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Insights of phytoconstituents and pharmacology activities of Salacca plants

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ABSTRACT

In the last 20 years, plant-based therapy had become the world's attention. Our country Indonesia is popular in its megabiodiversity, among which is *Salacca zalacca* Gaert. (Voss.), or *salak*. The fruit of this plant is generally utilized as pickles, chips, etc. However, its benefits for health remain unexplored. Library searches using PubMed, Google Scholar, Science Direct, and Google resulted that *S. zalacca,* which contains flavonoids, alkaloids, terpenoids, and sitosterols exerts various pharmacology activities, e.g., antioxidant, cholesterol reducer, antidiabetic, skin whitening, antihyperuricemia, antibacterial, immune system enhancer, cancer cell growth inhibitor, and adsorbent.

INTRODUCTION

Treatment of diseases using natural ingredients begins to be popular and furthermore, becomes the world's attention. World Health Organization (WHO) states that 65% of treatment is carried out by people in developed and developing countries using natural materials (Republik Indonesia, 2007). It was estimated that 25% of medicinal products were made of empirically used plants (WHO, 2013).

Indonesia is a country which is abundant in plant biodiversity as supported by its tropical geographic conditions (located between two continents and two oceans). Salak [*Salacca zalacca* Gaert. (Voss.)] is a native plant whose fruit is the most favorable and generally utilized as dried fruit, pickles, chips, canned fruit in syrup, etc., (Zaini *et al*., 2013). Some mixtures for medicine in Indonesia consist of salacca fruit, seeds, and bark (Joshua and Sinuraya, 2019). Salacca fruit is often called snake fruit because of its dry and flaky peels which resemble snake skin (Aralas et al., 2009).

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However, its benefits for health remain questionable; therefore, this review article will give insights into the botanical aspects, phytochemicals, and pharmacological activities of *S. zalacca* Gaert. (Voss.).

METHODS

This review is based on the literature obtained from the Google Scholar database using the keywords "Salacca" AND "Snake Fruit" AND "Antioxidant"; PubMed using keywords salacca [All Fields] AND ("antioxidants" [Pharmacological Action] OR "antioxidants" [MeSH Terms] OR "antioxidants" [All Fields] OR "antioxidant" [All Fields]) AND activities [All Fields]; Science Direct using keywords "Salacca" AND "Snake fruit" AND "Antioxidant" AND "Toxicity". The following exclusion criteria were applied: articles <2,000 and unrelated article. The flowchart of the literature search can be seen in Figure 1.

BOTANICAL ASPECTS

Origin and botanical classification

Salacca is a species of the palm tree (Arecaceae) native to Java and Sumatra in Indonesia. It contains dietary fiber and carbohydrates that are good for the body (Chareoansiri *et al*.,

2009). The taxonomy of salacca plants is (Cronquist, 1981) as follows:

Kingdom	: Plantae
Division	: Spermatophyta
Subdivision	: Angiospermae
Class	: Monocotyledoneae
Order	: Palmae
Family	: Palmaceae or Arecaceae
Genus	: Salacca
Species	: *Salacca zalacca* (Gaert.) Voss.
Synonym	: *Salacca edulis* Reinw.

Parts of the salacca plants can be seen in Figure 2 (Naharudin, 2019).

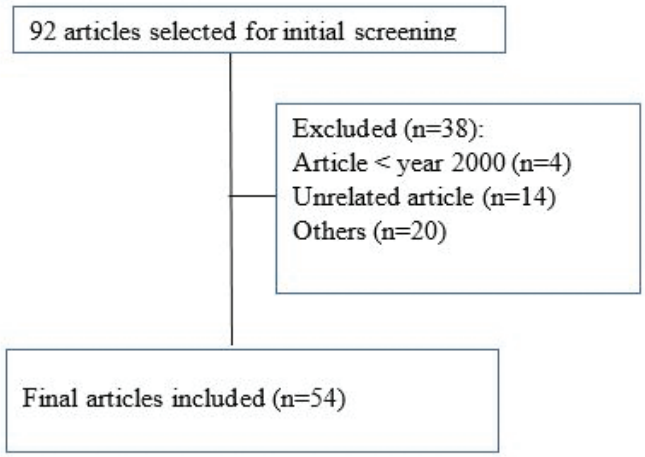

Figure 1. Flow chart of the reference search.

Morphology and structure

Salacca plant grows with thorns and its height can reach 6 m. This plant can be productive for 50 years. They grow at low altitudes and high humidity. The trunk is large and pinnate with shiny dark green leaves. The fruit, oval in shape, assembled in groups at the base of the tree. The seed is dark brown segmented in the fruit (Zaini *et al*., 2013). Raw fruit, which has a sharp, bitter taste due to its tannic acid content, is usually prepared for pickles. However, the ripe fruit is sweet and has a pleasant aroma (Horn *et al*., 2009).

NUTRITIONAL CONTENTS

Salacca fruit, like other exotic fruits, contains vitamins, minerals, fiber, and sugar which are needed for daily needs in overcoming various types of diseases (Dembitsky *et al*., 2011). The proximate analysis of 100 g of zalacca resulted in sucrose (7.6%), fructose (5.9%), fructose (3.9%), total sugar (17.4%), soluble dietary fiber (0.3%), insoluble dietary fiber (1.4%), water (80%), calories (77 kcal), protein (0.7%), ash (0.6%), and fat (0.1%). The contents of vitamins and minerals in 1 kg of the salacca fruit are ascorbic acid (400 mg), carotene (5 mg), thiamine (20 mg), niacin (240 mg), riboflavin (0.8 mg) and folate (6 mg), phosphorus (1.161 mg), potassium (11.339 mg), calcium (220 mg), magnesium (607 mg), sodium (231 mg), iron (12.0 mg), manganese (10.4 mg), copper (3.36 mg), zinc (10.4 mg), boron (5.07 mg), and sulfur (5.07 mg) (Chew *et al*., 2012; Gorinstein *et al*., 2009; Janick and Paull, 2008).

Phytoconstituents

NMR study of the dichloromethane extract of *Salacca wallichiana* Mart. revealed the presence of monogalactosyl diacylglycerols, β-sitosteryl-3β-glucopyranoside-6¢-O-ester fatty acid, β-cytosterol, and triacylglycerol in the fruit peels, whereas in

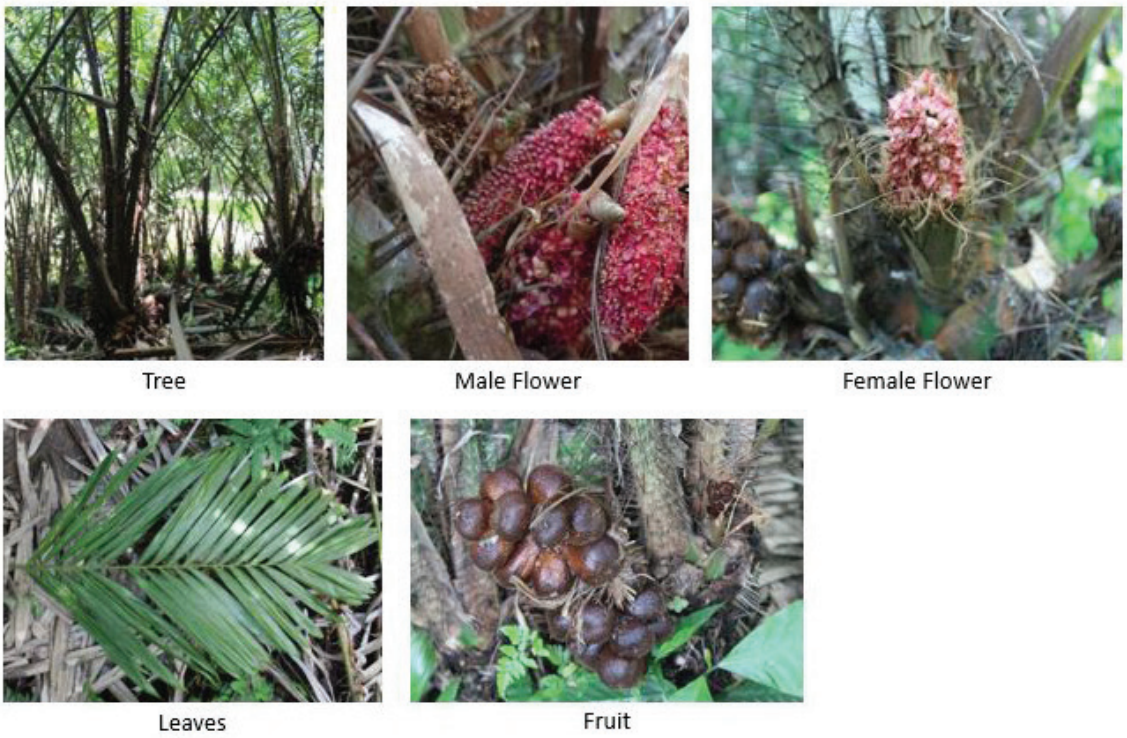

Figure 2. Parts of salacca plants.

the roots, several compounds, e.g., β-sitosterol and stigmasterol, had been reported. Moreover, β-cytosteryl-3β-glucopyranoside-6¢-O-ester fatty acids, triacylglycerol, and linoleic acid had been isolated from the seeds (Ragasa *et al*., 2016; Suica-Bunghez et al., 2016). Polyphenolic compounds and vitamin C were also reported to be significantly abundant in salacca fruit (Gorinstein *et al*., 2011).

The pleasant aroma of salacca fruit is generated by the combination of several phytochemicals; however, methyl esters of pentanoic acid (e.g., 3-methylpentanoate, methyl-3-methylpentanoate, methyl-3-methyl-2-pentanoate) and butanoic acid (e.g., methyl-3-methyl-2-butanoate and 2-methylbutanoate) are considered responsible for this characteristic odor. Other aromatic compounds, e.g., 2,5-dimethyl-4-hydroxy-3[2]-furanone, methyl dihydrojasmonate, and isoeugenol might also contribute to the overall aroma of salacca fruit (Wijaya *et al*., 2005). These methyl esters of carboxylic acids are also responsible for the sweet aroma of other salacca species, e.g., *Salacca edulis* Reinw Cv (Supriyadi *et al*., 2002). Moreover, 2-methylester-1-h-pyrolle-4-carboxylic acid compound has reported its presence in the ethylacetate extract of salacca var. bongkok as well as flavonoids, alkaloids, tannins, terpenoids, and quinones (Afrianti *et al*., 2015). Epicatechin, proanthocyanidine, and chlorogenic acid were detected in the fruit extract by high-performance liquid chromatography (Shui, 2005). Compounds elucidated from salacca fruit is summarized in Table 1.

PHARMACOLOGY ACTIVITIES

Antioxidant

Salacca fruit extract was reported possessing a high antioxidant activity by scavenging DPPH free radical and/or reducing ferric ion in plasma (Afrianti *et al*., 2010; Aralas, 2009; Gorinstein *et al*., 2009; Kanlayavattanakul *et al*., 2013; Suica-Bunghez *et al*., 2016; Zubaidah *et al*., 2017), and reducing ABTS (2,2-azinobis (3-ethylbenzothiazoline-6-sulfonic acid). Furthermore, other study indicated that the ethanol extract and fractions of salacca fruit contained phenols, flavonoids, and tannins. The strongest antioxidant activity was shown by 100% methanol fraction (IC_{50} = 110.16 µg/ml) (Werdyani *et al*., 2017). Salacca seed might be potential to be proposed as a local competitive coffee product due to its antioxidant activity (IC_{50} = 9.37 mg/ml). It has low caffeine (0.207%), low fat (2.95%), high carbohydrates (80.98%), water (6.24%), ash (3.49%), and protein (6.34%). However, the ethyl acetate fraction of *S. edulis* peels indicated the most potent antioxidant property ($DPPH_{IC50}$ = 2.932 ± 0.030 g/ml, $ABTS_{IC50}$ = 7.933 ± 0.049 g/ml, and $FRAP_{EC}$ = 7844.44 ± 40.734) (Dikta, 2015).

The 100% ethanol extract of salacca was reported containing higher phenolic level (116.70 ± 0.764 µg/ml) and antioxidant activity (IC_{50} = 49.45 ± 3.87 µg/ml) compared to the 60% ethanol extract (Misra *et al*., 2018). High phenolic compounds in salacca fruit were also reported by other workers (Leontowicz *et al*., 2006). Other salacca cultivars, e.g., Nglumut, Bali, and Sumalee, also contained high phenolic compounds and vitamin C. Reducing the power of salacca Nglumut cultivar is significantly higher than that of Balinese or Pondoh cultivars (Gorinstein *et al*., 2009).

Table 1. Phytoconstituent of Salacca fruit.

Part of plants	Compounds	References
Fruit pulp	3β-hydroxy-cytosterol	Priyatno et al., 2007
	2-methylester-1-H-pyrrole-4-carboxylic acid	
Fruit pulp	Anthocyanin	Gorinstein et al., 2011
	Polyphenols	
	Tannin	
	Flavanols	
	Flavonoids	
Fruit pulp	Alkaloid	Afrianti et al., 2015
	3-hydroxystigmastan-5(6)-en	
	Terpenoid	
	Pyrolle-2,4-dicarboxylic acid-methyl ester	
	Quinones	
Fruit pulp	β-cytosterone	Ragasa et al., 2016
	β-cytosteryl-3β-glucopyranoside-6'-O-fatty acid ester	
	Triacylglycerols female flower	
	β-cytosterol roots	
	Linoleic acid	
	Stigmasterol	
	Monogalactosyl diacylglycerols	
Peel	Quercetin	Kanlayavattanakul et al., 2012
	Chlorogenic acid	
	Gallic acid	
	Ferulic acid	
	Caffeic acid	
	Rosmarinic acid	

Cholesterol-lowering activity

In vivo assay of salacca fruit and/or peel extract indicated a cholesterol-lowering activity (Dhaneswari *et al*., 2015; Leontowicz *et al*., 2006; Nuranti *et al*., 2014). Flavonoids are compounds that play an important role in reducing cholesterol levels in the blood by decreasing HMG-CoA enzyme activity and increasing cholesterol activity 7-α hydroxylase (Honda et al., 2013).

Heart histopathologic of white rats treated with *Salacca edulis* extract indicated less fat infiltration compared to that of the control group (Hardjana et al., 2016).

Antidiabetic activity

Salacca fruit peel extract, which contains alkaloids, flavonoids, saponins, steroids and triterpenoids, phenolic hydroquinone, tannins, and cinnamic acid, indicated antidiabetic activity (Sahputra, 2008). Ferulic acid and proline found in the salacca fruit peel could stimulate the formation of collagen and elastin, while cinnamic acid derivates increase cell regeneration, and arginine stimulates cell division as well as increases protein biosynthesis. Moreover, pterostilbene could lower blood sugar level (Rohaeti *et al*., 2017).

All salacca vinegars were capable of reducing blood sugar (from 25.1% to 62%) and low density lipoprotein (from 9.5 to 14.8

mg/dl), triglyceride (from 58.3 to 69.5 mg/dl), malondialdehyde (from 1.1 to 2.2 mg/dl), and total cholesterol (from 56.3 to 70.5mg/dl) as well as increasing high density lipoprotein on streptozotocin (STZ)-induced diabetic Wistar rats (from 52.3 to 60 mg/dl). Various salacca vinegars were also capable of regenerating pancreatic cells. Nevertheless, the ability of Swaru salacca vinegar to manage hyperglycemia and dyslipidemia appeared to be superior to other salacca vinegars. Swaru salacca vinegar is a potential therapeutic agent to manage hyperglycemia and dyslipidemia on STZ-induced diabetic rats (Zubaidah *et al*., 2014; 2017).

Antimicrobe

Extract of *Salacca edulis*, which contains tannins, flavonoids, and alkaloids, has inhibited the growth of *E. coli*. The highest inhibition zone was obtained at a concentration of 100% (average diameter 18.783 mm), although, it was smaller than that of positive control (average diameter 31.367 mm) (Nurina *et al*., 2014).

Immunostimulants

Salacca peel extract showed high stimulation of the immune system. It enhanced the phagocytotic activity of murine macrophage-like J774.1 cell. Production of cytokine such as tumor necrosis factor (TNF)-alpha and interleukin (IL)-6 was also stimulated (Wijanarti et al., 2016; 2017).

Antihyperusemic activity

Two compounds isolated from salacca fruit, i.e., 3 β-hydroxy-sitosterol and 2-methylester-1-H-pyrrole-4-carboxylic acid indicated good inhibitory activity against xanthine oxidase (IC_{50} 48.86 µg/ml) (Lasekan and Abbas, 2012). The ethanol extract of salacca fruit also significantly decreased serum uric acid levels compared to the control group (Priyatno *et al*., 2012).

Anticancer and cytotoxic activity

Salacca fruit has been proven in exhibiting the growth of human Hepoma (HepG2), human colon cancer (HT-29), human lung cancer (A549), and human breast cancer (MCF-7) (Li *et al*., 2013). Moreover, pyrolle-2,4-dicarboxylic acid-methyl ester and 3-hydroxystigmastan-5(6)-en (β-sitosterol) isolated from *S. edulis* fruit showed cytotoxic activity against MCF-7 and T47D cell lines (Gorinstein *et al*., 2011). Brine shrimp lethality test of the liquid smoke of salacca seed showed toxicity towards *Artemia salina* Leach larvae (LC_{50} = 23.44 ppm) (Wagania *et al*., 2018).

Additionally, salacca fruit extract demonstrated cytotoxicity against Vero cells and normal human fibroblast cell line that was correlated with its antioxidant capacity (Kanlayavattanakul *et al*., 2013).

CONCLUSION AND FUTURE PERSPECTIVES

Salacca fruit, which is cultivated and consumed in tropical countries, has been reported as a good source of antioxidant compounds. Salacca contains flavonoids, alkaloids, tannins, terpenoids, sitosterols, carboxylic acids, and its methyl esters, and quinones. Salacca exhibits antioxidant activity and could reduce blood cholesterol level. It has also potential as antidiabetic, antihyperuricemia, antibacterial, enhances the immune system, and inhibits the growth of cancer cells. This tropical fruit needs further exploration, particularly the mechanism of its biological activity, to be proposed as a nutritional beverage.

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CONFLICT OF INTEREST

The authors declared that they have no conflict of interest.

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