

Plant Review

A Review on *Artocarpus altilis* (Parkinson) Fosberg (breadfruit)

Mukesh S. Sikarwar¹, Boey Jia Hui², Kumutha Subramaniam², Bavani Devi Valeisamy², Ling Kar Yean², and Kaveti Balaji¹

¹ Unit of Pharmaceutical Chemistry, Faculty of Pharmacy, AIMST University, Semeling, Kedah Darul Aman, Malaysia. ² Research Student, Unit of Pharmaceutical Chemistry, Faculty of Pharmacy, AIMST University, Semeling, Kedah Darul Aman, Malaysia.

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ABSTRACT

Artocarpus altilis (Family: Moraceae) is commonly referred to as breadfruit as it is similar to freshly baked bread. Synonyms of *Artocarpus altilis* are *Artocarpus communis* and *Artocarpus incisus*. Basically *Artocarpus* species consists of phenolic compounds which include flavonoids, stilbenoids, arylbenzofurans and Jacalin, a lectin. Breadfruit (*Artocarpus altilis*) is originated from *A. camansi* Blanco (bread nut) which is native to New Guinea, Moluccas (Indonesia) and the Philippines. Many on-going researches are testing the pharmacological activities of *Artocarpus altilis*. Some of the researches that are being carried out on this plant includes anti-inflammatory, antioxidant, antifungal, sexual behavior, immunomodulatory effect, antidiabetic effect and antibacterial effect. This review will help to provide detailed information on recent researches done on this plant.

INTRODUCTION

Herbal Medicine

Herbalism is an ancient practice that actually predates our recorded human history. According to the records, herbalism has been accepted as back as Sumerian practices dated back to 5000 years. History of herbal drugs in India dates back to 1900 B.C. which comprises of many herbs that are used in conventional herbal medicinal system.

In modern era, herbal ingredients are sometimes marketed for condition and ailments that were never considered in the traditional systems of medicines. Use of ephedra for weight loss or athletic performance enhancement is one of the examples. In Germany, herbal drugs are considered as 'phytomedicines', in which they are subjected to quality control measurement for safety, quality and efficacy. Most of the herbal/food products are sold and regulated as nutraceuticals, which does not require pre-approval for these above criteria (Glatz, 2011).

Artocarpus altilis

Most of the plants in the universe are known to possess therapeutic properties and have been used since ancient times to treat various human diseases effectively and efficiently. One such plant is *Artocarpus altilis* which belongs to the family, Moraceae. It is commonly referred to as breadfruit as it is similar to freshly baked bread. Breadfruit is a tropical fruit and the breadfruit tree produces fruits from March to June and from July to September (Akanbi et al., 2009). Breadfruit is also known to be a traditional starch rich crop. The genus *Artocarpus* (Moraceae) comprises of approximately 50 species and is widely distributed in tropical and subtropical regions (Timothy, 2014). The generic name of the species comes from the Greek words 'artos' (bread) and 'karpos' (fruit) and the fruits eaten are commonly called breadfruit (Jones, 2011). Synonyms of *Artocarpus altilis* are *Artocarpus communis* and *Artocarpus incisus* (Orwaet et al., 2014). Basically *Artocarpus* species consists of phenolic compounds which includes flavonoids, Jacalin, a lectin and stilbenoids. *Artocarpus* extracts and metabolites from leaves, stem, fruit and bark contain numerous beneficial biologically active compounds and these compounds are used in the various biological activities including antibacterial, antitubercular, antiviral, antifungal, antiplatelet, antiarthritic, tyrosinase inhibitory and cytotoxicity (Jagtap and Bapat, 2014).

* Corresponding Author

Dr. Mukesh S. Sikarwar, Unit of Pharmaceutical Chemistry, Faculty of Pharmacy, AIMST University, Semeling, Kedah Darul Aman, Malaysia.

E. mail: mukeshsikarwar@gmail.com.



Fig. 1 *Artocarpus altilis* (Parkinson) Fosberg (breadfruit) in natural habitat.

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. Although breadfruits are rich in carbohydrates, but they are substituted partially for wheat flour in many products such as snacks, pastries and bread.

Artocarpus altilis is a suitable crop for the hot, humid, tropical lowlands areas. Rain is a crucial factor that plays an important role in the flowering and rate of growth of the fruit. It requires rainfall of fairly equal distribution. *Artocarpus altilis* grows best in equatorial lowlands; it is occasionally found in the highlands, but the production and the quality of the fruits decreases in cooler conditions. Good drainage is essential, and trees may bear fruits when the soil is wet. The soil conditions required for the proper growth of the plants are sand, sandy loam or loam. This plant grows best at temperature 21- 32 °C. The soil should be neutral to alkaline in condition, pH 7.4-6.1.

TAXONOMICAL CLASSIFICATION (Nayeem *et al.* 2013)

Kingdom: Plantae
 Subkingdom: Mracheobionata
 Division: Magnoliophyta
 Class: Magnoliopsida
 Subclass: Hamamelididae
 Order: Rosales
 Family: Moraceae
 Genus: *Artocarpus*
 Species: *altilis*

Breadfruit (*Artocarpus altilis*) is originated from *A. camansi* Blanco and *A. Mariannensis* Trecul. *A. camansi* Blanco (bread nut) is native to New Guinea, Moluccas (Indonesia) and the Philippines. Around 3000 years ago, breadfruit was first cultivated in the western Pacific and spread throughout the tropics by migrating Polynesians where it has been cultivated widely by the Pacific islanders. Several seedless Polynesian breadfruit varieties and bread nut from New Guinea were introduced in the Caribbean in the late 1700s, where the breadfruit is considered as food for the

poor people. Later on, it has been distributed widely in Central and South America, Africa especially in Senegal, Ghana and Liberia, India mainly in the coastal regions of Karnataka and Kerala, Southeast Asia, Malaysia, Madagascar, Maldives, Seychelles, Indonesia, Sri Lanka, Northern Australia and South Florida (Deivanai and Bhore, 2010).

MORPHOLOGY (Diane, 1997; Ragone, 2006)

Tree

In general, breadfruit trees are very large, evergreen which can reach to heights of 15 to 20 meters. The tree comprises smooth, light-colored bark, and the trunk is large in 1.2 m in diameter, occasionally growing to a height of 4 m before branching. The wood is gold in colour, but when contact with air, turns to a darker colour. Latex can be seen in all parts of the tree which are milky in nature.

Leaves

The leaves are thick and leathery with a dark-green colour on the dorsal side, which often appears to be glossy. The underside is dull with an elevated midrib and main veins. The leaves varies in size and shape even on the same tree. At the end of the branches, the leaves are seen as clusters. The crown is conical in shape when the trees are young or grown under shaded condition and they become rounded and irregular when it turns older. Blade is generally smooth, glossy dark green with green or yellow-green veins and many white to reddish-white hairs on the midrib and vein.

Flowers

Breadfruit tree bears a multitude of tiny flowers. The breadfruit is monoecious which means the female and male flowers grows on the same plant. Club shaped spikes which are 5 cm in diameter and 45 cm in long are found in Male flowers whereas the female flowers are elliptical, green, prickly head measuring about 2.5 in (6.35 cm) long. Flowers undergo cross pollination with small powdery pollen grain spread by both the wind and insects. Once both the male and female flowers are fused together, it develops into a fleshy and edible fruit. Although the reproduction of flowers involves cross pollination, but pollination does not require the fruit to form.

Fruits

Fruits of *Artocarpus altilis* are of a very specific structure. In fruit, the central part contains many latex tubes and large vascular bundles. These vascular bundles can rapidly discolour upon cutting because of the oxidative enzyme activity. The fruits are variable in size, shape and surface texture. Mostly they are round, oval and oblong in shape ranging from 9-20 cm, more than 30 cm in long and usually weighing around 0.25-6 kg. Aggregate fruit (syncarp) is formed by the enlargement of the entire female head. The ripe fruits of these female flowers are roundish in shape and are 4 to 8 inches in diameter. The ripe fruits have yellow or yellow-brown skin and the fruits are soft and sweet

at the same time. The colour of the breadfruits are usually light green, yellowish green or yellow in colour when mature and the fruit (Afa) found in Society Island is pinkish or orange-brown in colour. The flesh of the fruit is usually creamy, soft with a pleasant fragrant.

Seeds

Breadfruits are available with seeds and also without seeds. The seeded types of breadfruit are available in south western Pacific, whereas seedless types of breadfruit are common in Micronesia and Eastern islands of Polynesia. All the breadfruit varieties elsewhere especially in topic region are of seedless type. Seeds are brown in colour, shiny, round or ovoid in shape and irregularly compressed. Moreover, the seeds have little or no endosperm, no period of dormancy and they can germinate immediately. Since they can germinate immediately, they are not able to be dried or stored. Trees that grow with the help of seeds can produce their fruits in a timeline of 6-10 years or sooner. On the contrary, asexually propagated trees can start to produce their fruits in 3-6 years of time.

PHYTOCHEMICAL CONSTITUENTS OF *ARTOCARPUS ALTILIS*

Phytochemicals are secondary metabolites. Wide varieties of phytochemicals are produced by plants. They function to attract animals or prevent infection, parasitism and predation but not necessary for basic metabolism. The *Artocarpus* genus can produce a large number of secondary metabolites usually rich in phenylpropanoids such as flavonoids and flavones. They also produce phenolic compounds including flavonoids, stilbenoids and arylbenzofurans. Over 130 compounds are identified in various organs of the tree of *Artocarpus altilis*, more than 70 of which derived from the phenylpropanoid pathway. Many of the isolated compounds exhibit biological activity such as inhibit platelet aggregation, anti-bacterial activity, anti-fungal properties, inhibition of leukemia cells and as an anti-tumor agent (Handa *et al.*, 2008). Nutritional compositions of the seeds have water, protein, carbohydrate, fat, calcium, phosphorus, iron, niacin, thiamine and vitamin C (Rahul, 2013)

Artocarpus altilis contains some chemical constituents such as morin, moracin, dihydromorin, cynomacurin,

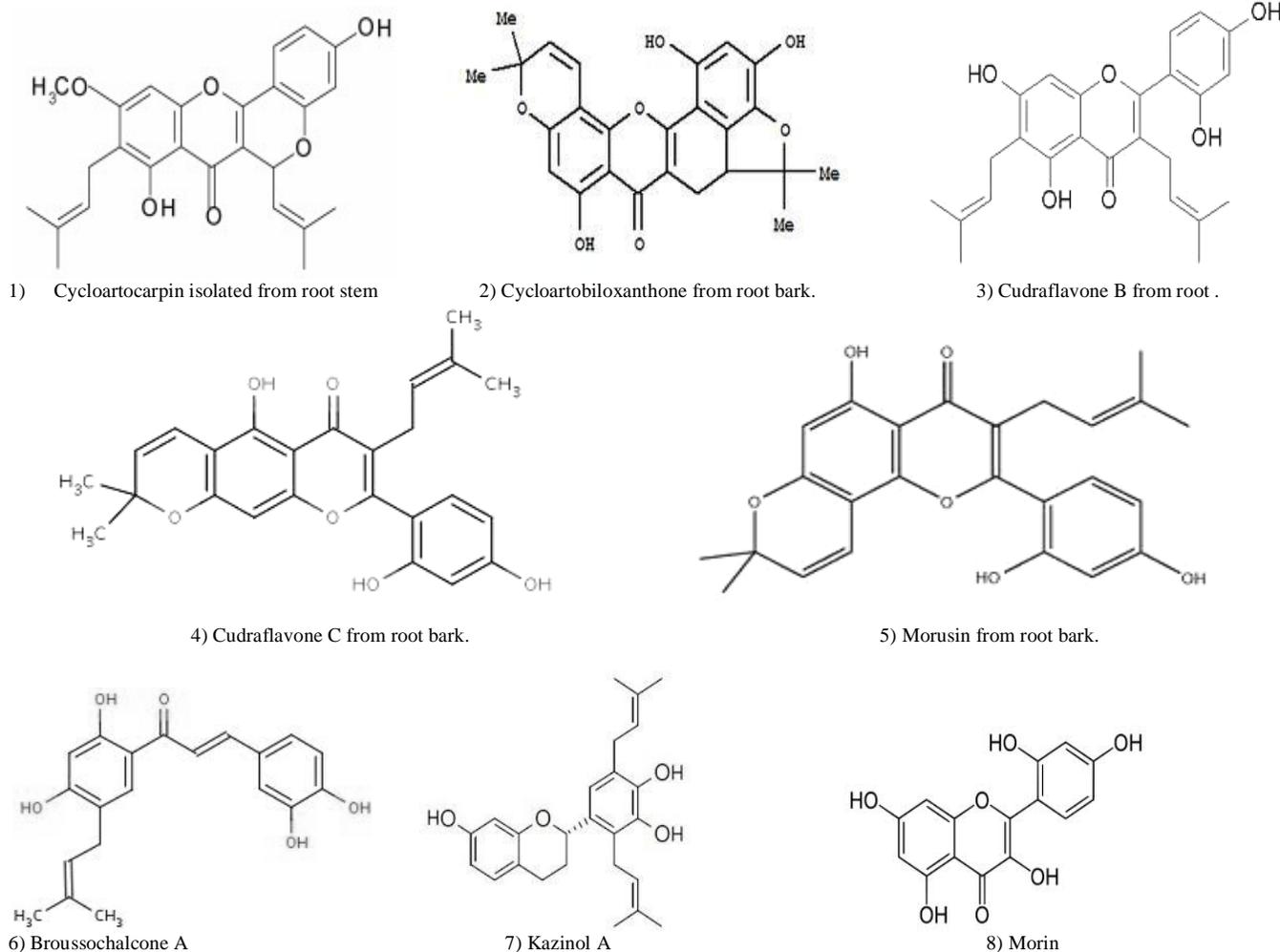


Fig. 2 Structures of some isolated compounds. Continued...

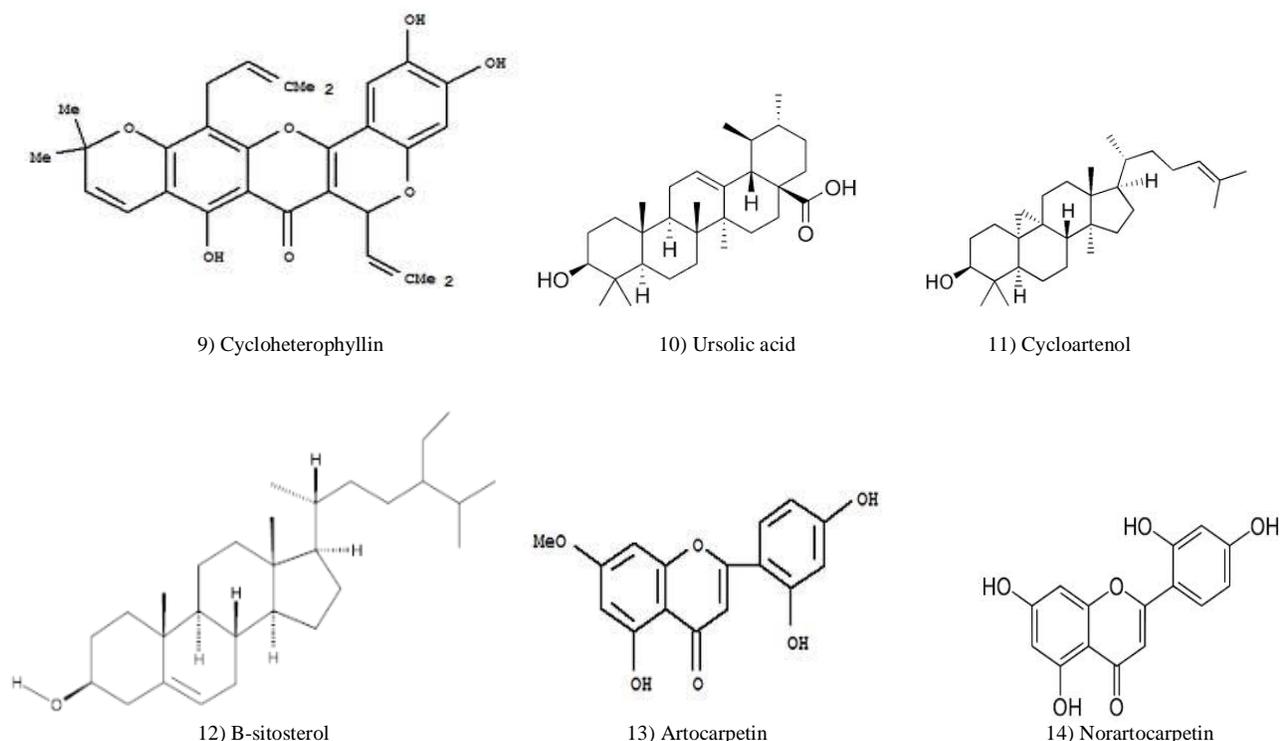


Fig. 2 Structures of some isolated compounds.

oxydihydroartocarpesin, artocarpetin, norartocarpetin (20, 40, 5, 7 tetrahydroxyflavone), cycloartinone, cyclogeracommunin, cyclocommunol, cycloartenyl acetate, β -sitosterol, sitosterol- β -D-glucopyranoside, ursolic acid, betullic acid acetate, artocarpanone, cudraflavone, artoflavon, orartocarpanone (20, 40, 5, 7 tetrahydroxyflavanone), oxyresveratrol and artoindonesianin F(40-[3-methyl-1(E)-butenyl]-(E)-2,30,4,50-stilbenetrol) (Solanki and Nagori, 2012). This species also contains brousochalcone A, kazinol A, brousoaurone A, cycloartocarpin A, cycloheterophyllin and brousoflavonol F (Lewis, 1961)

Methanolic, ethyl acetate and petroleum ether leaf extract of *Artocarpus altilis* have steroids, phytosterols, gums and resins. Besides, the other constituents present in the leaf extract are 72.5% amino acids, 68.2% fatty acids and 81.4% carbohydrates. 15.52 g/100 g fresh weight of starch content is present in breadfruit. Essential amino acids like cystine, arginine, histidine, leucine, lysine, methionine, theonine, tryptophan, sucrose, fatty acids and ellagic acid are the constituents of *Artocarpus altilis*. Calcium, iron and sodium are the minerals in breadfruit (Huie, 2002). Isoprenylated flavonoids with an isoprenyl side chain at C-3, and 2', 4'-dioxygenation or 2', 4', 5' trioxigenation patterns in ring B of the flavone skeleton are specific to *Artocarpus* species. Prenylflavonoids and geranyl flavonoids are produced by this plant (Delazar *et al.*, 2012).

Breadfruits contains geranyl dihydrochalcones such as 1-(2,4-dihydroxyphenyl)-3-[3,4-dihydro-3,8-dihydroxy-2-methyl-2-(4-methyl-3-pentenyl)-2H-1-benzopyran-5-yl]-1-propanone,

1-(2,4-dihydroxyphenyl)-3-[8-hydroxy-2-methyl-2-(3,4-epoxy-4-methyl-1-pentenyl)-2H-1-benzopyran-5-yl]-1-propanone(51-(2,4-dihydroxyphenyl)-3-[4-hydroxy-6,6,9-trimethyl-6a,7,8,10a-tetrahydro-6H-dibenzo[b,d]pyran-5-yl]-1-propanone.), 2-[6-hydroxy-3,7-dimethylocta-2(E),7-dienyl]-2',3,4,4'-tetrahydroxy dihydrochalcone and 1-(2,4-dihydroxyphenyl)-3-[8-hydroxy-2-methyl-2-(4-hydroxy-4-methyl-2-pentenyl)-2H-1-benzopyran-5-yl]-1-propanone (Raymond, 2003).

USES

1) Pharmacological uses (Somashekhkar, 2013)

Many on-going researches are testing the pharmacological activities of *Artocarpus altilis*. Some of the researches that are being carried out based on these plants includes Anti-inflammatory activity, Antifungal potential, Sexual behavior study, Immunomodulatory potential, Antidiabetic activity, Antibacterial activity, Anti-cholinergic effect, Chelating activity, Nutritional assessment, as cosmetic agent, ACE inhibitors, Antioxidant activity, Toxicity to cancer cell, Anthelmintic potential, Protease inhibitors, Regulation of oestrogens and melanin biosynthesis inhibition.

INTERACTIONS (Natural Standard, 2014)

5-Alpha reductase inhibitors

Based on laboratory tests, heartwood extract of *Artocarpus altilis* may produce a potent 5-alpha reductase inhibitory activity, and care must be taken when using 5-alpha

reductase inhibiting herbs and supplements, as the additive effects may cause some adverse reactions.

1) Anthelmintics

In an *in vitro* study, breadfruit tree preparation of 10(-2)-2.10(-3) concentration interferes with *Hymenolepis nana* (dwarf tapeworm) motility by causing motor excitation, contracture, and finally leads to death. Concomitant use of breadfruit with herbs or supplements that exhibits anthelmintic activity may have additive effects.

2) Anticoagulants and antiplatelets

Based on an *in vitro* study, root extracted from *Artocarpus altilis* can inhibit the formation of thromboxane (an inducer of platelet aggregation). Furthermore, breadfruit may theoretically potentiate the effects of other herbs and supplements that increase bleeding risks.

3) Antifungal

Frutackin, a lectin present in the seed extract of *Artocarpus incisus* inhibits the growth of *Fusarium moniliforme* and *Saccharomyces cerevisiae*. Breadfruit seed extract may theoretically show synergistic activity when administered in combination with other antifungal herbs or supplements.

4) Antineoplastics

According to the laboratory test, chemical components found in the leaves of *Artocarpus altilis* exhibits cytotoxic and apoptotic effects on human cancer cells by increasing the expression of apoptosis-inducing proteins such as Fas, FasL, and p53 proteins. Leaf extracts of breadfruit may theoretically have synergistic effect on antineoplastic herbs or supplements.

5) Antioxidants

Based on laboratory research, Thai breadfruit's (*Artocarpus incisus*) heartwood extract exhibits antioxidant activity depending on the dose and they may have an additive effect when taken with antioxidant herbs and supplements.

6) Hematological agents

According to the *in vitro* studies conducted on animals and humans, frutackin shows hemagglutination activity against erythrocytes and therefore they may have additive effects with antihemagglutinin herbs or supplements.

7) Inotropes

Based on research done on animals, it is found that the leaf extracted from *Artocarpus altilis* exerts a weak negative chronotropic effect to reduce left ventricular pulse pressure and also exerts a negative inotropic effect on right ventricular myocardial strips. Breadfruit may theoretically potentiate the effects of other herbs and supplements that alter myocardial contractility.

8) Skin-lightening agents

An *in vitro* study conducted on melanocyte B16F1 melanoma cells has shown that *Artocarpus altilis* extract reduced melanin content in these cells by inhibiting melanin synthesis. On the other hand, in another study, it is found that when the heartwood extracts from *Artocarpus altilis* is applied on the back of guinea pig, melanin biosynthesis is inhibited without causing any skin irritation.

BIOLOGICAL ACTIVITY OF *ARTOCARPUS ALTILIS*

1) Antitubercular and Antiplasmodial

Pakawan Puangsombat *et al.* used dichloromethane to extract and isolate nine prenylated flavones, three from the root stems of *Artocarpus altilis* which are cycloartocarpin, artocarpin, and chaplashin; and six from the root barks, morusin, cudraflavone B, cycloartobiloxanthone, artonin E, cudraflavone C and artobiloxanthone. They performed the antitubercular activity against *Mycobacterium tuberculosis* H37Ra using the micro plate Alamar blue assay (MABA) and the antimalarial activity against the parasite *Plasmodium falciparum* (K1, multidrug-resistant strain) using the microculture radioisotope technique. They concluded that these prenylated flavones exhibited antitubercular and antiplasmodial activities, while exhibiting moderate cytotoxic activity towards KB (human oral epidermoid carcinoma) and BC (human breast cancer) (Boonphong *et al.*, 2007).

2) Antiatherogenic

Oluwatosin and Olubukola (2014) used methanol extract of *Artocarpus altilis* and also questran as standard to learn the plant's effect on the atherogenic indices and redox status of cellular system of hypercholesterolemic (HC) rats. They induced hypercholesterolemia in male rats by administering 30mg/ 0.3mL of dietary cholesterol by oral gavage for nine consecutive weeks. They concluded that extract of *Artocarpus altilis* has significant anti-atherogenic effect and also improves antioxidant system of hypercholesterolemic rats via their ability to produce favourable lipid parameters, significant increase in HDL-C and improved antioxidant system.

3) Antiatherosclerotic

Wang *et al* (2006) identified the main cytoprotective components by a bioassay guided isolation of the ethyl acetate extract which afforded β -sitosterol and six flavonoids. The cytoprotective effect suggested the promising medicinal applications of *Artocarpus altilis*.

4) Skin Lightening Agent

Gottumukkala *et al.* (2013) isolated dendrite elongation inhibitory compounds from the extracts of *Artocarpus altilis* with methanol and subjected the active fractions obtained to chromatography method. They conducted the dendrite elongation study by using melanocyte cells, B16F10.

Finally, they concluded that the crude methanolic extract, fractions and isolated compound showed good dendrite elongation activity and these active compounds can be used in skin care formulations for the lightening of the skin.

5) Antioxidant Agent

Hornig-Huey *et al.* (2013) evaluated the antioxidant activities of flavonoids isolated from heartwood and cortex of *Artocarpus altilis* including their inhibitory effects on mushroom tyrosinase and melanin biosynthesis in vitro. They assessed the ability of the prenylated flavonoids including 10-oxoartogomezianone, 8-geranyl-3-(hydroxyprenyl)isoetin, hydroxyartoflavone A, isocycloartobiloxanthone, and furanocyclocommunin, together with 12 other known compounds to scavenge the DPPH, ABTS⁺ radical cation, and the superoxide anion (O₂⁻), and their capabilities to inhibit tyrosinase and melanin production in order to identify the natural antioxidants and whitening agents. Their investigation resulted in compounds hydroxyartoflavone A, isocycloartobiloxanthone and artoflavone A having moderate DPPH-scavenging activity, whereas compound isocycloartobiloxanthone exhibits significant ABTS⁺-scavenging activity, and that norartocarpetin and artogomezianone exhibits moderate ABTS⁺-scavenging activity, with compounds 8-geranyl-3-(hydroxyprenyl)isoetin, norartocarpetin, and artocarpin displaying good superoxide anion-scavenging activity. They concluded that these flavonoids are suitable as antioxidants and/or skin-whitening agents. However, further investigations are required to determine their mechanisms of action.

6) Alpha Amylase and Alpha Glucosidase Inhibitor

Sindhu *et al.* (2013) evaluated the inhibitory activities of methanolic extracts of *Artocarpus altilis*, *Cinnamomum zeylanicum*, *Piper betel* and *Artocarpus heterophyllum* on Wheat alpha amylase and Baker's yeast alpha glucosidase at varying concentrations. They concluded that the methanolic extracts of the all the plants efficiently inhibited alpha glucosidase enzyme in vitro. However, only *Artocarpus heterophyllum* can be useful in the management of postprandial hyperglycaemia.

7) Anthelmintics

Carine *et al.* (2010) investigated the antiparasitic potential of the leaf of phenolics containing *Artocarpus altilis* (Parkinson) var. *seminifera* and var. *non seminifera* and *Terminalia cattapa L.*, against the gastro intestinal nematode (GIN) *Haemonchus contortus*. Their in vitro assay results showed the A extract of *Terminalia cattapa L.* dead leaves exhibited egg hatching inhibition compared with the negative control while the A extract of *T. cattapa L.* dead leaf and the M extracts of *T. cattapa L.*, *A. altilis* (Parkinson) var. *seminifera* and var. *non seminifera* dead leaf exhibited larval development inhibition compared with negative control.

8) Antimicrobial Agent

Chinmay *et al.* (2013) investigated the antimicrobial activity of *Artocarpus altilis* leaf extracts in different solvent

media (petroleum ether, methanol, and ethyl acetate). They concluded that the methanol extract of *Artocarpus altilis* leaf in high concentration has the highest antimicrobial activity while petroleum ether and ethyl acetate leaf extracts showed better effectiveness at low concentrations.

9) Antihypertensive

Nwokocha *et al.* (2012) proved that the breadfruit can be used as an antihypertensive by investigating the possible mechanisms of action of its aqueous extract and its effect on cytochromes P450 (CYP) enzyme activities. The aqueous leaf extract *A. altilis* was administered intravenously via cannulated carotid artery of anaesthetized normotensive Sprague-Dawley rats. The rats are subjected to atropine, mepyrmine, propranolol and N (G)-nitro-L-arginine methyl ester. Their result showed moderate inhibitions of cytochrome P450s (CYP3A4 and CYP2D6) enzyme activities and they concluded that the *A. altilis* produces negative chronotropic and hypotensive effects through α -adrenoceptor and Ca²⁺ channel antagonism.

10) Antiausteric Agent

Nguyen *et al.* (2014) has determined that the methanolic leaves extract of the *Artocarpus altilis* has maximum preferential cytotoxicity against PANC-1 human pancreatic cancer cells under nutrient-deprived conditions at a concentration of 50 μ g/mL. They successfully isolated eight new geranylated dihydrochalcones named sakenins A-H (1-8) together with four known compounds (9-12) from the methanolic leaves extract of *Artocarpus altilis*. They have identified sakenins F (6) and H (8) as potent cytotoxic candidates.

11) Mosquito Deterrent

Jones *et al.* (2012) investigated the chemicals in the dried male inflorescences of breadfruit which is responsible for mosquito, *Aedes aegypti* deterrence. They proved that the male breadfruit flowers and fatty acids has the ability as mosquito repellent via systematic bioassay-directed study of the hydrodistillate of *A. altilis* and all its fractions using adult *Aedes aegypti* females.

CONCLUSION

The genus *Artocarpus* (Moraceae) comprises of approximately 50 species and is widely distributed in tropical and subtropical regions. The generic name of the species comes from the Greek words 'artos' (bread) and 'karpos' (fruit) and the fruits eaten are commonly called breadfruit. 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. Although breadfruits are rich in carbohydrates, but they are substituted partially for wheat flour in many products such as snacks, pastries and bread.

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