Medicinal properties of Pitaya: a review

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ABSTRACT
Pitaya (also known as dragon fruit) is a nutritional fruit that consumed widely in many countries nowadays. It is oval in shape and the peel appears as scaly structure. The flesh of the fruit is juicy and sweet with numerous small and edible black seeds. Three species of pitaya are commonly consumed, namely Hylocereus polyrhizus, H. undatus and H. megalanthus. The 3 species are distinguished based on their shape, size and color of their flesh. H. polyrhizus or red pitaya comes with red peel and flesh, H. undatus (commonly known as white pitaya) has red peel and white flesh while H. megalanthus (yellow pitaya) contains yellow peel with white flesh. The nutritional values and medicinal properties of the fruits have been reported recently. Thus, this review summarizes their medicinal properties particularly on antioxidant, anti-cancer, hypocholesterolemic, prebiotic and anti-microbial effects.

Keywords: Anti-cancer; Anti-microbial; Antioxidant; Hypocholesterolemic; Pitaya; Prebiotic.

ÖZET

Anahtar kelimeler: Anti-kanser; Anti-mikrobiyel; Antioxidan; Hipokolesterolomik; Pitaya; Prebiyotik.

INTRODUCTION

Pitaya, which is also known as dragon fruit in English or ‘Buah Naga’ in Malay is classified under the Cactaceae family with the genus name of Hylocereus [1-3]. It has recently gathered much interest due to its attractive appearance and taste, as well as nutritional contents [4, 5]. Pitaya is oval in shape with scaly structure on its outer peel [2, 6]. The flesh of the fruit is juicy and sweet with numerous small and edible black seeds. There are three species of pitaya that have been commercialized, namely Hylocereus polyrhizus, Hylocereus undatus and Hylocereus megalanthus [2, 7-9]. Different Hylocereus species are distinguished based on their shape, size and color of their flesh [3].

H. polyrhizus or red pitaya comes with red peel and flesh, and it comprises plenty of soft and edible seeds [10]. The weight of this species ranges from 130 to 350 g with the length of 10 to 12 cm [3]. H. polyrhizus is believed to be indigenous from Costa Rica [3, 7], and it is largely cultivated in Southeast Asia currently [4]. The compositions of the edible flesh include large amount of moisture content (82.5-83.0 g), followed by crude fibers (0.7-0.9 g), fats (0.21-0.619 g), proteins (0.159-0.229 g) and vitamin C (8-9 mg/L) [1, 3, 7]. Besides, the sugar contents of H. polyrhizus varies in quantity, from glucose (41.9-64.9 mg/g), fructose (32.3-49.9 mg/g) to sucrose (4.2-6.8 mg/g) [7]. In addition, minerals such as phosphorus, calcium, potassium and iron [1, 11], as well as vitamin B1, B2 and B3 [1] are found in H. polyrhizus. The deep red color of the peel and flesh...
are contributed by a nitrogen-containing pigment known as betalains, or specifically the red betacyanins [4, 5, 7, 12, 13]. Betacyanin is commercially used as natural food coloring [14]. Recently, its antioxidant properties has been discovered to protect against certain oxidative stress-related diseases [2, 4, 7, 15]. Besides, polyphenol contents in H. polyrhizus are also highly valued for their antioxidant properties [7, 15, 16]. Studies also revealed that H. polyrhizus seeds oil contains functional fatty acids such as linoleic acid that is beneficial to human health [7, 11].

The second type of pitaya is the H. undatus, or commonly known as white pitaya owing to its white flesh [3, 8]. H. undatus is generally larger than H. polyrhizus, and it weighs 300 to 800 g, with 15 to 22 cm long. H. undatus is originate from southern part of Mexico and it is now widely introduced in Asia countries such as Taiwan, Malaysia and Vietnam as well as northern Australia [8]. The contents of H. undatus are similar to the H. polyrhizus. It contains large amount of moisture content (85.30%), protein (1.10 g), fats (0.57 g) and fiber (11.34 g). Besides, vitamin C and minerals such as calcium phosphorus, magnesium and sodium are present in this species. H. undatus has higher sugar content compared to the H. polyrhizus. The glucose, fructose and sucrose present in the fruit were about 64.3-104.3, 40.1-64.9 and 5.4-7.5 mg/g, respectively [8]. H. undatus showed to possess antioxidant properties that aid in scavenging free radicals [8], and this is essential in promoting health benefits.

H. megalanthus, or the yellow pitaya consists of yellow skin with white flesh [3, 9], is a plant that is native to Colombia and Peru. It is occasionally being exported to Europe countries and Canada [9]. Recent research suggested that H. megalanthus was the hybridization product of Hylocereus costaricensis and Selenicereus inermis, which are closely related to each other [17]. The medicinal properties reported for this species are very minimal, but it is discovered that its edible seeds contain the largest amount of polyunsaturated fatty acids (PUFA) compared to the H. polyrhizus and H. undatus [18].

A number of studies have reported the health benefits of peel, flesh and edible seeds of pitaya. Hence, this review summarizes a few medicinal properties of pitaya such as antioxidant, anticancer, hypcholesterolemic, antibacterial properties and its prebiotic effects.

**MEDICINAL PROPERTIES OF PITAYA**

**Antioxidant property**

Reactive oxygen species (ROS) for instance hydroxyl radicals, superoxide anion and hydrogen peroxide are known to cause damage to the vital molecules in the body such as DNA, leading to cell death and tissue injuries [12, 19-21]. Therefore, antioxidants such as polyphenols, tocopherols and flavonoids play a vital role in inhibiting or delaying the oxidation of the cellular constituents [5, 19, 20, 22].

High total phenolic content (TPC) in the fruit is usually correlated with high radical scavenging activity [23-25]. Previous studies showed that polyphenols are the main antioxidant compounds in Hylocereus species. These compounds terminated radical chain by acting as a reducing agent that donates electrons to the free radicals [19, 22, 24]. Besides, their singlet oxygen quencher properties and metal chelating ability make them a good antioxidant [13, 24]. On the other hand, betacyanins and flavonoids such as kaempferol, quercetin andisorhamnetin that possessed radical scavenging and metal chelating property [13, 24] are also found in the flesh of H. undatus [26].

Peel and flesh of Hylocereus species were proposed to have different antioxidant capacities [19]. In a research where the peel and flesh of H. polyrhizus and H. undatus were extracted using 70% ethanol, it was found that H. undatus peel showed the highest 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical scavenging activity of 87.02±2.24% at the concentration of 1.0 mg/mL, followed by H. polyrhizus peel (83.48±1.02%). H. polyrhizus flesh showed lower radical scavenging activity of 27.45±5.03% and H. undatus flesh had the least scavenging activity (16.56±2.96%). The DPPH radical scavenging ability of the samples tested was closely correlated with their TPC. As such, H. undatus peel showed to possess the highest TPC (36.12 mg of gallic acid equivalents (GAE) /100g), followed by H. polyrhizus peel (28.16 mg of GAE/100g), H. polyrhizus flesh (19.72 mg of GAE/100g) and lastly H. undatus flesh (3.75 mg of GAE/100g) [19]. These showed that high TPC leads to a stronger antioxidant activity.

Generally the peel of the pitaya was found to have greater antioxidative capacity as compared to the flesh. This might be due to the presence of different bioactive compounds in the peel and flesh. Previous study showed that polyphenolic compounds were found in both the peel and flesh [27] but flavonoids were present mostly in the peel. On the other hand, non-flavonoid compounds were found abundant in the flesh [19, 22, 28]. These may suggest that the variation in flavonoid content in the different fruit parts caused the difference in the antioxidant activities. The flesh of H. polyrhizus was found to have greater TPC as compared to H. undatus [5, 19,
This is because *H. polyrhizus* with red flesh contained more phenolic compounds and betacyanin, therefore contributed to the higher antioxidant activity. In contrast, *H. undatus* with white flesh contained the non-betains compounds, therefore the TPC was relatively lower than the *H. polyrhizus* [19, 29].

Besides DPPH radical scavenging activity, the antioxidant effect of pitaya was evaluated by metal ion chelating assay. The chelating effects ranged from 18.00 to 36.06% at 0.2 mg/mL of the extracts tested, with the peel of *H. undatus* showed the greatest chelating effects [19]. However, these chelating effects were considered as rather weak. Hence, the antioxidant compounds in *Hylocereus* species were good in radical scavenging activity but not the metal chelating ability.

Solvent used in the extraction process might affect the antioxidant activity of a sample. In a study conducted by Wu et al. [22], the bioactive compounds of peel and flesh of *H. polyrhizus* were extracted by 80% acetone. Results showed that TPC of the peel and flesh were 39.7±5.39 and 42.4±0.04 mg of GAE/100g, respectively; these results were not correlated with the previous studies [19]. The higher TPC detected in the study might be partially attributed to the presence of betacyanin, which also contributed to the total phenolics. Betacyanin contents were 13.8±0.85 and 10.3±0.22 mg of betanin equivalents/100g in the peel and flesh of *H. polyrhizus*, respectively. Moreover, Chavan and Amarowicz [30] showed that acetone-water system extracted considerably higher amounts of phenolic compounds from beach pea than the ethanol-water systems, suggesting acetone might be able to extract more phenolic compounds in pitaya than ethanol; and this might contribute to the high TPC in the acetone-extracted samples. The TPC of samples detected in the study was correlated with their antioxidant abilities. From the DPPH radical scavenging assay, half maximal effective concentrations (EC$_{50}$) of peel and flesh were determined as 11.8±4.12 and 22.4±0.29 μmol vitamin C equivalent/g dried extract, respectively. The results indicated better antioxidant property of peel extract than the flesh due to its slightly higher polyphenolic content. Another antioxidant assay, the 2,2′-azinobis-3-ethylbenzothiazoline-6-sulfonic acid (ABTS) radical scavenging assay also showed that the peel extract was a better antioxidant compared to flesh [22].

Sub-fractionation method provided higher values of polyphenolic contents and hence the technique was applied to the extracts from red pitaya peel and flesh [5]. The fractionated peel and flesh extracts showed greater DPPH radical scavenging activity (805.1±1.2 and 999.8±1.4 μmol trolox equivalents (TE)/100 g fresh weight, respectively) compared to the non-fractionated samples, which were only 95.2±1.2 and 166.4±1.1 μmol TE/100g fresh weight, respectively. Among the fractions tested, fractions contained betacyanins showed the greater DPPH radical scavenging activity. The TPC in the peel (645.6 mg±1.0/100 g fresh weight) was found approximately 10 times higher than the flesh (78.1 mg±1.4/100 g fresh weight) in these betacyanin-containing fractions. Hence, the reducing capacity of the peel fraction was higher as determined by ferric reducing antioxidant power (FRAP) test [5]. All in all, *H. polyrhizus* exhibited greater antioxidant effects when the active compounds were sub-fractionated, as compared to the conventional non-fractionated method. This is because sub-fractionation of compounds reduced the number of phytochemical classes in a single fraction and thus minimizing potential interferences during the test.

The antioxidant property of pitaya was comparable to a few commonly consumed fruits. A research was performed to compare the radical scavenging activity of 95% ethanol peel extract of *H. undatus* with seven types of fruits that can be easily found, namely Panica granatum (pomegranate), *Nephelium lappaceum* (rambutan), *Garcinta mangostana* (mangosteen), *Musa sapientum* (banana), *Cocos mucifera* (coconut), *Passiflora foetida* (passion fruit) and *Lansium domesticum* (long-gong). It was found that the half maximal inhibitory concentration (IC$_{50}$) for radical scavenging activity of *H. undatus* (0.084±0.016 mg/mL) was higher than pomegranate, rambutan, mangosteen, banana and coconut, in which their IC$_{50}$ were ranged from 0.003±0.002 to 0.047±0.005 mg/mL. However, passion fruit (0.104±0.014 mg/mL) and long-gong (1.290±0.001 mg/mL) showed weaker radical scavenging activity as compared to *H. undatus* [31].

In short, *Hylocereus* species possess promising antioxidant properties which provides health benefits to human. However, the antioxidant contents vary when different extraction methods are used. The geographical area that the fruit is cultivated may also cause the different antioxidant activity [2].

**Anticancer Property**

The anticancer properties of *Hylocereus* species were recently studied. Several evidences showed that polyphenols, flavonoids and betains that present in the *Hylocereus* species are responsible for the anticancer effects [22, 32, 33]. *H. undatus* peel extracted by ethanol-water (50:50, v/v) solvent system showed anti-proliferative activity towards human hepatocellular carcinoma cell line (HepG2) in a dose-
dependent manner and it recorded an IC\textsubscript{50} at 21.81±0.01 mg/mL after 48 hours of incubation. Polyphenols were believed to be the main phytochemical compound for such effect, although the exact compound was yet to be identified [32]. The polyphenols acted through scavenging nitric oxide (NO) free radicals [34] that promoted tumor vascularization and metastasis. Compounds that inhibited NO might be considered as potential anti-cancer agents. On the other hand, the presence of C2-C3 double bond and three adjacent hydroxyl groups in the flavonoids was suggested to be crucial for anti-cancer effects [35]. Betacyanins that have similar molecular structure as flavonoids were proposed to have the similar anti-cancer effects [22].

The <i>H. undatus</i> extract also exerted anti-cancer effects on other cells. Significant decrease in cell viability was noted when human breast cancer cells (MCF-7) were pre-treated with various concentrations (0-600 µg/mL) of <i>H. undatus</i> ethanolic flesh extract. To be more specific, <i>H. undatus</i> extract inhibited MCF-7 cell growth by approximately 85% at 600 µg/mL [33]. Another <i>in vitro</i> anti-proliferative study on melanoma cell (B16F10) suggested that the peel and flesh of <i>H. polyrhizus</i> that extracted with 80% acetone inhibited the cancer cell growth in a dose-dependent manner. The peel extract showed stronger effect, in which the EC\textsubscript{50} was recorded as 10.00 µg of GAE, while the EC\textsubscript{50} value was not detected in the flesh extract. These results suggest that the higher TPC in peel might contribute to the anticancer effects [19, 22].

The peel of <i>H. polyrhizus</i> and <i>H. undatus</i> prepared via supercritical carbon dioxide extraction demonstrated good cytotoxic effects against human prostate cancer (PC3), human breast cancer (Bcap-37) and human gastric cancer (MGC-803) cell lines in a dose-dependent manner. <i>H. polyrhizus</i> showed lowest IC\textsubscript{50} value of 0.43 mg/mL in MGC-803, whereas <i>H. undatus</i> demonstrated lowest IC\textsubscript{50} (0.47 mg/mL) in Bcap-37 cell line [23]. A few bioactive compounds were found in these extract. These include β-amyrin that was previously found to promote cytotoxic effects against several cancer cell lines [36-38], β-sitosterol and stigmas-4-en-3-one. β-Ammyrin was found in the peel extract of both <i>Hylocereus</i> species while β-sitosterol and stigmast-4-en-3-one were found in the <i>H. polyrhizus</i> peel extract. The β-sitosterol and stigmast-4-en-3-one inhibited the growth of MGC-803 cells at IC\textsubscript{50} of 43.8±0.63 and 56.9±0.81 µM, respectively. The present findings concluded that the bioactive compounds that contributed to the anticancer effects were β-amyrin, β-sitosterol and stigmast-4-en-3-one, in which β-sitosterol exhibited the greatest effects [23].

The exact anticancer mechanism exerted by <i>Hylocereus</i> species is still unknown. However, previous researches reported that the anti-cancer effects of polyphenol might be mediated through suppression of nuclear factor-kB and growth factor receptor-mediated pathway; cell cycle arrest and apoptosis induction; inhibition of angiogenesis and mitogen-activated protein kinases; as well as antioxidant and anti-inflammatory mechanisms [24, 32, 39-41].

**Hypocholesterolemic Effect**

Polyphenol contents in <i>H. polyrhizus</i> flesh were proven to be able to reduce cholesterol level in the body [11, 25]. Generally, ROS or free radicals in the body interact with lipid leading to the formation of lipid peroxidase. The lipid peroxidase in turn causes the oxidation of low-density lipoprotein (LDL) that interacts with platelet to develop into foam cells. Formation of foam cells increases the rate of atherosclerosis [24, 25, 42]. Polyphenols were found to be able to aid in the prevention of lipid peroxidation and LDL oxidation; hence reducing the risk of cardiac-related diseases [6, 24, 25, 42]. Polyphenols also possessed anti-thrombotic effects which further enhanced its cardio-protective properties [24].

Previous research showed that feeding of diluted freeze-dried <i>H. polyrhizus</i> flesh for 5 weeks in hypercholesterolemic rats reduced total cholesterol, triglyceride as well as LDL levels and increased high-density lipoprotein (HDL). Reduction in total cholesterol was found the highest in the rats fed with 1.17% of pitaya (from 3.448 to 1.412 mmol/L), followed by 0.83% of pitaya (from 3.435 to 1.487 mmol/L) and lastly 0.5% of pitaya (from 3.356 to 1.707 mmol/L). Rats fed with 1.17% pitaya showed significant reduction in triglyceride and LDL levels by 59.52% and 39.06%, respectively. On the other hand, increment in HDL level was found to be ranged from 19.31% to 34.42% [11].

Another <i>in vivo</i> study demonstrated the relationship between polyphenol and other antioxidant contents of <i>H. polyrhizus</i> with dyslipidemia in hypercholesterolemic rats. Pitaya flesh was heated at 95°C for 30 minutes (Pit95) and 105°C for 60 minutes (Pit105). The hypercholesterolemic rats were fed with fresh or the thermal-processed samples. It was demonstrated that the TPC and radical scavenging activity were significantly reduced and the ability to regulate lipid profile was dropped when the <i>H. polyrhizus</i> extracts were exposed to heat. In this study, decrease in LDL and total cholesterol levels were only seen in rats fed with fresh flesh extract. Interestingly, the triglyceride level was the same for...
the rats treated with fresh or thermal-processed flesh. Although the decline in total cholesterol and LDL levels were not significant in both Pit95 and Pit105 groups, it was discovered that Pit95 showed greater hypocholesterolemic effects compared to Pit105. Overall, the results corroborated the idea that the efficiency of cardioprotective effect of *H. polyrhizus* is associated with its antioxidant properties. The serum lipid level shown an overall decrease when the radical scavenging strength and polyphenol contents were reduced [15, 25].

PUFA, particularly linoleic acids make up the essential fatty acids that are required but not synthesized by the human body [43]. Numerous researches have proven that consumption of these essential fatty acids is able to counter the increase of cholesterol, specifically the LDL level. Consumption of PUFA also reduces the risk of cardiac-related diseases, especially when it acts as a substitution for saturated fatty acids [43-50].

Research has been carried out to investigate the composition of fatty acids in *H. polyrhizus* seeds and results showed that 50.8±0.53% of seeds oil consisted of PUFA, in which the linoleic acid (49.6±0.33%) comprised the largest proportion, followed by minute amount of linolenic acid (1.2±0.20%). A total of 25.6±0.88% of monounsaturated fatty acids (MUFA) that contained mostly oleic acid (21.6±0.53), *cis*-vaccenic acid (3.14±0.30%) and palmitoleic acid (0.91±0.05%) were also detected in the seed oil. Besides, 23.6±1.41% of saturated fatty acids (SFA) was discovered and it was dominated by palmitic acid (17.9±0.53%). Composition of fatty acids in *H. undatus* was also being studied, and the results suggested higher PUFA (51.1±0.45%), higher MUFA (27.2±0.25%) and lower SFA (21.7±1.03%) in *H. undatus* [51]. These observation were in line with other studies, in which the ratio of fatty acids content in pitaya shown in this study was found to be similar with the other studies [45, 52, 53].

Another study was conducted to compare the fatty acids composition in *H. polyrhizus*, *H. undatus* and *H. megalanthus* seed oil. The results showed that the PUFA composition is the highest in *H. megalanthus*, followed by *H. undatus* and *H. polyrhizus*. The MUFA content was higher than SFA in *H. polyrhizus* and *H. undatus*. The fatty acid content was found the lowest in *H. megalanthus* [18]. The composition of fatty acids in different *Hylocereus* species was shown in Table 1.

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<th>Fatty acids</th>
<th>Composition of fatty acids (%)</th>
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<tr>
<td></td>
<td><em>H. polyrhizus</em></td>
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<tr>
<td>SFA</td>
<td>50.8±0.53</td>
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<tr>
<td>Palmitic acid</td>
<td>15.9±1.37</td>
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<tr>
<td>Stearic acid</td>
<td>4.6±0.47</td>
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<tr>
<td>Arachidic acid</td>
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<tr>
<td>Behenic acid</td>
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<tr>
<td><strong>Total</strong></td>
<td><strong>50.8±0.53</strong></td>
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SFA, saturated fatty acids; MUFA, monounsaturated fatty acids; PUFA, polyunsaturated fatty acids

**Table 1.** Composition of fatty acids in different *Hylocereus* species

**Prebiotic Effect**

Prebiotics are non-digestible oligosaccharides that are beneficially affect the host by stimulating the growth of normal flora in the colon [54]. Several studies showed that prebiotics provide protective effects against colon cancer and reduce the tendency of inflammation-associated bowel diseases. Growth of microflora in the colon for instance lactobacilli and bifidobacteria prevents the invasion of pathogenic bacteria into the gastrointestinal tract, hence promoting healthy digestive system [55].

The mixed oligosaccharides content in the *H. undatus* ethanolic flesh extract was detected as approximately 85%. These oligosaccharides had higher resistance towards the human salivary *α*-amylase compared to inulin. The maximum hydrolysis of the samples in *α*-amylase of increasing pH (4, 5, 6, 7 and 8) were 2.90, 3.08, 3.28, 6.8% and 11.18%, respectively; while the maximum hydrolysis of inulin were 5.72, 8.03, 7.39, 12.32 and 16.22%, respectively. The oligosaccharides also showed higher resistance to the hydrolysis by the artificial human gastric juice. Approximately 50% of the consumed pitaya mixed oligosaccharides would reach the colon despite the hydrolysis by salivary *α*-amylase (16%), stomach acids (2.5%) and other brush-border enzyme in the small intestine (30%) [56].

The mixed oligosaccharides in pitaya also promoted the growth of good bacteria such as *Lactobacillus delbrueckii* and *Bifidobacterium bifidum*. The microbial count of ethanolic flesh extract was detected as cell/mL, respectively when...
using extracts obtained from *H. undatus* as carbon sources [56].

**Antimicrobial Property**

The antibacterial activity of ethanol, chloroform and hexane extracts from *H. polyrhizus* and *H. undatus* peel was studied. From the disc diffusion assay results, both of the *Hylocereus* species exhibited inhibition zone of about 7 to 9 mm against Gram-positive (*Staphylococcus aureus*, *Bacillus cereus*, *Listeria monocytogenes*, and *Enterococcus faecalis*) and Gram-negative (*Escherichia coli*, *Salmonella typhimurium*, *Yersinia enterocolitica* and *Klebsiella pneumoniae*) bacteria. Result of the minimum inhibitory concentration showed that all extracts inhibited the growth of bacteria in the range of 1.25-10.00 mg/mL [57].

Interestingly, *Camphylobacter jejuni* was found resistant towards all the extracts tested except for *H. undatus* chloroform extract. *C. jejuni* is a highly pathogenic bacteria with the cell wall composed of lipopolysaccharides that are broken down to secrete enterotoxins [58]. It is readily penetrating the gastrointestinal mucus [59] and causing the onset of gastroenteritis [60]. As such, chloroform extract of *H. undatus* that was able to inhibit the growth of the bacteria showing a great potential as an antimicrobial agent. Overall, chloroform extract of both *H. polyrhizus* and *H. undatus* peel showed the most potent antibacterial activity [57].

**CONCLUSION**

Pitaya is a promising source of alternative medicine that might serve as antioxidant, anticancer, hypcholesteroleric, antimicrobial as well as prebiotic agent. However, further studies on identification, purification and quantification of bioactive compounds from pitaya are necessary; and determination of its mechanism of action should be conducted to gain a better view on the fruit’s medicinal properties. The antioxidant property of pitaya was well elucidated but information on other medicinal properties was limited. For example, the anticancer properties of the fruit were only explored in a few types of cancer. Therefore, further studies on other cancer cell lines could be performed. In addition, most of the current reports focused on the two types of pitaya: *H. polyrhizus* and *H. undatus*. Reports on *H. megalanthus*’s medicinal properties were scarce, thus further works on this fruit would provide more information on the benefits of consuming pitaya.

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Medicinal properties of pitaya