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# Pharmacological Studies of *Durio Zibethinus*: A Medicinal Plant Review

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## ABSTRACT
Durio zibethinus is a family of Bombacaceae. It's usually called the fruit king. This plant has properties as a pharmacological remedy. Various parts of the D. zibethinus plant, especially its fruits and leaves, have a wide range of pharmacological properties in the treatment for a number of diseases. Many constituents of active phytochemicals of this plant have proven efficacy from a number of studies, including flavonoids, carotene, tannins, ascorbic acid, saponins, alkaloids, flavonoids, steroids, muchilago, glycosids, carbohydrates, reducing sugar, and phenols. Several studies prove the potential pharmacological activity of the fruit and leaves of D. zibethinus as antidiabetic, anticholesterol, antibacterial, antioxidant, digestiva, anti-inflammatory, and neuroprotective effects. The review of this article focuses on the knowledge of some of the pharmacological activities that D. zibethinus has.

Keywords: Durio zibethinus, Phytochemicals, Pharmacological studies.

## INTRODUCTION
The use of plants into medicinal ingredients has long been used by humans at least 60,000 years ago. In addition, plants in prehistoric times also used animals, microorganisms, and marine organisms. All these ingredients provide the activity of chemical compounds that are useful to activate their metabolic activity so that these ingredients can be useful as a treatment to relieve pain, treat diseases, maintain endurance, prevention of diseases, and early diagnosis for a disease.[1,2,3] In practice, 80% of the human population relies heavily on the use of traditional medicine derived from plants because it is associated with several factors, such as the availability of plants that are widely available in nature, the existence of easy access to obtainable, affordable, and knowledge of the benefits of plants that have been very much published.[4] More than 9,000 plants are already used as medicines in the world,[1] one of them is *Durio zibethinus*. *D. zibethinus* is genus *Durio* has a high economic value as well as some parts of plants including leaves, bark, roots, wood and fruits that can be used traditionally for treatment, and measurement of toxicity levels.[5] The genus *Durio* has 28 species, of which 19 are from the island of Borneo, 13 species are found in Peninsular Malaysia, 6 species are found in Thailand and 7 others in Sumatera. *D. zibethinus* is considered the "*King of fruit*" in various parts of Southeast Asia.[6] Of the 28 species, only six have been studied for secondary metabolites, including triterpenoids, steroids, lignans and phenolates.[7] *D. zibethinus* has activities as antidiabetic,[8] anticholesterol,[9] antibacterial,[10] antioxidant,[11] digestiva,[12] anti-inflammatory,[13] and neuroprotective effects.[14]

**Figure 1.** Fruits of *Durio zibethinus*

This review aims to provide up-to-date information on pharmacological potential of *D. zibethinus*.

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**Classification of Taxonomy and Common Name**[15]

Kingdom : Plantae

Division : Tracheophyta

Class : Magnoliopsida

Order : Malvales

Famili : Bombacaceae

Genus : *Durio*

Spesies : *Durio zibethinus*

## MORPHOLOGICAL STUDIES

*D. zibethinus* is a plant with the family *Bombacaceae* originating from Southeast Asia, especially Indonesia.[16] *D. zibethinus* is an annual fruiting plant that has a roux growth model characterized by the dominance of stem growth *continuous monopodial orthotrop* or commonly called sustainable growth.[17] *D. zibethinus* leaves are elliptical and oblong with the base of stalks and round leaves consisting of leaf stalks and leaf strands. Generally lamina is light green and dark green. The bottom of durian leaves has a different color with a surface dominated by green color. While on the surface of the lower leaves are greenish white, beige, brown, durian tree trunks are round, gray, brown, dark brown and moss green. *D. zibethinus* fruit shape has three types, namely round without lobes and petals, round with lobes without stamens and shirts. The textures of *D. zibethinus* meat are soft and coarse. While the color of fruit meat on local *D. zibethinus* is white, pale yellow and dark yellow.[18]

## PHYTOCHEMICAL STUDIES

Based on the the previous study,[19] the phytochemical content of the leaves of *D. zibethinus* with various kinds of solvents has different results, in the ethanol extract, the leaves of *D. zibethinus* contain flavonoids, terpenoids/steroids and glycosides. Meanwhile, n-hexane extract contains terpenoids/steroids. The aqueous extract consists of tannins and glycosides. While ethyl acetate extract contains flavonoids, terpenoids/steroids and glycosides. In *D. zibethinus* fruit with positive Petroleum ether solvent containing steroids, triterpenoids and fixed oil. In *D. zibethinus* fruit chloroform extract, there are steroid metabolites, saponins, triterpenoids and fixed oil, ethyl acetate extract contains saponins, flavonoids and triterpenoids. Meanwhile, methanol extract fruit of *D. zibethinus* is positive for secondary metabolites of carbohydrates, proteins, glycosides, saponins, flavonoids, and tannins.[20]

## PHARMACOLOGICAL STUDIES

### 1. Antidiabetic

Diabetes mellitus is a metabolic disorder in the endocrine, a complication of diabetes that can cause death in sufferers.[21] Antidiabetic are substances that are given periodically to reduce glucose levels in the blood.[22] *D. zibethinus* fruit has antidiabetic activity because it contains secondary metabolites such as polyisoprenoid alcohol.[23] In addition, *D. zibethinus* fruit contains flavonoids, namely catechins, quercetin, polyphenols and tannins. Quercetin has aldose reductase inhibitors activity which has the potential to be used in antihyperglycemia therapy.[8] This is evidenced by experimental research conducted by Muhtadi et al., ethanol extract of *D. zibethinus* fruit at doses of 125, 250, and 500 mg/kgBW has an antidiabetic effect on male white rats induced by alloxan.[8]

### 2. Anticholesterol

Cholesterol or also called hyperlipidemia is a condition in which blood protein levels increase due to genetic predisposition (heredity) or associated with individual diets. Anti-cholesterol are substances that can be used to lower blood lipid levels that exceed normal thresholds.[22] One of the fruits that has anticholesterol activity is *D. zibethinus* fruit. Based on the results of research conducted by Muhtadi et al., *D. zibethinus* fruit has activity as an anticholesterol, testing was conducted experimentally on albino male mice that weighed between 150-300 grams, then mice were fed high fat for 28 days. This results of research it showed that by giving *D. zibethinus* fruit extract with a dose of 500 mg/kg BW, it can lower blood cholesterol levels in mice. The results of this test showed significant activity when compared to the positive control used namely Cholesteramine.[9]

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### 3. Antibacterial

According to research that has been done by Chigurupati et al., *D. zibethinus* fruit contains active content of flavonoids as antibacterial which is tested by diffusion of wells, so that it can be known the antibacterial activity of *D. zibethinus* fruit against *Staphylococcus aureus* at MIC 250 µg/ml of 10.3±0.58 mm and *Bacilus subtilis* by 10.0±0.58 mm.[24] Then in other research, durian fruit has a bland zone against the *Pseudomonas aeruginosa* 11.2±0.76 mm and against the *Escherichia coli* sebesar 12.0±1.00 mm.[10]

### 4. Antioxidants

Testing the antioxidant activity of *D. zibethinus* fruit that has been done by Vinay et al., using DPPH method. The percentage of inhibition or capture of free radicals has antioxidant activity with an $IC_{50}$ value of 370 µg/ml.[25] Then in other studies, *D. zibethinus* fruit with ethyl acetate solvent has a percentage of inhibition $IC_{50}$ value 48.04 ppm, durian fruit has strong antioxidant activity.[26] *D. zibethinus* fruit ethanol extract has the best antioxidant activity against DPPH with $IC_{50}$ 11.21µg/ml compared to ascorbic acid standard which shows inhibition of 50% at a concentration of 6.56 µg/ml. Due to the high content of phenolates and flavonoids in *D. zibethinus* fruit ethanol extract, it is possible to donate electrons such as hydroxyl groups to reactive species to form non-radical DPPH-H forms in homogeneous systems.[27] In other studies, *D. zibethinus* fruit methanol extract shows effective antioxidant ability in a dose-dependent way, its inhibitor concentration value is calculated as 102.37±1.98, 19.50±1.44, 280.79±22.80, 154.67±5.84, 770.52±19.28, 324.63±17.61, 4.45±1.13 and 63.95±14.91 µg/ml, respectively, for DPPH, $ABTS^{+}$, reduction power ($Fe^{3+}$), reduction power ($Cu^{2+}$), superoxide anion scavenging ($O_2^{-}$), hydroxyl scavenging (OH), anti-lipid oxidation, capability test correcting ($Fe^{2+}$).[11]

### 5. Digestiva

Digestiva is a substance used to improve the digestive process of the stomach and intestines.[22] One of the active substances contained in *D. zibethinus* fruit is amylase. Amylase is thought to be involved in the initiation of digestion of intracellular starch granules in *D. zibethinus* fruit ripening plastids that have a function to accelerate starch molecules from carbohydrates to sugars. This α-amylase plastid from *D. zibethinus* named DzAmy3, DzAmy3 is what improves the digestive process.[12]

### 6. Anti-Inflammatory

Based on research Chingsuwanrote et al., to test the anti-inflammatory activity of *D. zibethinus* fruit, the ripe *D. zibethinus* fruit was extracted first and then the anti-inflammatory activity was tested using cell culture U937 that had been activated by using lipopolisaccharide (LPS).[13] The result was that at concentrations of 0.1 and 0.20 mg/ml of *D. zibethinus* fruit extract can reduce IL-8 secretion by 23-36%. This indicates that *D. zibethinus* fruit skin extract has anti-inflammatory activity.[13] This anti-inflammatory effect is due to the active polyphenol compounds contained in *D. zibethinus* fruit.[13]

### 7. Neuroprotective Effect

Alzheimer's disease is a multifaceted neurodegenerative disorder characterized by memory loss, progressive deficits in cognitive function, and severe behavioral disorders.[28] Polyphenols and flavonoids contained in *D. zibethinus* known to have several biological activities associated with Alzheimer's disease such as antioxidants, anti-Aβ aggregation, anti-acetylcholinesterase, and nerve protection.[14] According to research Plekratoke et al., *D. zibethinus* fruit has a neuroprotective effect that has a mechanism of action where the toxicity of amyloid antibeta peptide 1-42 is induced in SH-SY5Y neuroblastoma cells. Both ethanol extract and fat-eliminated ethanol extract can protect the same nerves as Aβ 1-42 peptide-induced neurotoxicity. The cell mechanism of SH-SY5Y and CE at concentrations of 1-100 µg/ml can reduce cell life loss caused by Aβ 1-42 peptides. then ethanol extract that is eliminated fat at a concentration of 10-100 µg/ml can reduce the loss of life power of cells caused by Aβ 1-42 peptides. Then from the anti-aggregation test it can be known that *D. zibethinus* fruit exposing can inhibit Aβ aggregation.[14]

## DISCUSSION

*D. zibethinus* contains many different secondary metabolite compounds consisting of flavonoids (caffeate, quercetin, flavanones, flavons, flavones, flavanols, anthocyanins), polyphenols (cinnamic acid, hydroxybenzoic acid), carotene, tannins, ascorbic acid and saponins,[29,30] alkaloids, flavonoids, steroids, muchilago, glycosides, carbohydrates, reducing sugar, phenol.[10] *D. zibethinus* leaves can treat abdominal pain, respiratory distress, wounds, and muscle aches or fatigue in women.[31] While the fruit serves as an antioxidant, antimutagenic, anticarcinogenic, anti-inflammatory, and antimicrobial.[32] Many studies today

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review some interesting pharmacological activities by a wide range of potential phytoconstituents of *D. zibethinus.*

*D. zibethinus* has antibacterial properties, according to Akiyama et al., tannins content of *D. zibethinus* has antibacterial activity through destruction of membrane bacterial cells.[33] The adstringent compound of tannins induces the formation of complex compounds bonding with enzymes or microbial substrates and the formation of complex bonds of tannins to metal ions that can increase the toxicity of tannins themselves as well as by shrinking the cell walls or membrane cells, thereby disrupting the permeability of the cells themselves.[33] While in alkaloids as antibacterial by disrupting the constituent of peptidoglican components in bacterial cells, so that the layer of cell walls are not formed completely causing cell death, in alkaloids there are components known as DNA intercellators that are able to inhibit the enzyme topoisomerase of bacterial cells.[34]

Meanwhile, the content of flavonoids (catechins, quercetin, polyphenols and tannins) contained in *D. zibethinus* can be used in the therapy of diabetic patients. One of the *D. zibethinus* content of quercetin can be used as an antihyperglycemic therapy because it has the activity of aldose reductase inhibitors that have the potential to be used in therapy.[8] Furthermore, *D. zibethinus* fruit can also lower cholesterol levels, but also unknown pharmacological mechanism.[9]

Next is one of the compounds contained in the fruit *D. zibethinus* is polyphenols. The high content of phenolates and flavonoids in *D. zibethinus* extract can be a potential source of antioxidants. *D. zibethinus* extract has the best antioxidant activity levels against DPPH with $IC_{50}$ 11.21 μg/ml compared to ascorbic acid standard which shows inhibition of 50% at a concentration of 6.56 μg/ml due to the high phenolic and flavonoid content in ethanol extract of *D. zibethinus* fruit makes it possible to donate electrons such as hydroxyl groups to reactive species to form non-radical DPPH-H forms in homogeneous systems, so that the fruit *D. zibethinus* has the potential as an antioxidant.[27]

In other studies, *D. zibethinus* fruit contains amylase enzyme that serves to digest starch. Amylase is thought to be actively involved in the digestive process (DzAmy3) which has activity against escherichia coli bacteria that are present in the intestine.[12] *D. zibethinus* also has an anti-inflammatory effect containing caffeic acid and quercetin. Caffeic acid has anti-inflammatory activity by lowering the secretion of interleukin 8, 1β, 6 and TNF-alpha by epithelial cells that have been activated by LPS. In addition, in topical treatment, it can suppress 12-O-tetradecanoyl-phorbol- 13-acetate (TPA) which induces inflammation of the skin by reducing the activity of myeloperoxidase in thickening of the skin. Then other active compounds such as quercetin also have the same activity, this has been proven by experimental research in mice who are on a diet then given 60 mg/kgBW of *D. zibethinus* extract for days can reduce inflammation in the liver of injured mice. In other studies, at doses of 10 μg quercetin can reduce the formation of TNF-α, NO, IL-6, and IL-8 induced ochratoxin A.[13] Furthermore, *D. zibethinus* fruit has a neuroprotective effect because at a concentration of 100 μg, *D. zibethinus* fruit is able to inhibit the acetyl cholinesterase function. This is because *D. zibethinus* prevents or reduces anti-beta aggregation, can inhibit Aβ aggregation by means of ThT fluorescence tests.[14]

In addition to being rich in health benefits, *D. zibethinus* fruit can provide harmful effects to the body when consumed excessively because it can increase body temperature. In addition, durian fruit consumed in conjunction with antipyretic drugs such as paracetamol can increase toxicity, due to the mechanism of work of paracetamol that inhibits the third cyclooxygenase enzyme in the brain that causes a decrease in body temperature, while durian fruit affects the hypothalamus which is the body thermostat so as to increase body temperature.[35] According to Manoharan, *D. zibethinus* fruit extract in polysaccharide gel preparations tested against mice with a dose of 2 g/kgBW mice did not see any toxicity to test animals.[36]

## CONCLUSION

Currently the interest in herbal medicine that has been through clinical trials in accordance with the bioactive content of pharmacological is increasing. *D. zibethinus* is a plant that is incompetricable from the content of various compounds that have efficacy as a medicine. The latest information about the efficacious *D. zibethinus* can serve as the basis for conducting extensive studies for the discovery of new compound poten and further research for its pharmacological content. Therefore, further research can be done on *D. zibethinus* to explore complete therapeutic activities.

## CONFLICT OF INTEREST

No conflict of interest to declare.

## ABBREVIATIONS

**MIC**: minimum inhibitory concentration; **DPPH:** 2,2 Diphenyl 1 picrylhydrazyl; **$IC_{50}$:** median inhibitory concentration; **LPS:** lipopolisaccharide; **IL:** interleukin; **DNA:** deoxyribonucleic acid; **TNF:** tumor necrosis factor; **TPA:** 12-O-tetradecanoyl-phorbol- 13-acetate; **NO:** nitric oxide; **ThT:** thioflavin T.

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