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# Salacca zalacca: A short review of the palm botany, pharmacological uses and phytochemistry

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#### ABSTRACT

Salacca zalacca (Gaertn.) Voss (family Arecaceae) is the snake fruit commonly known in Malay language as salak in Malaysia. This exotic fruit has diverse and potential pharmacological properties due to its high antioxidant content. It is often consumed due to its sweet taste. The abundant natural sugar and fibre along with minerals and vitamin makes it a nutritious fruit. Phytochemical investigation on this fruit has revealed the presence of flavonoids, phenolics, glycosides as well as some volatile and aromatic compounds, including gallic acid, quercetin, chlorogenic acid, epicatechin, proanthocyanidins, lycopene and  $\beta$ -carotene. Pharmacological studies on the fruit flesh and peel have shown some tremendous antioxidant, anti-inflammatory, anticancer and antidiabetic potential. This review provides the botanical information of Salacca zalacca as well as its scientific investigations involving the distinct pharmacological and phytochemical benefits. This could help in highlighting the lacking data and research gaps on this plant.

# 1. Introduction

# 1.1. Origin and botanical classification

The Arecaceae (syn. Palmae) is one of the leading families of

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Angiosperms, and comprises of flowering plants. The family consists of about 187 genera that are collectively known as palm species and about 2 522 species (theplantlist.org). The plant of this family can be found in tropical countries and are abundant in South East Asian countries like Indonesia, Malaysia, and Thailand.

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Different species that exist in this family are ecologically and economically important. They are the major cultivated crops that contribute in various industries including food, pharmaceutical, and cosmeceutical. Some crops in this family include the oil-palm (*Elaeis guineensis*), coconut (*Cocos nucifera*), pinang (*Areca catechu*), date-palm (*Phoenix dactylifera*) and salak [*Salacca zalacca* (*S. zalacca*)][1]. S. zalacca (Gaertn.) Voss has different synonyms which include Calamus zalacca Gaertn., Salacca rumphii Wall., Salacca edulis (S.

S. zalacca (Gaertn.) Voss has different synonyms which include Calamus zalacca Gaertn., Salacca rumphii Wall., Salacca edulis (S. sedulis) Reinw., Salacca blumeana Mart., Calamus salakka Willd., S. sedulis var. amboinensis Becca and S. zalacca var.

S. zalacca or locally known as salak in Malay language, is one of the common plant species in palm or Arecaceae family. Salak has various names. It is called 'pondoh' in Indonesia, 'rakam' in Thailand, 'sa laka' or 'she pi guo zong' in China, and 'yingan' in Myanmar[2]. Salacca wallichianna C. Martins is another related species of salak which is comparably shorter and compact with edible fruit[2].

Being native to South Sumatra and Southwest Java, it is widely distributed around Southeast Asian countries, including Malaysia, Thailand, and Myanmar in abundance. The fruit has also been introduced to countries of other regions including New Guinea, Philippines, Queensland and northern Territory of Australia, Ponape Island (Caroline Archipelago), China, Surinam, Spain, and Fiji. The fruit of salak palm is known as the snake fruit due to its scaly skin[3]. It is the most common variety of Salacca cultivated in Malaysia, which is widely distributed around the Borneo Island and east coast region[3]. This snake fruit has been the local's favourite for its honey-like taste. It is famous among the east coast civilians whereby they grow the salak tree to harvest its fruit and in fact it provides income to some of the families in this region.

Salak is a good source of carbohydrate and dietary fibre[4]. The fruit pulp has been reported to possess high antioxidant capacity as compared to other exotic fruits[3]. The pulps of salak fruit are mainly consumed either freshly or as juice. They are also processed into dried fruits, pickles, chips, canned in syrup as well as added as an ingredient in local food called rojak[5]. Besides, the seed kernels of young fruits of pondoh (Indonesian salak) are edible. Apart from the fruit, the salak palm bark of the petioles is also used for matting, while the leaflets are used for thatching[6].

# 1.2. Morphology and structure

Salak species are indigenous throughout Indonesia and Malaysia and are one of the fruit producers. The salak grows as extremely spiny palm with some of the variants that are almost stemless and short. This plant could grow up to 6 m height and expected to be productive for an average of 50 years. They are usually grown in low land with high humidity[5].

The leaves are about 10 m long, large, and pinnate with shiny and

dark green long petioles with spine and leaflets. The fruit bore by this palm grows in bunches at the base of tree. It is oval or spindle shaped with approximately 6 cm long with pale-yellow sweet pulp covered with elongated end and snake-like reddish brown scales that brings about the name of snake fruit. The pulps are yellowish-white and are segmented with a hard-brown seed inside[5]. The unripe pulps are sour and have sharp taste due to the presence of tannic acid. However, the ripe pulps are crunchy soft with sweet taste added to a distinct and pleasant aroma. The unripe pulps are usually made into pickles, while the ripe pulp is eaten raw[6-9].

#### 2. Nutritional contents

Fruits and vegetables are edible substances from the nature that brings goodness to human health. It is due to their nutritional contents that majorly provide biologically active constituents with distinct medicinal purposes. Fruits are comprised of various vitamins, minerals, fibres, and sugars that are required in daily servings. These nutrients are important to hinder different type of diseases. Most exotic fruits provide multiple proportions of those nutrients. To our concern, salak contains various phytoconstituents and nutrients in abundance, comparably with other local fruits[10]. The proximate analysis of salak fruit is sucrose (7.6 g/100 g), fructose (5.9 g/100 g), fructose (3.9 g/100 g), total sugar (17.4 g/100 g), soluble dietary fibre (0.3 g/100 g), insoluble dietary fibre (1.4 g/100 g), total dietary fibre (1.7 g/100 g), water (80 g/100 g) and fat (0.1 g/100 g)

The fruit of salak is a source of natural sugars and dietary fibre. Besides, salak pulp is reported to contain minerals and vitamins in abundance. The mineral content and vitamins that can be found in *Salacca*, that was previously measured phosphorous (1 161 mg/kg), potassium (11.339 mg/kg), calcium (220 mg/kg), magnesium (607 mg/kg), sodium (231 mg/kg), iron (12.0 mg/kg), manganese (10.4 mg/kg), copper (3.36 mg/kg), zinc (10.4 mg/kg), boron (5.07 mg/kg), sulfur (5.07 mg/kg), ascorbic acid (400 mg/kg), carotene (5 mg/kg), thiamine (20 mg/kg), niacin (240 mg/kg), riboflavin (0.8 mg/kg) and folate (6 mg/kg)[2,11,12].

### 3. Phytochemical contents

The *Salacca* cultivars have been studied for their phytochemical constituents using various techniques. Wong and Tie reported on the volatile compounds present in the pulp of *S. sedulis* Reinw. The identification of about 46 compounds were detected comprising of mostly carboxylic acids (15.9%), alcohols (1.3%), aldehydes (0.8%), ketones (0.7%), sulphur-containing compounds (0.2%), and aromatic hydrocarbons (0.3%). Specifically, the most prominent compounds

viz., methyl 3-hydroxy-3-methylpentanone and methyl (E)-3-methylpenta-2-enoate were found to be about 25.0% and 23.4%, respectively.

The growth, maturation, and harvesting age of a fruit plant is crucial in determining its phytochemical contents. Upon maturation, the composition of various compounds in the plant and its parts may be varied[7]. Likewise, the sugar and volatile compounds content in snake fruit were reported to change drastically. Salak have been reported that the sugars (glucose, fructose, and sucrose) levels were at the optimum levels towards the end of maturation period[13]. Some of the major volatile compounds that were identified in solvent-assisted flavour evaporation and solvent extracts were the methyl esters of carboxylic acids which include the butanoic acid, 2-methylbutanoic acid, hexanoic acid and pentanoic acid. The methyl esters were measurably increased during the maturation process initiated after about 5 to 6 months after pollination. Another minor aromatic compound identified in the solvent-assisted flavour evaporation extract was furaneol or 4-hydroxy-2,5-dimethyl-3(2H)furanone[13].

A subsequent study was carried out by the same group of researchers, where the volatile compounds of *S. sedulis* were identified using electronic nose device equipped with a sensor array and mass spectrometry fingerprinting. About 10 compounds were identified which include six methyl esters, two carboxylic acids, an alcohol, and furaneol with the most distinctive odour namely 2,5-dimethyl-4-4-hydroxy-3(2H)-furanone. A similar compound was also reported by the same group[14].

Apart from that, another study was conducted on *Salacca endulis* pulp to quantify the lycopene and  $\beta$ -carotene levels using chromatographic technique. Carotenoids are the precursor of vitamin A that play an important role as the antioxidant in quenching oxygen radical, anti-inflammatory agent, immunity regulatory process, and cancer prevention<sup>[15]</sup>. An investigation revealed that the salak pulp juice contains 1 130 and 2 997 µg in 100 g of sample of lycopene and  $\beta$ -carotene, respectively. The same study also measured the vitamin A activity which was expressed as µg of retinol equivalent in 100 g of the fruit. The result showed a significantly high content of the observed vitamin with 500 µg of retinol equivalent per 100 g, compared to other local fruits that were analysed along with other fruits including guava, mango, watermelon, papaya, sawo, jackfruit, kedondong, and orange. This indicates the potential of salak fruit as a rich antioxidant source<sup>[15]</sup>.

In another study, a new technique was applied in an effort to identify antioxidants present in salak. In this study, high performance liquid chromatography technique paired with mass spectrometry was used for the elucidation of compounds structure. Some of the bioactive constituents identified and elucidated for the first time in salak fruit were chlorogenic acid, (-)-epicatechin, and proanthocyanidins[16].

In the same year, compounds responsible for the characteristic aroma of three different cultivars of snake fruits (pondoh hitam, pondoh super, and gading) were analyzed through gas chromatography-mass spectrometry and GC-olfactometry using the nasal impact frequency. Twenty-four compounds strongly associated with the distinct snake fruit aroma were identified. A methyl ester namely methyl 3-methylpentanoate was found responsible for the authentic snake fruit odour. Apart from that, the compounds that cause a sweaty flavour were identified as 2-methylbutanoic and 3-methylpentanoic acids. Other compounds identified include methyl 3-methylbutenoate that occurs in over ripen fruit, methyl 3-methyl-2-pentanoate with woody smell, and 2,5-dimethyl-4-hydroxy-3[2]-furanone that gives the caramelised odour[16]. The new volatile compounds identified in snake fruit were methyl dihydrojasmonate and isoeugenol which have considerable odour impact on the fruit[17]. This study isolated a sterol (3β-hydroxy-sitosterol) and carboxylic acid (2-methylester-1-H-pyrrole-4-carboxylic acid) from the ethyl acetate extract of the snake fruit[18].

Other study conducted analysis on the bioactive compounds in salak fruit. The vitamin C and polyphenol content were found to be significantly high as compared to mangosteen fruit (*Garcinia mangostana*) with 13.28 mg ascorbic acid equivalent (AAE) and 8.46 mg gallic acid equivalent (GAE) per gram fruits, respectively. Along with this, flavonoids, anthocyanins, tannins, and  $\beta$ -carotene content were also measured to be 0.31 mg catechin equivalent (CE), 3.14 µg CE, 9.74 mg cyanidin-3-glucoside equivalent, 6.48 mg CE, and 1.17 µg per gram fruit, respectively[19].

In a comparative analysis using salak fruit and mangosteen fruit, the content of dietary fibres, mineral, and trace metals were measured. The polyphenols content of salak (217.1 mg of GAE) was higher than that of mangosteen (190.3 mg of GAE) while the flavonoids content reported were 61.2 mg and 54.1 mg CE per 100 g fruit, respectively. Meanwhile, the trace elements analysis showed the level of sodium (1.9 mg), potassium (191.2 mg), manganese (2.5 mg), and zinc (0.3 mg) per 100 g of fruit, which were significantly higher in salak fruit than mangosteen. Apart from the fruit of salak, the juice of the ripe aril of Salacca was investigated for its total phenolic and vitamin C. The amount measured was 176.0  $\mu$ g GAE and 98.28  $\mu$ g AAE per gram sample[20].

Meanwhile the two isolated compounds obtained from the Indonesian cultivar of *S. sedulis* of Bongkok variant were studied. The compounds were purified from ethyl acetate fraction and identified as 3-hydroxystigmastan-5(6)-en that belongs to the β-sitosterol group (white crystal) and pyrolle-2,4-dicarboxylic acidmethyl ester (orange solid- amorphous). Besides, the same variant of snake fruit was also reported to contain several phytoconstituents in abundance including the terpenoids, flavonoids, tannins, alkaloids, and quinones. However, saponins were not detected during the phytochemical screening[21].

Another species of *Salacca* that was investigated for its bioactive compounds was the *Salacca wallichiana* Mart. The fruit flesh, female flower, root, and seeds were used to obtain dichloromethane extracts from which the bioactive compounds were isolated. Compounds isolated from the fruit flesh include the monogalactosyl diacylglycerols,  $\beta$ -sitosteryl-3 $\beta$ -glucopyranoside-6'- $\theta$ -fatty acid esters,  $\beta$ -sitosterol, and triacylglycerols. The  $\beta$ -sitosterol and  $\beta$ -sitosterone were obtained from the female flower extract, a mixture of  $\beta$ -sitosterol and stigmasterol was isolated from the root, and  $\beta$ -sitosteryl-3 $\beta$ -glucopyranoside-6'- $\theta$ -fatty acid esters, triacylglycerols, and linoleic acid were isolated from the seeds[22].

The spectroscopy instrumental analysis of the salak fruit flesh and shell using UV-VIS and FT-IR showed the peak absorbance at the wavelengths that correspond to phenolic acids and their derivatives (flavonols, flavones, phenylpropenes, quinones), flavonoids, quinines, coumarins, polysaccharides, and protein<sup>[23]</sup>. Evidently, the salak fruit is rich with various bioactive compounds that may benefit to human health by means of its natural sugar, minerals, vitamins, and antioxidants contents. All reported compounds identified and/or elucidated from the salak fruit are tabulated in Table 1.

#### 4. Pharmacological uses

#### 4.1. Antioxidant potential of salak

The human body is comprised of a complex system undergoing various cellular activity or metabolism that produces free radicals, such as reactive oxygen and nitrogen species. These radicals involve in the pathogenesis of certain oxidative stress that are closely related to the diseases like neurological degenerative and cardiovascular diseases, carcinogenesis, rheumatoid arthritis, and ulcerative colitis[27]. Sufficient intake of dietary antioxidants is important to combat the free radical activity in the body. Plants provide a variety of antioxidants that may benefit human health. There are various analytical methods that can effectively be used to analyse the antioxidants potential of these plant sources[27].

Various *in vitro* scientific studies have been carried out to investigate the antioxidant capacity of salak, especially in the fruit flesh. Antioxidant effect of salak fruit through 2,2'-azinobis-(3-ethylbenzothiazoline-6-sulfonic acid) (ABTS•+) assay in which it exhibited about 260 mg ascorbic acid equivalent antioxidant capacity (AEAC) and 2.4 mg ascorbic acid per 100 g sample through HPLC quantification. The same study reported the DPPH scavenging activity with >250 AEAC (mg/100 g). The correlation between the assays was ascertain to be good with high activity as compared to other local fruits investigated along[23].

Table 1
Phytoconstituents content in salak fruit.

- I nytoconstituents content in salak irut.		
Compound(s)	Plant part(s)	References
Methyl 3-hydroxy-3-methylpentanone	Ripe fruit	[7]
Methyl (E)-3-methylpenta-2-enoate		
Sugars: Glucose, Fructose, Sucrose	Ripe fruit	[13]
Butanoic acid		
2-Methylbutanoic acid		
Hexanoic acid		
Pentanoic acid		
4-Hydroxy-2,5-dimethyl-3(2H)- furanone		
Methyl 3-methylbutanoate	Fruits (from	[14]
Methyl 3-methylpentanoate	different stages	[24]
Methyl 2-methyl-2-butenoate	of maturity)	. ,
2-Methylbutanol		
Methyl hexanoate		
Methyl 3-methyl-2-pentenoate		
2-Methylbutanoic acid		
3-Methylpentanoic acid		
Methyl 3-hydroxy-3-methylpentanoate		
Furaneol		
Methyl 4-hydroxy-3-methyl-2-pentenoate		
Acetic acid		
	Pulp juice	[15]
Lycopene  B. Carotene	r urp Juice	[15]
β-Carotene	Davit anda	[19]
Chlorogenic acid	Fruit pulp	[23]
(-)-Epicatechin		
Proanthocyanidins  Method dilectories assessed to	Emile 1	[17]
Methyl dihydrojasmonate	Fruit pulp	[17]
Isoeugenol	P. 1.	F1.03
3β-Hydroxy-sitosterol	Fruit pulp	[18]
2-Methylester-1-H-pyrrole-4-carboxylic acid		54.03
Polyphenols	Fruit pulp	[19]
Flavonoids		
Flavanols		
Anthocyanin		
Tannin		
3-Hydroxystigmastan-5(6)-en	Fruit pulp	[21]
Pyrolle-2,4-dicarboxylic acid-methyl ester		
Terpenoid		
Alkaloid		
Quinones		
p-Cresol	Fruit pulp	[5]
Catechol		
4-Methyl catechol		
Chlorogenic acid		
Caffeic acid		
Epicatechin		
I-DOPA		
Gallic acid		
	Fruit pulp	[22]
Monogalactosyl diacylglycerols  8 Sitosteryl 38 glycopyraposide 6' O fotty	Fruit pulp	[22]
β-Sitosteryl-3β-glucopyranoside-6'- <i>O</i> -fatty acid Esters	Seeus	
β-Sitosterol	Roots	
Triacylglycerols	Female flower	
β-Sitosterone	- c.i.mic ilowel	
Stigmasterol		
Linoleic acid		
Gallic acid	Peel	[25]
Caffeic acid	r cci	[25]
Ferulic acid		
Chlorogenic acid		
Quercetin		
Rosmarinic acid	-	FA 63
Xanthophyll	Fruit	[26]
Zeaxanthin		

In vivo study was carried out which characterised the snake fruit for its polyphenols content (14.9 mg GAE/g) and antioxidant potential [72.9 μmol trolox equivalent (TE)/g]. Its effect on plasma lipid and antioxidant activity in hypercholesteraemic rats was investigated. After approximately 4 weeks of diet supplemented with snake fruit, a significant reduction in plasma lipid and increase in antioxidant activity were observed. Some of the parameter observed include the fibrinogen fraction (solubility and mobility of the protein bands in SDS electrophoresis). It was concluded that the snake fruit contains bioactive compounds with positive effect on hypercholesteraemic rats[39].

A comparative study on the antioxidant assay was performed using DPPH and ABTS between the snake and mangosteen fruits. The snake fruit showed significantly higher activity than mangosteen with the DPPH and ABTS activities of 110.4 and 2 016.3  $\mu$ g TE/g, respectively. Other *Salacca* sp. that was studied and reported includes the *Salacca conferta* (assam kelubi) which grows in swamp areas. The phenolic content measured was 1 455.29 mg GAE per 100 g of the edible portion, while the antioxidant capacity was measured based on the  $\beta$ -carotene bleaching assay as 84.68% $\pm$ 8.69%[28].

The investigation on salak fruit juice using its ripe aril showed a remarkable antioxidant activity with the initial screening of total phenolic content of 175.99 µg GAE and 98.28 µg AAE of vitamin C per g sample, respectively. Meanwhile, the DPPH and FRAP activities were observed as 421.56 µg vitamin C equivalent antioxidant capacity per gram and 1 556.79 µg TE antioxidant capacity per g sample, respectively[18]. This is followed by a study where the salak core (fruit flesh) and shell were analysed for their antioxidant activity using the DPPH scavenging activity and total flavonoid content. The core and shell hydro-alcoholic extracts were found to be active in the DPPH assay at 82.67 and 73.13%, respectively[18].

The antioxidant capacity of four different varieties of this species available in Sabah were investigated and compared. Their study reported that the total flavonoid content of the four varieties ranged from 4.9-7.1 mg CE/g of dry sample, while the total phenolic content was of 12.6-15.0 mg GAE per g dry sample, both in dry basis. Meanwhile, the DPPH scavenging activity was expressed as ascorbic AEAC and FRAP as µM ferric reduction to ferrous in 1 g sample, in dry basis, respectively. The DPPH activity was measured to be between 691.5-922.5 AEAC mg per 100 g sample, while the FRAP value was between 113.3-91.6 µM FeSO<sub>4</sub>/g. Conclusively, their results displayed a very good antioxidant activity of the *Salacca* varieties although slight variations were observed among different varieties[3].

Antioxidants are also strongly related to skin whitening and lightening agents. Ascorbic acid is one of the potential compounds that has been reported to have skin whitening effect. However,

due to its toxic effect in excessive amount, the usage of it has been limited[29]. Therefore, the naturally occurring compounds especially the antioxidants from the plant source have been extensively evaluated in recent times. Majorly, the anti-tyrosinase compounds which are effective in lightening the skin colour. Commonly, the polyphenols and flavonoids are known to be the best tyrosinase inhibitors[29]. Snake fruits are known to possess high antioxidants as compared to apple and grapes[3]. In a randomised double-blinded, the skin lightening cream was prepared and optimised with 3% of the *Salacca* ethanolic extract. The skin melanin index showed a significant reduction comparably better than the base cream used in the study. The finding showed that the *Salacca* fruit extract can be used as the potential material in the preparation of skin whitening cream in cosmeceutical industry[29].

Apart from the pulp, the peel of salak fruit has been reported to possess various polyphenols that are responsible for its antioxidant activity. Evaluated the ethyl acetate extract of the *S. sedulis* peel on DPPH (IC<sub>50</sub>: 2.93 μg/mL), ABTS (IC<sub>50</sub>: 7.93 μg/mL), and FRAP (EC: 7844.44) activities. The result showed the potential good antioxidant capacity of the peel[25].

#### 4.2. Antidiabetic potential of Salacca zalaaca

Along with hyperglycaemia condition, dyslipidaemia is also another common feature related to diabetes mellitus (DM) type 2. Dyslipidaemia is a common metabolic abnormality of body fat. In the case of DM, the glucose is unable to provide energy. Thus, the lipolysis will actively provide energy to the DM patients where the breakdown of fat leads to the uncontrolled elevated level of free fatty acids, cholesterol, and triglycerides that increase the risk of cardiovascular diseases[30]. Therefore, it is crucial to control lipid level among DM patients. With this respect, an *in vivo* study was carried out to understand the role of snake fruit in the management of dyslipidaemia. The results of the study revealed that the diet supplemented with 5% snake fruit improves the plasma lipid level of the rats fed with high cholesterol diet[31].

Another variant of *Salacca* was investigated for its effect on the lipid profile in diabetic subjects induced with streptozotocin (STZ). Vinegar was prepared using *Salacca* fruit and the STZ-induced rats were treated with it. The study concluded that the high content of polyphenols in the vinegar has significant effect on the lipid profile as well as the blood glucose level in the STZ-induced diabetic rats. Conclusively, the blood glucose level was found to decrease upon treatment with about 0.4 and 0.7 cubic centimetres of the *Salacca* vinegar. Besides, the LDL, triglycerides, and cholesterol levels were effectively decreased while the HDL was increased after the treatment[30]. This indicates the effectiveness of the *Salacca* fruit on the observed condition.

Vinegar prepared from fruits of different variants of *Salacca* further showed significant results with improved lipid profile and controlled glucose level along with potential capability of the Swaru *Salacca* vinegar to regenerate damaged pancreatic cells in the STZ-induced rats. Vinegar produced using the snake fruit showed effective action in regulating the blood glucose level thus reducing the glycaemic index in the treated diabetic subjects. The antioxidants and acetic acid present in the vinegar exhibited the antidiabetic potential of the snake fruit vinegar through regenerating the pancreatic beta cells and regulating the lipid profile[32].

The antidiabetic potential of salak fruit was also assessed through in vitro assays using  $\alpha$ -glucosidase (digestive enzyme). As a matter of fact,  $\alpha$ -glucosidase breaks down starch and disaccharides to glucose. Hence, an inhibitor of the digestive enzymes is of therapeutic interest in type 2 diabetes, since it helps to slow down the release of glucose from oligosaccharides, thereby lowers post-prandial levels of glucose in diabetic patients. In this regard, the flesh of salak fruit was extracted using six different ratios of ethanol-water (100%, 80%, 60%, 40%, 20% and 0%) and their inhibitory effect against  $\alpha$ -glucosidase was ascertained. The results showed that 100% and 60% had the lowest IC<sub>50</sub> values viz., 15.94 µg/mL and 19.15 µg/mL, respectively against  $\alpha$ -glucosidase. While, the water extract showed the lowest activity with IC<sub>50</sub> at 271.46 µg/mL[33].

#### 4.3. Antihyperuricemic potential of salak

Studies have indicated the capacity of salak fruit in stabilising the elevated uric acid level thus managing the gout inflammation. Xanthine oxidase is the enzyme that is responsible for the breakdown pathway of purine bases thus generates the reactive oxygen. In the form of xanthine oxidoreductase, it catalyses the oxidation of hypoxanthine to xanthine that subsequently produces uric acid. Excess production of uric acid leads to the formation of uric acid crystals which are accumulated in the joints, thereby causing the inflammation and intense pain of a gout attack[24,34]. The two compounds isolated in snake fruit namely  $3\beta$ -hydroxy-sitosterol and 2-methylester-I-H-pyrrole-4-carboxylic acid were tested for their xanthine oxidase inhibition activity to alleviate the symptoms associated with gout. The first compound was regarded inactive and the latter exhibited a good activity with the IC<sub>50</sub> value 48.86 µg/ mL[24].

The *in vivo* investigation of antihyperuricemic effect of salak fruit ethanol extract showed significant reduction in the serum uric acid level as compared to control group upon administration at 200 mg/kg body weight, after induction using potassium oxonate intraperitoneally and oral uric acid simultaneously. The urine uric acid level was also determined which showed significant increase in the urine uric acid excretion as compared to the control group, however it was found lower than the control drug (probenecid)

used. This suggests that the mechanism of action of salak fruit's ethanol extract as an anti-hyperuricemia agent is via the inhibition of xanthine oxidase activity[35].

#### 4.4. Anticancer potential of S. zalacca

Cancer is one of the major leading causes of mortality and morbidity globally. Despite the advancement in the medical field and treatments, significant deficiencies can still be observed which require more improvement. Chemotherapy remains the routine therapy for the treatment of cancer, however, the unavoidable deleterious side effects associated with the chemotherapy during the treatment process still remain great challenge to overcome cancers. Alternative treatments to reduce the cancer cells are still relied upon the plant sources. Plants have been reported to possess enormous potential to provide effective anticancer action. Likewise, the salak fruit has been found to exhibit an anticancer effect against human lung cancer (A549), human hepatoma (HepG2), human colon cancer (HT-29), and human breast cancer (MCF-7) cell lines. The antiproliferative effect of salak pulp, peel, and seed extracts were significant on all cell lines[36].

The two compounds isolated from the *Salacca* fruit (*S. sedulis*) were pyrolle-2,4-dicarboxylic acid-methyl ester and 3-hydroxystigmastan-5(6)-en ( $\beta$ -sitosterol). The first compound was discovered to possess cytotoxic activity against MCF-7 and T47D (breast cancer stem) cell lines. The latter was then investigated for the similar anticancer effect, whereby the cytotoxicity assay revealed that 3-hydroxystigmastan-5(6)-en ( $\beta$ -sitosterol) inhibited the proliferation and viability of MCF-7 and T47D cell lines with an IC<sub>50</sub> value of 45.414 0 and 1.194 2 µg/mL, respectively[19].

#### 4.5. Cytotoxicity study

The salak fruit extract has been analysed for its cytotoxicity level against Vero cells and normal human fibroblast (NHF) cell line correlated to its antioxidant capacity. The Vero cells showed non-cytotoxic effect at 50 μg/mL concentration. Meanwhile, the cytotoxicity of salak fruit extract in NHF cell line was based on the biosynthesis of collagen and elastin, fibres in NHF cells function in the elasticity and firming. These fibres production and degradation are influenced by the collagenase and elastase which can be altered by free radicals. However, the salak plum ethyl acetate extract which showed viability of more than 75% at the concentration between 5-40 μg/mL was observed to be effectively reduce the oxidant (H<sub>2</sub>O<sub>2</sub>-mediates the NHF cell death) content. This indicates the cellular antioxidant potential of the salak fruit extract that was effectively measured by the reduction in the content of observed oxidant which was considered the main reason for cell apoptosis and necrosis[25].

#### 4.6. Other uses

Plant parts can be used for other purposes in different industries in addition to their medicinal effects. Likewise, the salak fruit has been reported to be used in the food industry to isolate yeast meant for bread leavening agent. It relatively showed better quality than the commercial baker's yeast by means of desired leavening ability and colour development of the bread crust and crumb[37].

The salak fruit is also used in the making of fruit tea with combination of other local fruits (pineapple and longan) and hed krang (Schizophyllum commune) as the main ingredient. The composition of high antioxidants has driven this product development which is then optimised. The optimum formula of desired fruit tea contains the ratio of pineapple, salak, and longan of 20:20:60, respectively, added with 20% (w/w) of hed krang. Upon analysis of the chemical, physical, and microbiological properties as well as the sensory evaluation, the product seems to have great potential of acceptance by consumers and could be a power packed healthy drink[38].

#### 5. Conclusion

Salak (S. zalacca) fruit have been cultivated in various countries for its fruits that are consumed for nutritious content as well as for its sweet taste and distinct flavour. It has also been commercialised in local and international markets thus vastly contributes to economic value. Despite its taste, the fruit has also been reported to be a good source of antioxidant with potential bioactive compounds as well as natural sugar. This review has presented a comprehensive information on the nutritional and phytochemical contents with the pharmacological uses of the snake fruit. However, the investigation on the mode of action is still lacking, thus critical further studies are required to fulfil this gap and also to validate other traditional uses of the salak (S. zalacca) along with the isolation techniques shall provide more details on the bioactive compounds that are yet to be discovered in this plant of high medicinal value.

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#### **Conflict of interest statement**

The authors declare no conflict of interest.

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