Nutritional and Health Benefits of Breadfruit (Artocarpus Altilis) Leaves: A Literature Review

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Abstract

Based on the availability of many nutrients, Artocarpus altilis leaves have been widely employed as nutrients and nutraceuticals in recent years, or well known as Breadfruit or in Indonesia called Sukun. According to habits of community use A. altilis leaves in various way as a medicine, this article make respresentations as commonly known literature review about Artocarpus altilis leaves chemical constituent with health potential. This literature review utilizing academic databases such as PubMed, ScienceDirect and Google Scholar, included all journals recorded, classified, and analyzed in 12 years, from 2010 to 2022. The diversity of secondary metabolites present in this plant species especially flavonoids, terpenoids, steroids, phenols, saponins, alkaloids and tannins show that Artocarpus altilis leaf is a good candidate for source of health cause its compounds are used as a antioxidant, antiinflammatory, hypoglycemic properties, some cardiovascular problems, and many others. More research is needed for utilization as well as to study medicinal effects and bioaccesibility of these leaves for development of various drugs and functional foods.

Key Words: Nutritional, Health, Artocarpus Altilis.

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Introduction

The past decade has witnessed an explosion of clinical research to show specifically what health benefits individual foods can offer, identifying the various nutrients and phytochemicals associated with these benefits and how they can be incorporated in the diet. One of the major issues of the WHO was to deepen investigation of plants as a promising source of therapies for human disease management (Mboso et al, 2010).

Medicinal plants are plants that have active components and are believed by the community to cure diseases. Plants provide not only essential nutrients needed for life, but also other bioactive phytochemicals that contribute to health promotion and disease prevention. Plant extracts have been used for thousands of years because of higher bioactive components, which are responsible for certain physiological activities in human body. Numerous phytochemicals exist in edible fruits, flowers, seeds, and leaves, which are related to health-promoting benefits with protective properties of the neurological, hepatic, cardio, and gastro systems. Chemical components present in them have physiological functions in living plants, and hence they have superior compatibility with human body. Various examples of animal model studies are also discussed to show the potency of the plant extracts against several ailments (Majeed and Naseer, 2022).

Indonesia has the largest biodiversity in the world. Of the 30 thousand plant species, 1000 of them have been used for medicine and medical treatment.

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Breadfruit (Artocarpus altilis) is one of the most commonly used plants (Palimbong, et al, 2020). The breadfruit is a member of the genus Moraceae which contains about 50 species of trees. The breadfruit tree is fast-growing with the capability of reaching 26 m in height and often buttressed at the base. There are many spreading branches. This Plants belonging to the family Moraceae This contains efficacious compounds. The leaves, evergreen or deciduous depending on climatic conditions, are situated on thick, yellow petioles, entire at the base, then more or less deeply cut into 5–11 pointed lobes (Badrie and Jacklyn, 2010).

Breadfruit leaves (Artocarpus altilis), extremely common in Indonesia, contain polyphenol, flavonoid, tannin and alkaloid substances which accelerate the wound healing process because of their anti-inflammatory, anti-bacterial and anti-oxidant properties. Thus, this plant is one of the traditional medicines than has been widely known to the people especially can grow in tropical climates (Jagtap and Bapat, 2010). Previous studies have shown that breadfruit has anti-cancer, anti-austeric, antioxidant, anti-inflammatory, anti-bacterial and anti-atherosclerotic properties (Fakhruddin, et al, 2015). Another study indicated that 16% breadfruit leaf gel extract administered to Wistar rats induced effective anti-inflammatory activities (Abdassah et al., 2009).

Breadfruit (Artocarpus altilis) has many benefits, the extracts and metabolites of Artocarpus, especially leaves, barks, stems, and fruits, have been shown to be useful bioactive compounds. In the West Indies, yellowing breadfruit leaves are used as tea to treat diabetes, high blood pressure and asthma (Kumaraswamy and Senthamarai, 2020). The breadfruit leaves infusion has an effect on reducing blood glucose levels in white male mice with type 2 diabetes mellitus (Simanjuntak, and Kasta, 2020). The objective of this study is to find references about the chemical contents related to the effects of Artocarpus altilis leaf extract in Health.

Methods

This study uses a literature review approach. The stages of implementing a literature review include the stages of collecting, identifying, evaluating, and interpreting information about breadfruit leaves. The research articles obtained were then screened and selected according to the inclusion criteria which included: 1) research articles published in 2010-2021; 2) full text that can be accessed freely; 3) using experimental methods. While the exclusion criteria are articles that are the result of a review or the published articles are not in their original form such as letters to the editor, abstracts only, and book reviews. The literature review was carried out on PubMed, Science Direct and Google Scholar. To make the process of researching relevant journals efficient, keywords used are according to the title of the writing such as Artocarpus altilis leaf, Breadfruit Leaves Extract, Bioactive Compounds, Nutrition and Health Benefit.

Results and Discussion

The search results obtained as many as articles. From the Science Direct database, 581 articles were obtained, from Google Scholar in English, 13 articles were obtained from Science Direct, and from Pubmed, 14 articles were obtained. From several search results articles, a review was carried out and obtained 27 articles that matched the inclusion and exclusion criteria.

Nutritional Content and Bioactive Profile of of Artocarpus Altilis Leaves

Table 1. Nutritional composition of A. altilis leaf

Nutritional Content	Leaf Infusion	Leaf Powder
Carbohydrates (%)	0.13	0.45
Proteins (%)	0.1	0.01
Fats (%)	0.2	0.07
Ash (%)	0.04±0.01	15.92 ± 0.01
Moisture content (%)	99.53±0.23	14.88 ± 0.53

Values are expressed as mean ± standard deviation of three replicate measurements.

For nutritional composition, the A. altilis leaf infusion at 100°C and leaf powder contained carbohydrates, proteins, fats, ash and moisture content values respectively at table1 (Simanjuntak and Kasta, 2013 and Ayeni, et al, 2018). Fats content obtained in the sample indicated that there are phytosterols and steroid in the leaf of A. altilis (Azli, et al, 2016).

Table 2. Mineral composition of A. altilis leaves

Nutritional Content	Values
Phosporus	24.31±0.03
Calcium	20.08±0.01
Magnesium	5.76±0.01
Potassium	26.00±0.02
Sodium	7.20±0.02

Values are expressed as mean ± standard deviation of three replicate measurements.

Mineral compositions of the leaves of the breadfruit leaves revealed high concentration of Potassium, Calcium and Phosphorus with moderate quantity of Magnesium and Sodium (Ayeni, et al, 2018). Magnesium is an important mineral element which acts as a cofactor of many enzyme (McDonald et al., 1995). Calcium is also helpful in the formation of blood, intracellular and extra cellular fluids within and outside the cell of the body (Olayiwola et al. 2009).

Table 3. Qualitative and Quantitive analysis of A. altilis leaves

Phytochemical	Results	Values
Alkaloids	+	14.80 ± 0.00
Saponin	+	3.90 ±0.00
Tanin	+	1.89± 0.00
Flavonoids	+	3.70± 0.14
Terpenoids	+	
Steroids	+	
Total Phenol	+	1.09 ±0.00

Values are expressed as mean ± standard deviation of three replicate measurements.

The results of phytochemical screening contained in the breadfruit leaf infusion consist of flavonoids, saponins and tannins, and terpenoids (Simanjuntak and Kasta, 2013). Qualitative and quantitative test prove that the ethanol extract of breadfruit leaves also contains alkaloids, tannins and total phenol (Ayeni, et al, 2018). Extract A. altilis leaf with methanol and etanol shown that steroid and flavonoid are indicated by using qualitative method (Siddesha, et al, 2011). Breadfruit leaves are often used to treat various diseases because of the high antioxidant phytochemical. Antioxidants can stop the process of cell damage by giving electrons to free radicals (Kadir, Kasimo and Ilmi, 2020). Phytochemical screening of extracts and fractions stuck yellow leaves of breadfruit also contains, monoterpenes and sesquiterpene (Setiawati, 2017). Phytochemicals can have complementary and overlapping mechanisms of action, including modulation of detoxification enzymes, scavenging of oxidative agents, stimulation of the immune system, regulation of gene expression in cell proliferation and apoptosis, hormone metabolism, and antibacterial and antiviral effects (Waladkhani, 1998). Phytochemicals have been shown to have roles in the reduction of platelet aggregation, modulation of cholesterol synthesis and absorption, and reduction of blood pressure. Recently, C-reactive protein, a marker of systemic inflammation, has been reported to be a stronger predictor of cardiovascular disease than LDL cholesterol (Ridker, et al, 2002).

Most of the bioactive compounds in A. altilis originated from the phenylpropanoid pathway, and they are phenolics and flavonoids (Sikarwar, et al 2015). Phenolic and flavonoid compounds are bioactive compounds found in many plants and have the potential to reduce free radicals (Tungmunnithum, et al 2018). A. altilis leaf contains more phenolic and prenylated flavonoids than the fruit and bark parts. Which may play a role in scavenging free radicals, were phenolic non-flavonoids.

Gaschromatography–mass spectrometry (GC-MS) analysis revealed three major bioactive compounds existed in A. altilis extract. The extract demonstrated antioxidant and antibacterial properties with 2,3-diphenyl-1-picrylhydrazyl (DPPH) scavenging activity, ferric reducing ability of plasma (FRAP), hydroxyl radical scavenging activity, tyrosinase mushrrom inhibition of 41.5%, 8.15±1.31 (µg of ascorbic acid equivalents), 32%, 37% and inhibition zone diameter of 0.766±0.06cm (B. cereus) and 1.27±0.12cm (E. coli). Based on the results, the major compounds such as hexadecanoic, cinnamic and cis-13-octadecenoic acid can protect the autoxidation or lipid oxidation by donating an electron to reactive radicals so that they can be converted into stable species (Ahmad, Mohammad Norazmi, Et al. 2020).

The study by Rafaela, et al (2019) has demonstrated the presence of other metabolites in idioblasts through histochemistry, such as phenolic compounds triterpenes, steroids and lipophilic substances. Histochemistry was also important to reveal that the two species of Artocarpus leaves present the same types of metabolites, however, located in different tissues. Identification of the chemical composition of the crystals by histochemical test and by SEM-EDS is an important diagnostic feature for genus and species of Moraceae.

Health Benefits of Artocarpus Altilis Leaves

Anti-Cancerous Properties

The Artocarpus altilis dried and stems leaves extracts and the partially purified fraction have been shown to inhibit STAT3 activity and the phosphorylation of STAT3 in a dose-dependent manner. To identify the active components, a bioassay-guided isolation of the partially purified

fraction resulted in the identification of a geranyl dihydrochalcone, CG901. Its chemical structure was established on the basis of spectroscopic evidence and comparison with published data. The partially purified fraction and the isolated a geranyl dihydrochalcone, CG901, down-regulated the expression of STAT3 target genes, induced apoptosis in DU145 prostate cancer cells via caspase-3 and PARP degradation, and inhibited tumor growth in human prostate tumor (DU145) xenograft initiation model. These results suggest that A. altilis could be a good natural source and that the isolated compound will be a potential lead molecule for developing novel therapeutics against STAT3-related diseases, including cancer and inflammation (Jeon, et al, 2015).

Artocarpus altilis leaves could have a potential utility for the development of drugs against pancreatic cancer by the result of the microscopic images were analyzed under phase-contrast and fluorescence mode using ethidium bromide/ acridine orange (EB/AO) reagent. AO is a cell permeable dye and gives a green or orange fluorescence in live cells. EB is permeable to dead cells only and gives a red fluorescence. The cells in control were alive and stained with AO giving a green fluorescence. However, the morphology of PANC-1 cells was distinctly altered with an increasing population of dead cells. The phase contrast image of PANC-1 cells treated showed rounding of the cell membrane, rupture, and disintegration of cellular contents to the medium (Nguyen, et al, 2014).

Anti Hypertension

The ACE-inhibitory potential of Artocarpus altilis leaf extracts shore up its utilisation in the folk medicine for the better treatment of hypertension. The correlation between the phytochemical analysis and ACE-inhibitory activity in this investigation suggests that the high content of phytoconstituents, glycosidic and phenolic compounds in the leaf extracts could be involved in exerting the ACE-inhibitory activity such as (Siddesha, et al. 2011).

By using Male Sprague–Dawley rats, Nwokocha, et al (2012) research shown that the calcium ion concentration-response curve constructed in a calcium ion free medium on rat aorta was shifted to the right. Intravenous administration of A. altilis leaf extract caused a dose-dependent reduction in systolic blood pressure (SBP), diastolic blood pressure (DBP) and MAP. HR showed a similar reduction at increasing dose of the A. altilis extract. The mechanism of the hypotensive activity is probably through endothelium and adrenergic mechanisms. Breadfruit leaves extract decreased the phenylephrine induced contraction in aorta suggesting the involvement of calcium ion mechanism.

Anti Diabetic

Study by Indrowati, et al (2017) shown that ethanolic extract of Artocarpus altilis leaves decreased the level of blood glucose and increased the insulin expression in pancreas beta-cells. By using completely randomized design and male Sprague Dewley rats, this study devided rats into normal control group and diabetic rats groups. Levels of bood glucose were measured using strip rapid test. The insulin expression in beta-cells was assessed using immunohistochemistry. The active compounds Gamma Amino Butyric Acid (GABA) and ethanolic extract of A. altilis leaves with a minimum dose of 400 mg k-1 b.wt., can be used as an antidiabetic. Pancreas is the target organ was affected by GABA and A. altilis leaves as antidiabetic agents.

Breadfruit leaf powder has an inhibitory effect on the concentration of blood glucose, α-glucosidase, α-amylase, and increases G6PD activity in diabetic rats. Breadfruit leaf extract at a dose of 400 mg / kg BW has better activity in protecting the pancreas and reducing the effects of pancreatic damage in rats compared to metformin. The infusion of breadfruit leaves at a dose of 300 mg / kg BW, 400 mg / kg BW and 500 mg / kg BW showed a decrease in blood glucose levels.This is due to the presence of secondary metabolites found in breadfruit leaf infusion which has an antidiabetic effect (Simanjuntak and Kasta, 2013).

The potential hypoglycemic activity of breadfruit leaves (Artocarpus altilis (Parkinson) Forberg) was tested in vitro by inhibiting the activity of α-glucosidase enzyme. Acarbose is used as a comparison which is an antidiabetic agent that works by inhibiting the action of the α-glucosidase enzyme. The activity test results showed that the ethanol extract of the yellow breadfruit leaves and the green breadfruit leaves showed the best activity compared to the green and yellow breadfruit leaf n-hexane extract with IC50 values of 9.07 ppm and 11.01 ppm, respectively. The high activity of ethanol extract compared with n-hexan extract is thought to be due to the many compounds that have the effect of inhibiting the activity of

α-glucosidase enzymes. In the condition of hyperglycemia, the inhibition of the action of the α-glucosidase enzyme can help overcome the condition of hyperglycemia because the amount of monosaccharide absorbed by the intestine becomes less and less (Rante, et al. 2015).

The diabetic status was associated with an increase in blood glucose concentration, as there was an observed significant increase in the blood glucose of untreated-diabetic rats. The A. altilis leaf powder supplemented diet mitigated the increase in blood glucose concentration but the group pre-treated with the A. altilis leaf powder supplemented diet had a greater impact in controlling the increased blood glucose concentration caused by DM similar to the reference drug (100 mg/kg metformin). This leaf have been shown to be involved in the stimulation of the ß-cells and the subsequent secretion of preformed insulin (Ajayi and Godwin, 2019).

Chemical compounds suspected to act as amylase inhibitors in Breadfruit leaves are flavonoids. Flavonoids could form complex compounds with starch, which causes the inhibition of hydrolysis of polysaccharides into monosaccharides. In Conclusion, 70% ethanol extract of breadfruit (Artocarpus altilis) leaves exhibited antioxidant activity and potential as an α-amylase inhibitor (Dwita, et al, 2018). The administration of A. altilis leaf extract at all given doses appeared to alleviate the atrophy and increase the number and size of pancreatic islets. This pancreatic protection of A. altilis leads to the restoration of plasma insulin levels and improvement of blood glucose levels following treatment (Djabir, et al, 2021).

Cardiovascular and Hematological Activity

The usefulness of Artocarpus atilis, as having a beneficial cardiovascular and haematological outcome in experimental myocardial infarction, and as such, a potential drug discovery for diseases of cardiovascular & hematological involvement. Artocarpus altilis treatment ameliorated the ISO induced increases in viscosity, increased the ISO induced decreases blood flow and influenced oxygen release through its effects on the P50 of the oxygen hemoglobin dissociation curve, AA treatment also reversed the ISO induced weight loss (Thomas, 2022).

Oral administration of aqueous extract of Artocarpus altilis has cardio-protective functions in myocardial injury by ISO, in part, by decreasing the heart rate and the sympathovagal balance, restoring the ECG distortions, and decreases the levels of the cardiac biomarkers (ALT, AST, CPK and LDH). Which could be due to a normalization of cell automatic sinus node function, as well as, sympathovagal balance. These findings have potential clinical effect for the therapy of cardio-protection from isoproterenol induced myocardial damage. The location of the myocardial injury was located in the subendocardial, perivenular, subepicardial regions, with maximum number of foci and maximum diameter of degenerated areas seen with the ISO treated group. Histological features of myocardial injury presented with oedema, interstitial haemorrhage, myocyte degenerations and inflammatory reactions in these tissues. All of these injuries were reduced with by A. atilis treatment (Nwokocha, et al 2017).

The results of Mozef, et al (2015) in vivo study show that the ethyl acetate fraction of Artocarpus altilis can lower the serum total cholesterol level and prevent the lipid deposition in aorta could occur which are potential to prevent atherosclerosis. Its content of flavonoid especially 2-geranyl-2',3,4,4-tetrahydroxydihydrochalcone is suggested to contribute to this effect by acting as antioxidant.

Anti Inflammatory and Antimicrobial

Artocarpus altilis leaf extract has the potential to be used as complementary therapy of inflammatory-related diseases (such as autoimmune), due to the insignificant side effects on body weight and suppression effect on the immune system compared to methylprednisolone. Macrophages as professional antigen-presenting cells are components of the innate immune system that play a role in the process of phagocytosis. Study results by showed that Artocarpus altilis extract affected phagocytic activity in macrophage function (Palupi, D H S, et al. 2020).

Antimicrobial activity of seedless breadfruit leaves extracts using agar dilution technique showed that the ethanol extract had a higher inhibitory activity against the test organisms used for the analysis than the n-hexane and water extracts as compared to the two methods used for the antimicrobial analysis (Nwaoha, and Onwuka, 2014). The green synthesis of Artocarpus altilis silver nanoparticles (BAgNPs) using aqueous leaf extract of Artocarpus altilis showed moderate antimicrobial and antioxidant activities. These BAgNPs seemed to exhibit bacterial inhibitory effect comparable to that of streptomycin and antifungal inhibitory

effect similar to that of amoxicillin against human pathogens and also free radical scavenging activity comparable to that of ascorbic acid (Ravichandran, et al, 2016).

The antibacterial activity of ethanol extract of breadfruit leaf can inhibit the growth of P. aeruginosa bacteria in the concentration range of 25 - 300 µg/mL. The antibacterial activities of Artocarpus altilis leaves were verified by the presence of glycosides, alkaloids, and flavonoids. This study by Putra, et al. (2021) proposed that phytochemical components of plants that might either kill or hinder disease development be evaluated as possible antimicrobial medication options. An antibacterial effect is produced by the alkaloid, tannin and flavonoid in the leaves used. It is believed that the antibacterial effect of breadfruit leaves is caused by their elevated alkaloid content. Alkaloid can disrupt bacteria cell membranes as well as inhibit DNA and RNA synthase, while also being toxic to microorganisms (Aniszewski, 2015).

Conclusion

Generally, herbal preparations are considered safe and without adverse effects because they are considered natural products. Artocarpus altilis are highly recommended as natural dietary supplements, functional food because of their high nutritional value and low anti-nutritional factors. No adverse effects of breadfruit leaves have been observed in human studies so far. This leaves also contain key phytochemicals, which makes this plant an essential therapeutic agent with properties such as antioxidant, anticancerous, antimicrobial, antidiabetic, and anti-inflammatory properties. As the human clinical evidence is still limited, future research needs to define the actual magnitude of health benefits, establishes the safe range of breadfruit leaves consumption associated with these benefits, and elucidates the mechanisms of action.

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