin, glycosides, steroids, anthraquinones, phenols	Ethanol, methanol, *n*-hexane
Artocarpus hirsutus Lam.	Stem	Sterols, flavonoids, tannins, triterpenoids, saponin	Ethanol
	Leaves	Flavonoids, tannins, triterpenoids, saponin, glycosides, alkaloids, steroids	Acetone, ethanol, methanol
	Fruits	Flavonoids, terpenoids, saponin, glycosides, alkaloids, steroids	Acetone, methanol
Artocarpus camansi	Leaves	Friedelinol, squalene, stigmasterol, phytol, polyprenol, cycloartenol	Acetone
	Stem		
	Peels	Steroids, triterpenoids	*n*-Hexane
Artocarpus altilis	Bark	Prenylated, Stilbenoids	Methanol
	Peels	Alkaloids, flavonoids, phenols, tannins, glycosides	Ethanol
	Heartwood	Artocarpin, norartocarpin, cycloartocarpin, artonol B, cyclomorusin, artoflavone A, cyclogera communin, and artonin M, prenylated Stilbenoids, flavonoids	Ethanol, methanol
	Cortex		
	Fruits	Flavonols, tannins, catechin, monoterpene	Methanol
	Leaves	Phenols, flavonoids, prenylated aurone, artocarpaurone, prenylated chalcone, prenylated flavanone, triterpenes, Hexadecanoic acid and cinnamic acid	Ethanol, methanol
	Root	Prenyl flavonoids, triterpenoids	Ethanol
	Seeds		Ethanol

* Source: [3, 13, 38, 50, 117].

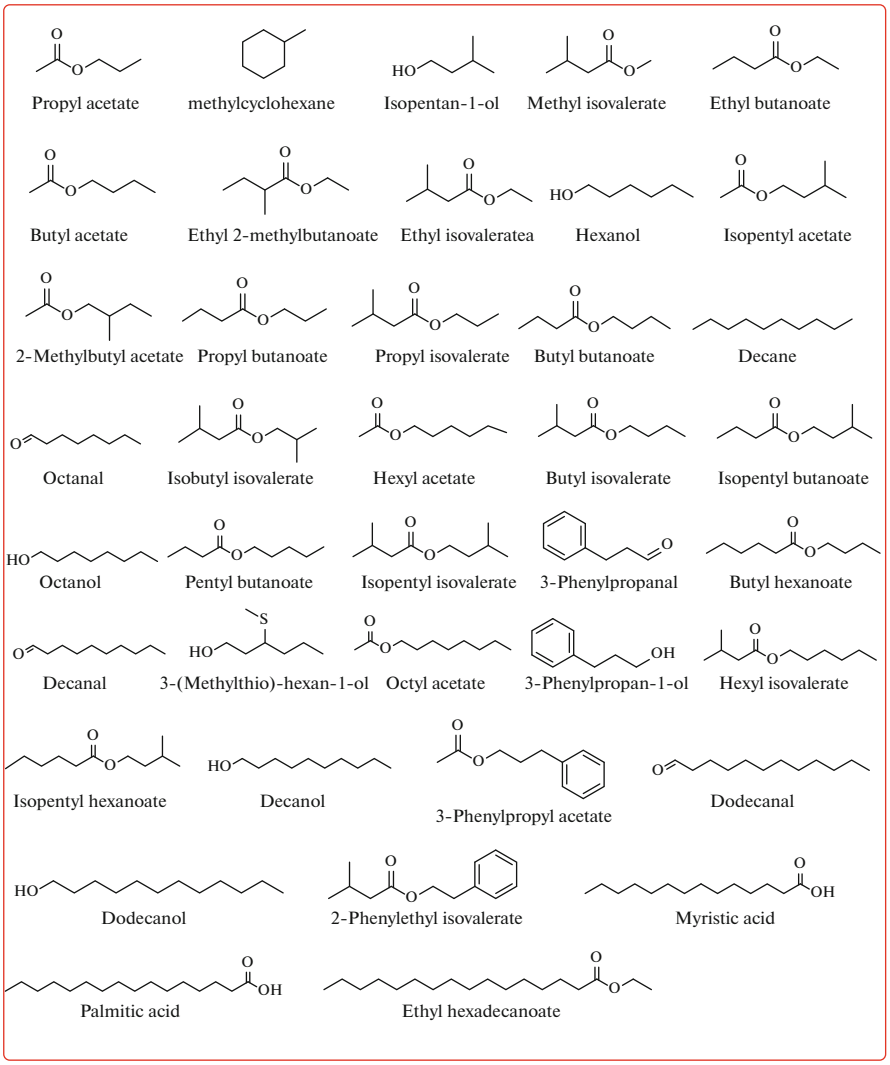


Fig. 4. Volatile constituents of *Artocarpus heterophyllus*.

acid, quercetin, Gallic acid, vanillic acid, cinnamic acid, ferulic acid, and kaempferol, etc. [27]. Albanin A [28], isoartocarpesin [29], cudraflavone C [30], norartocarpin [31], cudraflavone B [32], and catechin A [31], were reported from same plant as per the study [33]. Using membrane application, the oxyresveratrol component was isolated and purified from the obtained solution of AL petroleum ether extract of fruits and foliage. This included triterpenoids and phytosterols, which had larvicidal action [34, 35].

The heartwood extract can be used as an innovative skincare ingredient having antityrosinase and skin whitening activities in human previous screening studies of AL heartwood using thin layer chromatography (TLC), with capillary zone electrophoresis were identified Oxyresveratrol as the main active component, along with benzoic acid.

In one of studies, using a 70% ethanolic-extract system, various flavonoid or phenolic compounds were extracted [36], wherein this study was focused on an active component like catechin, flavonoid, or isoflavone. The active ingredients discovered in the AL extract were rutin, pyrogallol, gallic acid, phenol, flavonoid, catechin, and caffeic acid [37].

Phytochemical Profile of Artocarpus altilis

Artocarpus altilis showed the presence of steroids, anthraquinones, tannins, glycoside, and flavonoids [38]. The heartwood and cortex of AA comprises of artocarpin, norartocarpin, cycloartocarpin, artonol B, cyclomorusin, artoflavone A, cyclogera communin, and artonin M, prenylated stilbenoids, flavonoids [39]. Flavonols, tannins, catechin, monoterpene were commonly reported in fruits [40].

Various phytoconstituents like phenols, flavonoids, prenylated aurone, artocarpaurone, prenylated chalcone, prenylated flavanone, triterpenes, hexade-

Table 4. Composition of jackfruit (100 g edible portion)*

Composition	Ripe fruit
Water, g	72.0–94.0
Protein, g	1.2–1.9
Fat, g	0.1–0.4
Carbohydrate, g	16.0–25.4
Fibre, g	1.0–0.6
Total sugars, g	20.6
Total minerals, g	0.87–0.9
Calcium, mg	20.0–37.0
Magnesium, mg	27.0
Phosphorus, mg	38.0–41.0
Potassium, mg	191–407
Sodium, mg	2.0–41.0
Iron, mg	0.5–1.1
Vitamin A (IU)	175–540
Thiamine, mg	0.03–0.09
Riboflavin, mg	0.05–0.4
Vitamin C, mg	7.0–10.0
Energy (Kj)	88–410

* Source: [120].

canoic acid and cinnamic acid were also reported in leaves of AA. Prenyl flavonoids, triterpenoids were found from same plant as per the one study carried using roots and seeds [41–43]. Prenylated, Stilbenoids were commonly testified in bark. Peels alkaloids, flavonoids, phenols, tannins, glycosides were also described in abundance in the AA peels in previous studies [44].

Phytochemical Profile of Artocarpus hirsutus

Artocarpus hirsutus (Ah) showed the presence of sterols, terpenoids, saponin, tannins, lactones and flavonoids [45]. Cudraflavone C, a prenyl flavone was isolated from its stem bark [46]. Some of the primary bioactive components were reported from stem extracts, which include sterols, flavonoids, tannins, triterpenoids, and saponin. Ah leaves include flavonoids, tannins, triterpenoids, saponin, glycosides, alkaloids, and steroids Table 5.

These components were extracted with acetone and methanol as solvents from Ah fruit [47, 48].

Phytochemicals from Artocarpus camansi

Artocarpus camansi was reported to have polyprenol, sqallene, and β-sitosterol [49]. A variety of known

Table 5. Preliminary phytochemical screening of *Artocarpus hirsutus*

Phytochemical Class	Test/reagent used	Leaf		Fruit	
		acetone	ethanol	acetone	ethanol
Alkaloids	Wagner's test	+	+	+	+
	Mayer's test	+	+	+	+
Flavonoids	Alkaline reagent	+	+	+	–
	Lead acetate test	+	–	–	–
	Ferric Chloride test	–	+	–	–
Glycosides	Borntrager's test	+	–	+	+
	Legal's test	+	+	+	+
	Killani test	+	–	+	+
	Libermann's test	+	–	+	+
	Salkowski's test	+	+	–	+
Saponins	Foam test	+	+	+	+
Anthocyanins	Borntrager's test	–	–	–	–
Tannins	5% $FeCl_2$	–	+	–	–
	Gelatin test	+	–	+	+
Phenols	Ferric chloride test	–	+	–	–
Terpenoids	Salkowski test	+	+	–	+
Carbohydrates	Molisch's test	–	–	–	–
	Benedict's test	+	+	–	+
Leucoanthocyanin	Borntrager's test	–	–	–	–

chemicals were found in the leaves, fruit, and seed of *Artocarpus camansi* leaves were reported for friedelinol, sqallene, β-sitosterol, stigmasterol, and phytol. The stem yielded polyprenol, cycloartenol, and cycloartenol acetate. The seeds of the fruit encompassed lectin, while the triterpenoids leupeol acetate was extracted from the fruit peels [50]. Steroids and triterpenoids were isolated from its peels [51].

PHARMACOLOGY

Antibacterial Activity

Multi-drug resistance is an important issue in treatments of varieties of microbial infections, therefore potent antibiotics with unique mechanisms of actions are required. The use of silver nanoparticles as an effective antibacterial methodology can aid in the control of antibiotic-resistant pathogenic microorganisms. The bactericidal ability of these nanoparticles were tested using the agar well diffusion technique, which authors detailed in further using morphological and structural analysis. For human prostate adenocarcinoma (PC-3) cells, the anticancer activity was tested using the 96-well plates MTT assay with flow cytometry-assisted apoptosis.

A change in colour from mild yellow to brown were noticed as a insecticidal activity triggered by nanoparticles, which was studied by authors using ultraviolet-visible (UV-Vis) spectroscopy at the wavelength of 415 nm. These developed nanoparticles were found to have noticeable zones of inhibition on PC-3 cells as well as good antibacterial properties. The IC_{50} values for annexin v/PI were found at30.62 μg/mL, and 48.11 ± 0.7%, 24.92 ± 0.5%, and 1.19 ± 0.4% [52] studied for early, late apoptosis and necrosis analysis using a flow cytometry assisted annexin v/PI. Green AgNPs can be used to alleviate microbial and cancer-related illnesses in the near future [52].

The Indonesian native plant *Artocarpus kemando* (AK) is high in flavonoid contents, which was reported for varieties of bioactivities. The flavonoid compound artonin E is being extracted from branches and root bark of the plant. Diazomethane was also used to modify compound (artonin E), which resulted in modified artonin E. The UV-Vis, Fourier transform infrared (FT-IR), Hydrogen-1 (^{1}H), and Carbon-13 nuclear magnetic resonance (^{13}C NMR) spectra of both compounds were compared to published data [53].

Silver nanoparticles were also prepared utilizing AH seed extract, and their characterizations revealed that the nano-particles has spherical shapes (size range from 30 to 45 nm) [54]. The antibacterial investigation showed that these NPs were more effective against *Enterobacter aerogenes* (EA), with a larger maximal inhibition zone, than the *Listeri amonocyto genes*. The scanning electron microscope micrographs revealed that the *EA* bacterial strains were more vulnerable to silver nanoparticles. The size and charge NPs make them easy to penetrate the cell wall of bacteria [54, 55].

The bark of AL was tested for antibacterial efficacy against number of microorganisms. In *Shigella soneii*, *E. coli*, *Bacillus pumilus*, *Proteus mirabilis* AM 198, *Bacillus subtelis* American Type Culture Collection (ATCC) 6633, and *E. coli* Row 7/22 species, methanolic extracts were exerted minimum inhibitory concentration (MIC) values around 200 μg/mL. According to earlier findings, the methanolic extracts of AL at doses of 200 μg/mL as well as 400 μg/mL had strong antibacterial activity against varieties of Gram-negative bacteria [56, 57].

Various solvents such as petroleum ether, dichloromethane, ethyl acetate, and butanol were used to partition methanolic extract samples of AH (stem, root barks, heartwood, leaves, fruits, and seeds). This extract was found to capable of exerting an antibacterial property against *Bacillus cereus*, *Bacillus coagulans*, and other bacterial strains (Fig. 5). The butanolic portions of AH roots bark and fruits were found to be more active tested with disc diffusion methods [58].

Antifungal Activity

A traditional microbiological approach for assessing bioactive substances using antifungal activity usually takes a long time. Calculating various kinetic parameters is similarly tricky. That particular study used toxic agar as well as isothermal microcalorimetry (IMC) assays to assess the tolerance for plant pathogenic fungi towards an ethanolic extract from jackfruit leaf. The link between the two strategies was determined using Pearson coefficients. The phase and Max are substantially associated (>0.51) with the in vitro % inhibition, according to correlations. As a result, their findings contributed to the use of IMC as a supplement to traditional techniques of fungal inhibition by giving real-time data [59].

AA being known to have antifungal properties, and the goal of the study was to see if it was effective against AN, which causes black moulds in onions. T1—control (only AN inoculated); T2—25% AA leaves extract; T3—50%; and T4—75% were the varying samples used for this analysis. Indications were appeared after three days of inoculation, and the zone of inhibition was examined and recorded. The results showed that there were no significant variations in the inhibition zone between the treatments, and it was classified as resistant to AA antifungal activity [60]. However, those treated with 50% AA leaf extract had fewer symptoms after 51 days of observation, whereas those treated with 75% AA leaf extract had major shrivelling, suggesting that the application of 50% AA leaves extract is still the optimum concentration for controlling black moulds in onions. The effectiveness with AA extracts against AN through onions might be

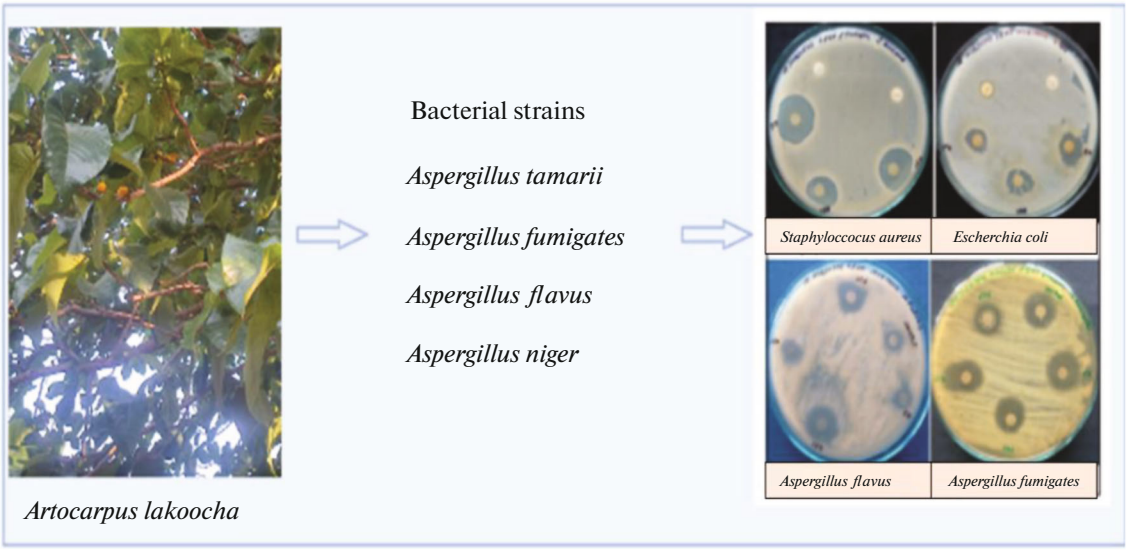


Fig. 5. Antibacterial activity of AL extract.

advantageous in shelf-life extension for onions within market and reducing post-harvest losses [61].

C. gloeosporioides was inhibited by catechin as well as chlorogenic acid components isolated from AH leaf extracts with the high percentage inhibition [62].

The presence of silver nanoparticles were confirmed by the UV-vis absorption spectra of such phytochemical-mediated reduced reaction mixture, which revealed a surface Plasmon peak at 428 nm. Taking 2 mL of jackfruit rind extracts, Ag^+ 1.0 mM, and 180 min of reaction time, the silver nanoparticles production was found to be excellent at pH 9 conditions. The presence of acid, esters, alcohols, pyrazine, and other compounds that can act as capping agents surrounding the nanoparticles was discovered using FT-IR. The face centred cubic and oxygen frameworks with metallic silver nanoparticles were checked by X-ray diffraction (XRD) investigation [62].

According to high resolution transmissions electron microscopy, the size of nanoparticles was found around 18 nm, which accords well with the average crystallite size estimated using XRD technique. With pathogenic *Phytophthora capsici*, *Colletotrichum acutatum,* and *Cladosporium fulvum*, antifungal activity demonstrated 8-, 11- and 16-mm inhibition zones against produced silver oxide nanoparticles at 200 μg/well, respectively [62, 63]. Catechin suppressed cyclic adenosine monophosphate (cAMP) synthesis and disturbed the mitogen-activated protein (MAP) kinase cascade pathway in fungal cells [63].

Antimalarial Activity

Finding alternative medicines to treat the malaria has continued to grow in importance. Among other natural sources, the plant source is considered as a reliable source that could yield pharmaceuticals. The *Artocarpus* species demonstrated excellent pharmacological potentials such as a good antimalarial activity. In one of works, extraction of potent antimalarial components from the stem bark of *Artocarpus sericicarpus* (AS) were achieved by utilizing *n*-hexane, dichloromethane, plus methanol as solvents with the stem bark from AS. This was extracted using an ultrasonic-assisted extraction technique. By employing gradient acetonitrile-water as the mobile phase and octadecyl silica as the stationary phase, open column chromatography was used to fractionate the concerned dichloromethane extract. The lactate dehydrogenase (LDH) method was used to test the antimalarial activity of such extract against the *Plasmodium falciparum* (Pf) 3D7 strain. Thirteen fractions were produced after fractionating this dichloromethane extract. These 13 fractions were then evaluated, and seven of them showed antimalarial activity [58] fraction 6 was demonstrated the strongest inhibition (with an IC_{50} value of 1.53 ± 0.04 μg/mL). Fraction 6 was including flavonoid, polyphenols, plus terpenoids components, which might have contributed to its antimalarial activity. Antimalarial compounds found in AS, particularly in fraction 6, severely inhibited the growth of Pf [58].

Artocarpus champeden was also used in the malarial treatment, which has typically been done with stem bark. The purpose of said previous research was to obtain fingerprints of metabolites present in *A. champeden* bark extract from various locations throughout Indonesia, and also in addition to specify and manage the extract's quality. The HPTLC (high-performance thin layer chromatography)—densitometry technique was used to develop fingerprints. Further, MTT and HRP2 assays were used to test in-vitro toxicity activity.

Compounds with retention factors (RF) values of 0.66 and 0.63, in addition to morachalcone-A, were thought to be supplementary markers as they found to be responsible of both antimalarial activity as well as toxicity. Finally, *A. champeden* from Maluku region had the best antimalarial activity (60.41 + 5.67 μg/mL) [65] and was shown to be safe at a therapeutic level of 10 ppm [65].

The leaves of AA have previously been investigated as a promising antimalarial medication. Inhibition concentrations (IC_{50}) and effective dosage values (ED_{50}) versus Pf and *Plasmodium berghei* (Pb), respectively, have been reported using chromatography methods. Moreover, the active ingredient was separated out from ethanolic extract of AA, and the chemical composition of the isolated molecules was determined using NMR and Mass spectroscopy data. Antimalarial activity towards Pf 3D7 was assessed using a microscopic technique, and molecular docking investigations. Dihydrochalcone, a flavonoid component, was eventually extracted with AA. This phytochemical strongly reduced Pf growth in antimalarial activity tests, with an IC_{50} value of 1.05 μM. An in-silico analysis of the compound's mechanism of action found the presence of a 3BPF receptor with a cysteine protease inhibitor of Falcipain-2.

Various compounds have also been isolated from *Artocarpus niger* leaves. AA could be a promising new source for antimalarial medication development. Prior to a clinical trial, an animal investigation using such phytochemical may be recommended. The IC_{50} value of 1.32 μg/mL at a dose of 0.82 mg/kg [66] indicated that an ethanolic extract of AA leaf could inhibit Pf growth [66]. The antimalarial activity of three *Artocarpus* species bark extracts were also examined in one of the studies reported. The antimalarial in-vitro test was carried out with Pf (3D7 strain) cultivated in RPMI-1640 medium, while the malaria in-vivo test was carried out with Pb infected mice using Peter's test. Antimalarial activity was reported for varieties of isolated compounds from *Artocarpus* leaves and stem bark. AA leaf extracts had the best antimalarial activity, with an IC_{50} of 1.32 μg/mL Pf and ED_{50} of 0.82 mg/kg Pb [67] body weight. AA leaf extract is a viable candidate for a new antimalarial medicine [67, 68]. Possible targets for antimalarial drug treatment (Fig. 6).

Immunomodulatory Activity

Immune system imbalances are usually caused by pollutants and bad dietary habits, which can be avoided by consuming a diet rich in vitamins and antioxidants. Traditional medicinal use of natural compounds as immune boosters has the potential to modify the body's normal defence system [69]. In one of analysis, oligo-peptides were significantly increased. The CoA-mediated spleen lymphocyte proliferation, footpad thickness, macrophages phagocyte capacity, and phagocyte rate were also parameterized and compared this data to whey protein-treated mice [70].

Swiss female mice were used to test an immunomodulatory activity. For seven days, the treatment group received an infusion with AA (100 and 200 mg per kg) [71], and normal saline for control group. Methylprednisolone at a dose of 40 mg per kg was given to the control group. On the eighth day during observation (day 8), the animals were killed, as well as the average significance of the organ was computed for 100 g body weight [71]. The MTT assay demonstrated that ALL (*Artocarpus lingnanensis* lectin) had a high mitogenic potential. Meanwhile, the healthy human leukemic Jurkat T-cells lines were also used to investigate ALL's anticancer efficacy. ALL had a high affinity for the cell membrane (nearly, 97%). With a lower population of S and G2/M phases, ALL could cause morphologic changes but also raised the hypo diploid cell population. The stimulation of caspase-8 and -9 verified its apoptosis-causing action by promoting phosphatidyl serine externalisation and PARP cleavage. ALL-induced apoptotic cells may be rescued by inhibiting caspase-9 but not caspase-8. ALL suppressed the production of Bcl-xl as well as Bcl-2 genes, while having no effects on Bax. Furthermore, it was discovered that activation of the p38/JNK MAPK signalling pathways is required for ALL apoptotic activities. ALL, on the other hand, was unable to cause apoptosis in normal T cells. This data showed that ALL has a different effect on Jurkat as well as normal T cells, implying that it may have therapeutic potential in leukaemia [72].

Antitubercular Activity

Isolations of 12 new compounds were achieved by chromatographic separation of acetone preparations of twigs as well as barks of AL. With IC_{50} values of 36.7 and 33.9 μM, respectively, lakoochanone and Moracin. Moracin as well as sanggenofuran, with IC_{50} values at 15.0 and 57.1 μM, respectively, displayed cytotoxic actions against the A2780 cell line. In addition, cyclocommunin had retained a minimum inhibitory concentration (MIC) value of 12.3 μM against *Mycobacterium tuberculosis* H37Ra strains [73].

The conventional antibiotics such as rifampicin, isoniazid, and kanamycin, were retained with MIC values of 0.0024, 0.1, and 2.5 μg/mL [74], and employed as standards. Cycloartocarpin, artocarpin, and chaplashin were extracted from a dichloromethane extract of the roots and stem of same plant; however morusin, cudraflavone B, cycloartobiloxanthone, artonin E, cudraflavone C, and artbiloxanthone were separated from the roots of AA [74], Micro plate Alamar Blue Assay (MABA) assay was used to assess an antitubercular activity against *Mycobacterium tuberculosis* H37Ra [75].

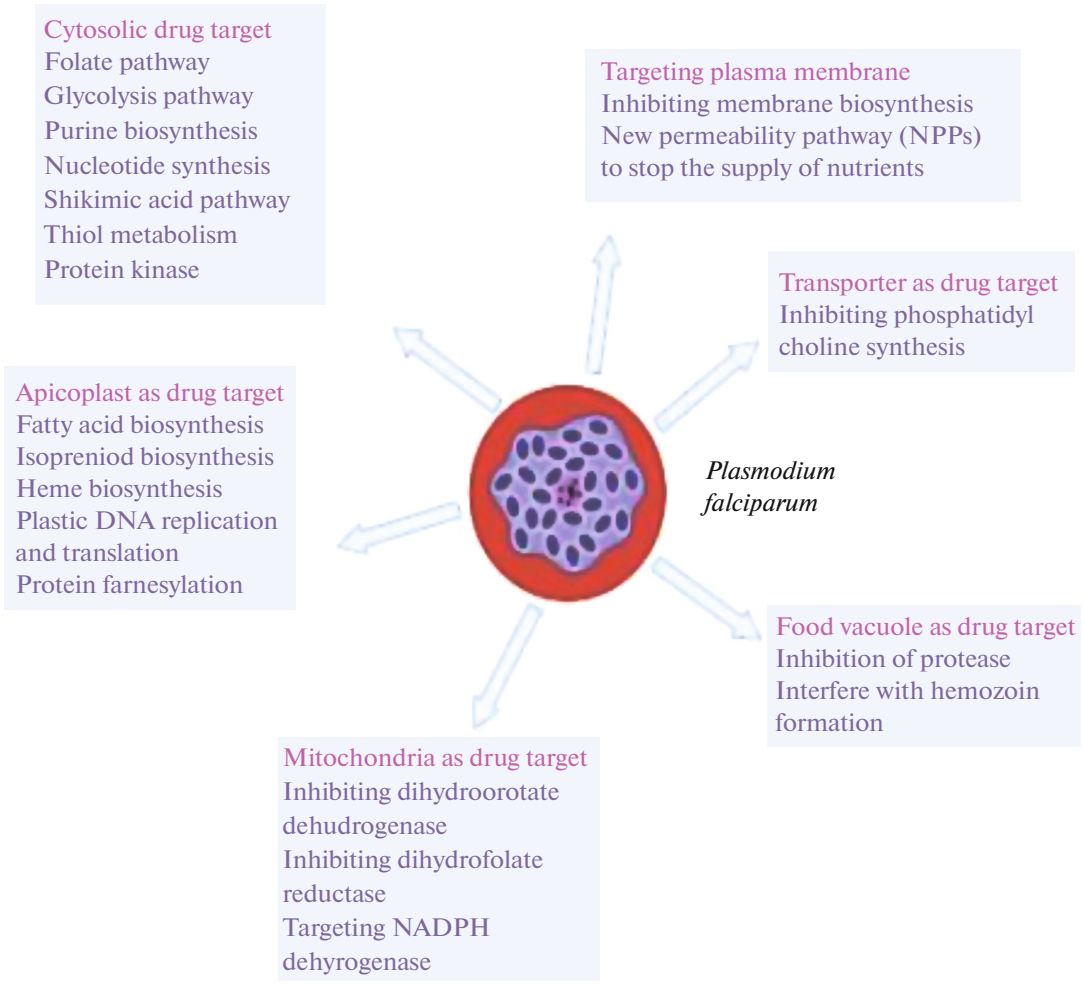


Fig. 6. Possible targets for antimalarial drug treatment.

Antiviral Activity

Direct-acting antivirals (DAAs) have vastly enhanced the sustained virologic response (SVR) in chronic hepatitis C virus (HCV) patients; yet, DAA treatment is still costly, and drug-resistant HCV cases are still being a major problem. As a consequence, there is a need for more economical and effective HCV treatments to be developed. A solution of AH leaves has previously been shown to be a good antiHCV candidate. Authors refined this crude extract further in their study, and looked at which sub-fraction it had the best antiviral activity. They also afterwards tested its potency at different stages of the HCV life cycle. They also looked at whether the AH extracts as well as commercially available antiHCV medications had synergistic antiviral effects [76]. AA, AC, and AH extracts were studied for their antiviral properties against HCV strains. The antiviral activity of the isolated compounds was tested utilizing Huh7it-1 cells as well as HCV genotype 2a strains using a cell culture technique. Time-of-addition tests were used to determine its mode of action with antiHCV activity. Quantitative rapid transcription-PCR as well as western blotting methods was used to measure the influence on HCV RNA replication as well as HCV accumulation in cells, respectively. With no visible toxicity, the dichloromethane (DCM) extracts of AH depicted substantial antiHCV activity. The antiHCV activity of DCM extracts from AA as well as AC was found to be modest IC_{50} values of 6.50 ± 0.3 μg/mL and 9.71 ± 1.1 μg/mL [77], where in time-of-addition study was, conducted [77]. AH showed strong antiHCV activity with IC_{50} values of 1.5 ± 0.6 μg/mL

HCV was infected in Huh7it-1 cells in the presence of different plants extracts. The cells were rinsed with water after 2 h of viral absorption as well as cultured for 46 h in medium containing same extracts. The cells were only administered extract-containing medium during viral injection for time-of-addition studies. The virus titration was done two days after infection on culture supernatants. The IC_{50} was determined using SPSS analysis [78–80].

Cytotoxicity Potentials

In Asian countries, AH has already been utilized as a folk medicine. Flavonoids were shown to have a wide range of medicinal activities and they could be used to treat a variety of ailments, including cancer prevention. The flavonoid, artocarponanone was extracted mainly from heartwoods of AH. In earlier study, authors analysed how this natural phytochemical and a commercial anticancer drug, cisplatin, interacted with cancer cell lines. The cytotoxic activity of this combination was determined using the MTT test. The effect over cancer cell lines was predicted using isobologram analysis. Using the AO/PI staining procedure, overall impact of such a combination was then validated. Artocarpanone was found to be cytotoxic to (Non-small-cell lung cancer cell lines) H460 as well as (Michigan Cancer Foundation-7) MCF-7 cell lines. Cisplatin, on the other hand, had a cytotoxic impact [81].

The ethyl acetate preparation of *Diaporthe lithocarpus*, an entophytic fungus obtained from leaves of AH was fractionated and purified, yielding one new compound, diaporthindoic acid, as well as seven known compounds. The novel molecule was identified and described using a variety of spectroscopic techniques, namely NMR and HRMS (high resolution mass spectroscopy). Emodin had the strongest cytotoxicity against P-388 cells from murine leukaemia, with an IC_{50} of 0.41 μg/mL [82]. Antimicrobial activity was also investigated on all of the 8 compounds. This will be the first chemical examination of fungal Diapor the produced from *Artocarpus* that we are aware of [82, 83].

Panzer root bark from *Artocarpus rotunda* Hout., revealed a new prenylated flavones, artoindonesianin L, and also four well-known phenolic, artonin M, E, cycloartobiloxanthone, andartonin O [84].The catechol-containing compounds artonin E and artbiloxanthone, as well as the prenylated flavonoid artonin (E and O), artbiloxanthone, and cycloartobiloxanthone, have been separated from bark extract of AK and sometimes showed cytotoxic effects against KB (human oral epidermoid carcinoma) with IC_{50} values of 3.0, 0.5, 3.5, and 2.5 μg/mL [85].

Antidiabetic Activity

With limited scientific evidence, AH stem bark is used locally to manage diabetes mellitus. The antioxidant capacity of phenolic extracts of AH bark extract, as well as its antidiabetic action using streptozotocin-induced diabetic rats, are investigated in this study. Fifty males hyperglycaemic Wistar rats (streptozotocin, 45 mg/kg body weight) were treated with 400 mg/kg of free and bound phenols from AH stem bark. The animals were sacrificed using the cervical dislocation method on the 28th day of the experiment, and the antihyperglycaemic and antiinflammatory parameters were measured.

The polyphenolic extracts showed substantial inhibitory effects against amylase and glycosidase and antioxidant potential. In diabetic rats given the extracts and metformin, there were a substantial ($P < 0.05$) rise in glycogen, insulin concentrations, pancreatic β-cell scores Homeostasis Model Assessment (HOMA-β), antioxidant enzymes, hexokinase activities, and glucose transporter concentration. In diabetic rats given the extracts and metformin, there was a significant ($P < 0.05$) [85] drop in fasting blood glucose, lipid peroxidation, glucose-6-phosphatase, and antiinflammatory markers. The extracts were found to have antidiabetic properties, which could be beneficial in treating *diabetes mellitus* [64, 85, 86].

Hyperglycaemia was induced with streptozotocin in rats aged two to 2–3 months, and the blood glucose levels were measured 14 days later. A 400 mg/kg dose of such ethanol extracts of AH plant seeds were given to diabetic rats. The extract has an antidiabetic effect, as evidenced by a drop in blood glucose of 61.73% [87].The anticancer activities of the various *Artocarpus* species have been tested in-vivo using different animal models (Fig. 7).

Saponin can help lower cholesterol and blood glucose levels. An aqueous extract of AH restored blood glucose levels and metabolic profiles over 21 days of therapy, demonstrating its antihyperglycemia and antihyperlipidemic potential. We can keep looking for important antidiabetic drug leads in AH. A more comprehensive biological study is required to determine the mode of action [88].

Antidiarrhoeal Activity

Diarrhoea is a disease in which have watery fluids, accompanies with loose stools over than three times a day. Salam leaves and perhaps jackfruit leaves have been utilized as herbal cures for a variety of ailments from Indonesian traditional medicine, including antidiarrheal medicine. In one of experiment conducted, authors used to see if a mixture of Salam leaf as well as jackfruit leaves infusum generated by castor oil had an antidiarrheal effect in rats or not. The rats were placed into nine groups, with a negative control group receiving 1% CMC, a positive control group receiving tannin, and five test groups receiving the infusum, with five dose comparisons provided orally. Castor oil was once used as a diarrhoea stimulant. The results reveal that jackfruit leaves also have antidiarrheal effects in all mixtures of salam leaves, with lower intensity of defecation, faeces texture, and faeces weight at proportions of 1 : 1, 1 : 2, 1 : 3, 2 : 1, as well as 3 : 1 compared to negative control ($p < 0.05$). The infusum showed positive tannins in a phytochemical test. Both infusum may have antidiarrheal activity due to the presence in tannin, which have an antisecretory action inside the intestinal lumen. In rats provoked by Castor oil, therapy with a mixture of Salam leaf and jackfruit leaf infusum had an antidiarrheal effect. The optimum

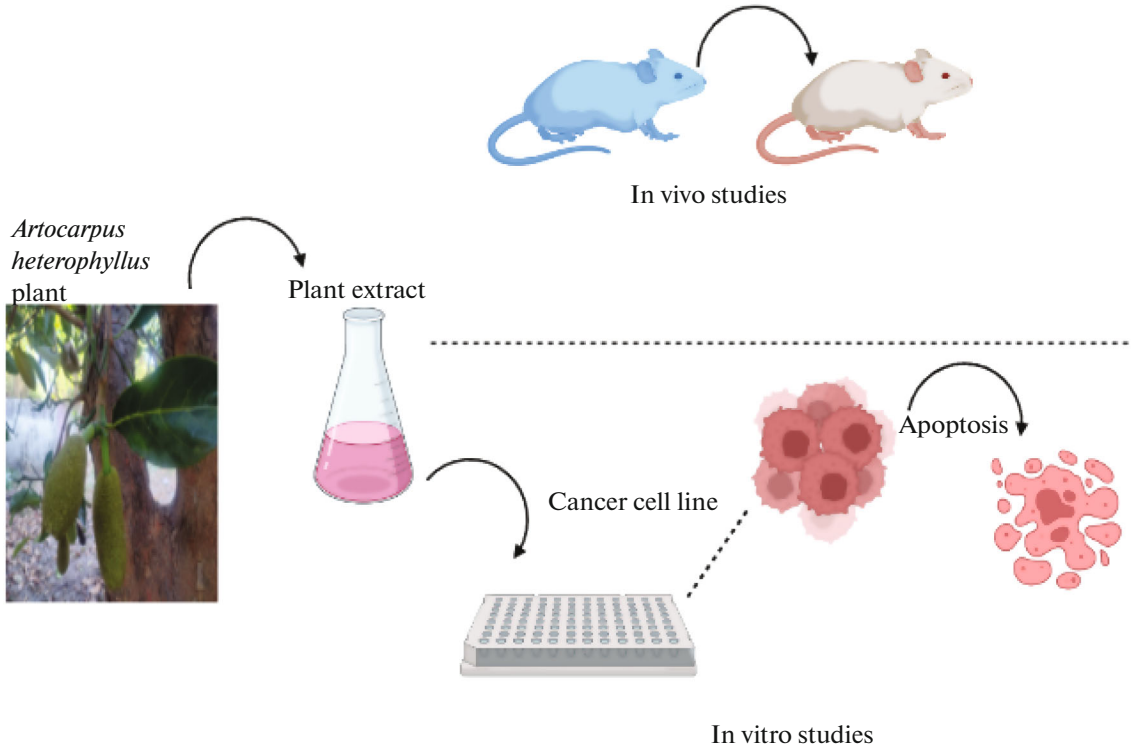


Fig. 7. The anticancer activities of the various *Artocarpus* species have been tested in-vivo using different animal models. Adapted from open assess article.

effect occurred from a 3 : 1 ratio of Salam leaves infusum to jackfruit leaves infusum [89].

AH methanolic extract possesses potent antioxidant and antidiarrheal effects. More research is needed, however, to understand the mechanisms underlying antidiarrheal antioxidant activities and to identify the active compounds involved for these pharmacological advantages [90].

Antimicrobial Activity

The use of plant latex as a natural herbivore defence exudates has a long-dated history. However, there is a scarcity of on-going study on its bioactive properties and its use as a therapeutic adjuvant. In previous study, authors collected latex mostly from (jackfruit) and examined them for their antibacterial and antioxidant activities. Aqueous extracts and trifluoroethanol extracts (TFE) of jackfruit latex were prepared using distilled water and trifluoroethanol. Both extracts were analysed using TLC, UV-Vis spectroscopy, as well as Gas Chromatography Mass Spectrometry (GC-MS). Antimicrobial and antioxidant activities of the extracts were also tested. *P. aeruginosa*, *S. aureus*, as well as *Bacillus* sp. were all inhibited by TFE [91].

Study found that TFE had lesser antioxidant activity than AE. The silver oxide nanoparticles (Ag_2O-NPs) were produced in that work via a green technique, since it was an environmentally benign, less harmful, and inexpensive. Moreover, plants were utilized as capping agents containing such phytochemicals that act as a stabilising and reducing agent. Natural ingredients can also be employed to synthesise Ag_2O NPs from AH plant extract. The solution mixture was heated and stirred for 60 min at 60–80°C. For the formations of Ag_2O NPs, the temperature, pH, as well as period of time of a reaction mixture were found to be critical parameters. The existence of Ag_2O NPs formed in a Face-centred cubic structure can be seen using XRD technique, which agreed well with the (Joint Committee on Powder Diffraction Standards) JCPDS Card no. 004-0783. The DLS (Dynamic light scattering) demonstrated that as-synthesized Ag_2O NPs had a hydrodynamic diameter of 212 nm along with monodispersity (Polydispersity index <1.0). In the future, the antimicrobial properties of such silver oxide nanoparticles at varied concentrations could also be studied [92].

To qualitatively and quantitatively investigate the phytochemical compositions in AL leaf, authors confirmed from their study for its significance as a strong antioxidant and antibacterial agent. Using the solvent fractionation method, various phytochemicals were extracted and isolated from leaves of AL. Following that, conventional methods were used to investigate antioxidant, antibacterial, antioxidative activity, and

quantitative as well as qualitative phytochemical profiling. For sustainable agricultural and pharmaceutical uses, one can use methanol portion of AL and could use as a powerful antioxidant and antibacterial agents [93].

Antiinflammatory Activity

Previously, AH seeds were gathered, cleaned, dried, and ground into powder by one of author groups. Methanol, an organic solvent, was used to extract the dry powder. Using four distinct antiinflammatory assays, including the HRB membrane stabilisation test, the nitric oxide scavenging test, the protein denaturation test (inhibition of albumin denaturation), and the proteinase inhibition test, crude extract was analysed. Results were analysed with respective IC_{50} values. Aspirin, ascorbic acid, and diclophenac sodium are commonly used medications that have antiinflammatory actions. Significant antiinflammatory activity was discovered from the methanolic seed extract of AH [94].

Stilbenoids, particularly oxyresveratrol, have long been known for their abundance in AL plants. The ancient Thai medical system had been long utilizing AL plant parts. However, the function of AL in controlling inflammation is yet unclear. The molecular mechanisms of AL ethanolic extract's antiinflammatory effects are still unclear and needs to be assessed with higher studies. The plant was high in oxyresveratrol, according to the HPLC data reported previously. The AL ethanolic extract had also retained antiinflammatory qualities when studied. The synthesis and release of cytokines and chemokines, including IL-6, TNF-, and MCP-1, that are mediated by lipopolysaccharide (LPS), were in particular found to be reduced by AL extract. Within supernatants of LPS-stimulated cells, the extract consistently reduced the generation of nitric oxide (NO) radical species.

Results from the immunofluorescence investigation demonstrated that AL extract decreased nuclear factor-kappa B (NF-B) translocation after LPS induction. Western blot analysis results further supported the finding that AL extract significantly inhibited the LPS-induced breakdown of I-B, which is typically necessary for such activation of NF-B. The addition of AL extract significantly reduced the protein function for iNOS as well as cyclooxygenase 2 **(**COX-2) in responses to LPS stimulation.

It was discovered that AL extract reduced inflammation in part by preventing Akt activation brought on by LPS. The extract had very little effects on the pathways that activate mitogen-activated protein kinase (MAPK). In particular, merely 3 h of extract treatment in cells showed how quickly the extract inhibited overall phosphorylation of Akt but not ERK1/2. To somewhat lessen perhaps the phosphorylation of such ERK1/2, p38, as well as JNK MAPKs, a longer exposure to AL extract (24 h) was necessary.

These findings suggested that the main mechanisms by which AL extract controls its antiinflammatory actions are by blocking the PI_3K/Akt and NF-B signal transduction pathways. Collectively, authors believed that AL extracts might be a viable alternative treatment for reducing excessive inflammation in a variety of diseases, which are related to inflammation [25].

In one study, authors carried an experiment to see if phenolic compounds isolated using ethanolic extract preparations from AH fruits had any in-vitro antiinflammatory activities or not. Three phenolic compounds had been identified by them as artocarpesin, norartocapetin, and oxyresveratrol. These three compounds were found to have significant antiinflammatory properties. Artocarpesin, as a result, can be used to cure inflammatory conditions [95].

Inhibitors of Tyrosinase Activity

Natural cosmetic products that are non-invasive, highly effective, and reasonably priced are having huge demands, nowadays. In earlier study, 15 ethanolic extracts from the leaves, peels, and stem bark of five Malayan *Artocarpus* species—AA, AH, *A. integer, Artocarpus elasticus* (AE), and *Artocarpus rigidus* (AR) were examined for their potential use in skin-lightening cosmeceuticals. These activities were tested for antimelanogenesis, radical scavenging, and UV protection effects.

Effects of AH bark extract and peel extracts were found to be four times more effective than kojic acid in their investigation, reducing melanin level to 23.62 ± 0.69% and 24.10 ± 3.96% at 50 μg/mL, respectively. All extracts were 1.42 to 1.85 [96] times more effective than kojic acid at 50 μg/mL in inhibiting cellular tyrosinase activity. While DPPH, and ABTS radicals were all significantly reduced by an extract from the peel of AE. Overall, their findings suggested that AH bark extract and peel extracts have promising antimelanogenesis capability for the application in skin-lightening cosmeceuticals. Whereas AE peel extract could be regarded as a strong antioxidant for usage in cosmeceuticals products [96].

Tyrosinase inhibitory activity including melanin pigment reduction had also been observed for these extracts of AL and *Glycyrrhiza glabra* (Gg). In melanoma B16 cells, extracts of AL and Gg individually and in combination were examined for cytotoxicity and tyrosinase inhibitory actions, along with decrease of melanin pigments. In comparison to Al70, Al95 displayed larger amounts of oxyresveratrol, and had better antioxidant, and tyrosinase inhibitory action. It further also eliminated additional melanin pigmentation in B16 cells. In addition to having larger quantities of glabridin than Gg70, Gg95 suppressed oxidative stress as well as mushroom tyrosinase enzyme more effectively. AL and Gg extracts may be used in skin products for the treatment of hyper pigmentation [97, 98].

Using AL wood extract, human volunteers were able to reduce melanin synthesis. AL extract seemed to have a faster beginning of substantial whitening impact than other tyrosinase inhibitors widely used in whitening solutions, including kojic acid and liquorice extract, requiring only 2–4 weeks of administration depending on the kind of composition and application area. The concerned developed oil-in-water dispersion appeared to have a better whitening effect than that of the polypropylene glycol-based solution. Although the little amounts of extract were used in that study, it has a lot of promising effects in the cosmetics industry and can be used as a reliable, effective, and cost-effective whitening agent [36]. The compound artocarpanone, which would be a great contender for curing hyper pigmentation in human skin, was investigated using activity-guided fractionation. Changes in melanogenesis may be responsible for some of the clinical as well as histological aspects unique to malignant melanoma. Artocarpanone inhibited two very different fungal tyrosinase enzymatic activity and melanin formations in B16 melanoma cells (with IC_{50} values of 80.8 and 89.1 μM) [31].

Inhibitors of 5α-Reductase Activity

A potent 5α-reductase inhibiting potential was noticed with Artocarpin (Ar), isolated from an extract from *Artocarpus incises* (AI) heartwood. Artocarpin was found to be partially penetrated the deeper epidermis that contains androgen receptors. In order to formulate alginate/chitosan (ACS) microscopic particles as targeted trans-follicular administration, the concerned work was undertaken. It was discovered that the ionotropic gelation approach may produce particles with an appropriate size range of 2 to 6 μm. Ar was effectively trapped in ACS micro particles at a rate of 18.7 ± 1.7%. A lengthy discharge of Ar inside the follicular ducts was possible because of the ACS micro particles, with release of 0.7% of the loading dosage over a period of 6 h [98].

The reduction of the rodent flank organs was accomplished by topical treatment of Ar-ACS tiny particulates with either a substance of 0.1 mg through 5 mg microscopic particles with one hamster flank. Ar with 0.1 mg quantity packed in ACS tiny particles was proven to have efficiency that was on par with Ar 1 mg applied as solution. However, contrast to a dermal exposure of such Ar mixture as well as a flutamide mixture (1 mg) as a positive control; Ar formed in tiny particles did not exhibit a meaningful systemic impact [98]. A diethyl ether extract from AI heartwood was found to contain an Ar component. Ar inhibited the 5α-reductase enzyme, preventing testosterone from being transformed mostly to 5-dihydro-testosterone [99].

Antiarthritic Effect

The Hmong ethnic group in North Vietnam carried out a traditional treatment called *Artocarpus tonkinensis* (At) leaves decoction. This tea extract is high in bioactive chemicals and may be useful for treating arthritis and backaches. Indeed, in an experimental model of collagen-induced arthritis, it has been demonstrated to prevent the growth of Th17 cells. They demonstrated that *Artocarpus tonkinensis* extract significantly decreased RAW 264.7 murine cells, nitric oxide synthase activation, and IL-6 production by using various in vitro disease models and osteoclastogenesis.

Additionally, the development of TRAP-positive osteoclasts was completely inhibited by At, and the expression of important genes related to osteoclasts was lowered. As the activation of non-receptor tyrosine kinase Src was decreased by exposure to RANKL-At, it was likely that this At activity depends on the suppression of the RANK downstream signalling cascade. The collagen-induced arthritis (CIA) experiment also revealed that, it had a protective effect with At against bone loss. Bone and cartilage were well-preserved in CIA+ at decoction. Osteoclasts marker genes were expressed at lower levels in mice and joint tissue compared to the CIA control group. Although to a lesser amounts of At decoction, maesopsin 4-*O*-D-glucoside (also known as TAT-2, one of the main decoction bioactive components) was also able to contrast NOS2 activity, IL-6 production, and osteoclasts development.

Overall, their study focused on macrophages as an additional At cell target in addition to Th17 cells. The antiarthritic benefits of At decoction likely result from its capacity to inhibit not just osteoclastogenesis but also inflammation [100].

This study had used qualitative phytochemical analysis to detect the presence of flavonoids and other active components in At. The young leaves of AH have such a considerable antiarthritic effect. Antiarthritic efficacy of this extract was evaluated with in-vitro models. According to findings, the extract suppressed proteins (albumin) denaturation at various doses. Phytoconstituents such as steroid, terpenes, flavonoid contents, phenols, and tannins have been studied with in-vitro models as antiarthritic agents. This activity could be attributed to steroid hormones, flavonoid, saponin as well as coumarin glycosides, and terpenoids. One of key objective of the concerned study to isolate the active ingredients that is responsible for the activity [101].

antiinflammatory effects were detected in all four drugs in varied degrees. The antiinflammatory effects were seen in the rat model of arthritis corresponds well with the reduction of mitogen-induced T-cell proliferation. Furthermore, the chemicals inhibited the secretion of cytokines including tumour necrosis factor as

Table 6. Antioxidant property of AL

Sample	Result	Reference
AL leaf methanol extract	IC_{50} value 41.35 ± 11.75 mg BHT/gm by hydroxyl IC_{50} value 0.47 ± 0.13 mg ascorbic acid/ gm by superoxide anion IC_{50} value 18.28 ± 4.22 μg/mL by DPPH	[127]
AL leaf ethanol extract	IC_{50} value 48.23 ± 0.46 μg/mL by DPPH IC_{50} value 6.72 ± 4.70 mg ascorbic acid/gm by DPPH IC_{50} value 2.32 ± 1.27 mg ascorbic acid/gm by ABTS	[126]
AL seed methanol extract	IC_{50} value 31.22 ± 0.89 μg/mL by FRAP IC_{50} value 111.98 ± 34.20 μg/mL by DPPH	[43]
AL leaf methanol extract	IC_{50} value 26.95 ± 0.009 μg/mL by DPPH	[128]
AL leaf *n*-hexane, ethyl acetate, and ethanol extract	IC_{50} value *n*-hexane (1062.03 ± 1.42 μg/mL); ethyl acetate (323.18 ± 0.02 μg/mL); ethanol (99.23 ± 0.07 μg/mL) by DPPH	[129]
AL seed methanol fraction	IC_{50} value 138.26 ± 0.66 μg/mL by ABTS	[93]

well as interferon in mitogen-stimulated T cells in a concentration-dependent manner [102].

Antioxidant Activity

The intake of antioxidant rich compounds in the modern diet has been increased as a result of the rising prevalence of diseases linked with oxidative stress throughout the population. With 50–80% ethanol as solvent, one study was conducted to ascertain the antioxidant property of cempedak fruit (skin) extract. The 1,1-diphenyl-picrylhydrazil (1,1-DPPH) assay was employed to test for radical scavenging potentials (vitamin C was used as a positive control). Phenolic, flavonoids, and tannins were found to be present when tested with the phytochemical screenings (Table 6).

These findings supported the fact that the cempedak fruit's skin has lesser or no antioxidant activity [103].

The flavonoid concentrations vary greatly among different types of *Artocarpus* species. The number of flavonoids in each plant part varies; for instance, the fruit has a high concentration of anthocyanins, particularly cyanidin glycosides; the leaf has a high concentration of flavonols and their glycosides, such like quercetin and kaempferol; and the roots and stems have a high concentration of flavonoids (their glycosides, such as apigenin and luteolin). In this family, mainly in the genus *Morus*, a number of flavonoids and Diels-Alder adducts of flavonoids were also discovered. Stems and roots of *Morus* plants have most of flavonoid contents, whereas the leaf of a *Ficus* genus has more flavonoids and Total Phenolic Content (TPC).

More intriguingly, the pathways for the production of flavonoids are strongly influenced by environmental factors, particularly altitudes, UV radiation, dry and wet seasons. Furthermore, due to the abundance of flavonoids in these plants, it has been demonstrated that they have potent antioxidant activity via a variety of mechanisms. This review sheds new light on the potential of herbs from the Moraceae family to treat a range of illnesses brought on by free radicals. We believe that higher studies can be carried out with various *Artocarpus* species in order to establish detailed antioxidant mechanisms [104]. The antioxidant activity of the protein component of bread fruit pulp was also tested using TLC methods [105]. Protein Fraction of Breadfruit Pulp (PFBp), quercetin, and Gallic acid were added to 3 TLC plates subsequently washed with a chloroform/ethanol different with solvent composition of 9 : 1. Plates were then nebulised with developing solutions to recognize phenolic compounds [106].

The current society's and the world market's demand for naturally occurring bio molecules is widely known. Resveratrol, a phenolic molecule, is in major abundances from various AL plants from North East India. Two distinct kinetic models were used to predict the extraction kinetics. Outcomes demonstrated that diffusive influence inside the sample was a factor in the extraction process. With an IC_{50} value of 53.24 μg/mL, one of isolated compounds demonstrated considerable antioxidant activity. As a result, authors suggested that resveratrol can be utilized as an antioxidant agent [107].

Antiatherosclerosis Activity

The plant AH is a member of the Moraceae family. This family is known to offer several health benefits, particularly for inflammatory conditions, infections, diabetes, and even other cardiovascular issues. Hypercholesterolemia is one of the risk factors for several cardiovascular illnesses. Previous in-vitro studies demonstrated that *A. altilis* ethyl acetate fraction had cytoprotective effects on human U937 cells that had been exposed to oxidised LDL. The same study sought to determine the impact of an ethyl acetate (EA) fraction from Sukun leaves on in-vivo lipid deposition in the aorta and blood total cholesterol levels. Wistar rats

aged 8 weeks, each received the EA fraction after being fed a diet rich in cholesterol for 30 days. The EA fraction had the potential therapeutic impact of preventing atherosclerosis; moreover it had lowered total blood cholesterol levels and prevented lipid build up in rat aorta. Additionally, it was hypothesised that its flavonoid content, particularly 2-geranyl-2',3,4,4'-tetrahydroxydihydrochalcone, was contributed to the said benefit by acting as an antioxidant [108].

The cytoprotective properties of several solvent extracts were assessed by various researchers around the World. By using 4-[3-(4-iodophenyl)-2-(4-nitrophenyl)-2*H*-5- tetrazolio] method, the cytoprotective effects were assessed in human U937 cells that had been exposed to oxidised LDL (OxLDL). In a bioassay-guided isolation of the ethyl acetate, researchers extracted beta-sitosterol along with six flavonoids, and tested for the primary cytoprotective components. Based on spectroscopic data and comparison with published data, the chemical structures were established. Their results presented promising possibilities for the therapeutic uses of AA [109, 110]. Plant sterol esters (PSE) in the diet were found to reduce plasma LDL-cholesterol (LDL-C) levels, and they can also slightly raise plasma plant sterol levels. In conclusion, diet-related PSE decreased plasma LDL-cholesterol (LDL-C) levels. Despite a rise of plasma plant sterol levels, they had no impact on the formation of aortic foam cells. In instance, dietary PSE dramatically reduced the growth of aortic foam cells. These results denote the idea that PSE inhibit atherogenesis [111].

Corneal Epithelial Wound Healing Activity

It may be possible to employ the secondary metabolites found in mobe leaves to aid in the healing of wounds. One of the secondary metabolites in mobe leaves, Artocarpin had been shown to influence the expression of the protein known as transforming growth factor-beta (TGF-β), promoted the proliferation of fibroblast cells and hastened the wound healing. Nanoemulgel dosage formulations are possible using ethanol extract from mobe leaves.

This reported study demonstrated the ability of mobe leaf ethanol extract in combination with nanoemulgel to treat wounds. In comparison to the negative control, a significant difference with proportion of wound diameter reduction and after 14 days, the numbers of fibroblast cells were observed ($p < 0.05$). In the course of a 14-day observation, results from the examination of platelet-derived growth factor (PDGF)-BB and TGF-1 immunoexpression were found substantially different from those of the Blank group ($p < 0.05$). Study also found that by significantly increasing TGF-1 and PDGF-BB expressions in burn sites, nanoemulgel-mobe can drive greater fibroblast cell proliferation [112].

The Ibo ethnic community of South and east Nigeria usually enjoys the flavour of African breadfruit, a neglected food security crop. Across West and Central Africa, this plant is frequently seen. It is a huge, evergreen tree that produces 20 to 30 pods per year containing edible seeds. This Ibo community in South East Nigeria uses these edible seeds in their specialised recipes. Meals made with African breadfruit are found to be highly nutritious.

Traditional medicinal uses of it include parts such as the roots, leaves, and pods. The leaves are notably abundant in minerals, flavonoids, phenols, cardiac glycosides, and anthraquinones. They are rich in antioxidant, antibacterial, and wound-healing components. This stem bark extract contains antibacterial qualities and used in a cough treatment. The root's aqueous and ethanolic extracts had been reported for hypoglycaemic-lowering abilities and also prevented the emergence of type 2 diabetes associated secondary problems. Although *Treculia africana* has considerable potential as a food, nutrition security and medicinal crop, several relatives of the mulberry family, particularly the *Artocarpus* species, needs attention by researchers [113, 114].

The wound healing capacity of the multi- herbal compound PACT was evaluated using excision wound and perhaps incision wound models. The wound shrinkage region and epithelialisation period were studied in the excision wound model, whereas wound fracture toughness and hydroxyproline concentration were assessed in the incision wound model. The PACT significantly increased wound closure, epithelialisation, wound possibly breaking power, and hydroxyproline content as compared with control group. This formulation had a strong wound healing potential in preclinical investigations, according the findings of this research [115]. It can be investigated further for therapeutic uses. Excision wound model and an ointment that was equal to standard (Betadine) ointment were used to investigate the wound-healing capabilities of methanol bark extract of AH in albino mice. The time of epithelialisation of the extract-treated group was found higher than the control group. These results suggested that extract had potent wound-healing activities [116].

FUTURE PROSPECTUS

The objectives of present review appear to be suitable for exploration of this plant genus in the near future. First, knowing the similar phytochemical structures of these plant chemicals will lead to more research into the metabolic pathways of these valuable products; second, knowing metabolic engineering will greatly improve both biosynthesis and the accumulation of these substances. This will be facilitated by the use of molecular marker technologies to find high-yielding clones that produce these phyto-products. Unfortunately, metabolic pathways that produce

active phytochemicals are generally unknown, and only a few genes encoding important enzymatic or regulatory stages have been identified. New findings and developments in these domains allow us to study for the biosynthesis [117].

Crude extracts and associated phytochemicals, and their application for nutraceuticals or active compounds for traditional and modern research, can be possible based on the biological properties of *Artocarpus* species, although clinical studies and product development are required at first step. The new research may primarily base on in-vitro studies. *Artocarpus* species are vital to biodiversity. The jackfruit is still a relatively untapped source for isolating and characterizing novel beneficial compounds. Other plant parts, such as the flowers, can also be investigated, as recent papers have emphasised on AL and AH (mostly as a source of bioactive chemicals) [13, 15].

Computational tools are gaining more popularity nowadays in order to establish possible correlations between the ligand/chemical components with proposed biological targets. Various techniques such as Density functional theories, Molecular docking, molecular dynamics, etc can successfully be employed for synthetic as well as natural compounds [131–155].

Recently, we have also performed in-silico pharmacokinetic and toxicities for a number of *Artocarpus lakoocha* polyphenols and it was determined that these analyses would provide (Brosimone as well as other *Artocarpus lakoocha* polyphenols)a possible therapeutic hit for varieties of receptor targets of malarial parasites [118].

CONCLUSIONS

This review summarizes pharmacological potentials of *Artocarpus* species as a source of important nutrients and bioactive phytochemicals. Traditional, phytochemical, and pharmacological data on many *Artocarpus* species are also compiled in this review. Phytochemicals, which were detected in an abundance from five *Artocarpus* species, encompassed flavonoids, glycosides, tannins, phenols, saponin, alkaloids, steroids, and triterpenoids, etc.

Experimental studies on this plant genus reported for edible and non-edible parts were also suggested to have varieties of pharmacological properties of same such as antioxidant, antiinflammatory, antibacterial, anticarcinogenic, immunomodulatory, antifungal, hypoglycaemic effects, inhibition of melanin biosynthesis, wound healing properties.

Artocarpus fruits, such as jackfruit, monkeyfruit, and bread fruit are less popular than other tropical fruits and usually, they are wasted in vast amounts. Despite being a nutritious fruit, the Jackfruit's lack of popularity is mostly owing to the perception that it causes stomach discomfort. More research on these plant species should be encouraged in order to establish scientific evidence for its numerous therapeutic benefits. To understand mechanisms of the flavonoids, glycosides, tannins, phenols, saponin, alkaloids, steroids, and triterpenoids triggering pharmacological activities, and more research required. Highly collaborative programs that integrate conventional and modern techniques would be crucial for the future applications of *Artocarpus* as a possible source of medicinal natural products.

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COMPLIANCE WITH ETHICAL STANDARDS

The authors declare that they have no conflicts of interest.

This article does not contain any studies involving animals or human participants performed by any of the authors.

CONFLICT OF INTEREST

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