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Dragon fruit: A review of health benefits and nutrients and its sustainable development under climate changes in Vietnam

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Abstract: Dragon fruit or pitaya is an exotic tropical plant that brings multiple benefits to human health thanks to its high nutritional value and bioactive compounds, including powerful natural antioxidants. Extracts from stems, flowers, peels, pulps of dragon fruit own a range of beneficial biological activities against pathogenic microbes including bacteria, fungi and viruses, and diseases like diabetes, obesity, hyperlipidaemia, and cancer. Moreover, dragon fruit extracts have cardiovascular and hepatoprotective properties, as well as prebiotic potential. Vietnam is a tropical country with favourable climate conditions for the development of pitaya plantations, which have great adaptability and tolerance to a wide range of environmental conditions (e.g. salinity adaptation, favour light intensity, drought resistance, etc.). The dragon fruit, thanks to its nutritional properties, biological activities, and commercial value has become a cost-effective product for the Vietnamese economy, particularly in the poorest areas of the Mekong Delta region, and a driving force in the sustainable development of Vietnam under the challenges posed by the global climate change such as saline intrusion and drought.

Keywords: pitaya; tropical fruit; nutrition; medicinal value; Mekong Delta; antioxidant

Dragon fruit or pitaya is the fruit of several different tropical climbing plants of the genus *Hylocereus*, family Cactaceae. Although the pitaya is native to the tropical areas of North, Central and South America, it is now cultivated worldwide due to its commercial interest, not demanding cultivation requirements, i.e. high drought tolerance, easy adaptation to light intensity and high temperature, a wide range of tolerance to different soil salinities, and benefits to human health (Nobel and La Barrera 2004; Nie et al. 2015; Crane et al. 2017; Mercado-Silva 2018). It is commercially cultivated in over 20 tropical and subtropical countries such as Bahamas, Bermuda, Indonesia, Colombia, Israel, the Philippines, Myanmar, Malaysia, Mexico, Nicaragua, northern Australia, Okinawa (Japan), Sri Lanka, southern China, southern Florida, Taiwan, Thailand, Vietnam, Bangladesh, and the West Indies (Mercado-Silva 2018).

Pitaya is an exotic fruit due to its shape and very attractive colours of flesh and skin e.g., red flesh with pink skin (*Hylocereus polyrhizus*; Britton and Rose 1920), white flesh with pink skin (*Hylocereus undatus*; Britton 1918) or red-purple flesh with red skin (*Hylocereus costaricensis*; Britton and Rose 1909) or yellow skin and white flesh [*Selenicereus megalanthus* (K. Schum. ex Vaupel) Moran 1953 *(synonym Hylocereus megalanthus*)] (Ortiz-Hernández and Carrillo-Salazar 2012; Muniz et al. 2019). However, the results of genetic analyses showed that *S. megalanthus* is tetraploid, whereas species of *Hylocereus* are diploid. The species is thereby considered a natural hybrid between *Hylocereus* and *Selenicereus,* and maybe it belongs to a distinct genus

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(Tel-Zur et al. 2004). The genus *Hylocereus* belongs to the family Cactaceae and includes numerous distinct species (Morton 1987), but only two of them, *H. polyrhizus* and *H. undatus*, are commonly grown in Vietnam. The exact origin of dragon fruit is unknown, but the plant is probably native to Mexico, Central America, and northern South America (Britton and Rose 1920; Morton 1987; Blancke 2016). Dragon fruit is a long day and perennial plant; one planting can harvest fruit in around 20 years (Jiang et al. 2012; Crane et al. 2017). The tree also produces fruits throughout the year thanks to off-season production technology like artificially lengthening daytime through electric lighting (Jiang et al. 2012; Jiang et al. 2016).

Dragon fruit was introduced to Vietnam by the French over a hundred years ago (Mizrahi et al. 1997). It is known as Thanh Long (Green Dragon) because the most common types of fruits are oval shaped with bright, red skin with green foliaceous bracts/scales resembling the skin of a dragon (Figure 1). This fruit has become the most profitable crop for Vietnamese farmers. Vietnam has the largest area of pitaya cultivation in Asia and it is grown in 63/65 cities/provinces of the country (Hoat et al. 2018; Hien 2019). Vietnam is the main exporter of dragon fruit worldwide due to high global demand (Ratnala Thulaja and Abd Rahman 2017).

A high proportion of the population and economic assets of Vietnam are located in coastal lowlands, deltas and rural areas, which explains why Vietnam has been ranked among the five countries likely to be most affected by climate change (World Bank Group 2020). Particularly, climate changes impact agricultural production due to the increase of saltwater intrusion and lack of irrigation water in the dry season. Moreover, droughts have become a recurrent problem in the Mekong River Delta, already threatened by the increased saline intrusion in the dry season, seriously affecting the crops (US Forest Service 2011).

Interestingly, pitaya has been successfully cultivated in mangrove areas of Vietnam (Figure 2), due to its high adaptation capacity to grow under harsh environmental conditions, becoming a valuable asset for the sustainable development of the country and par-

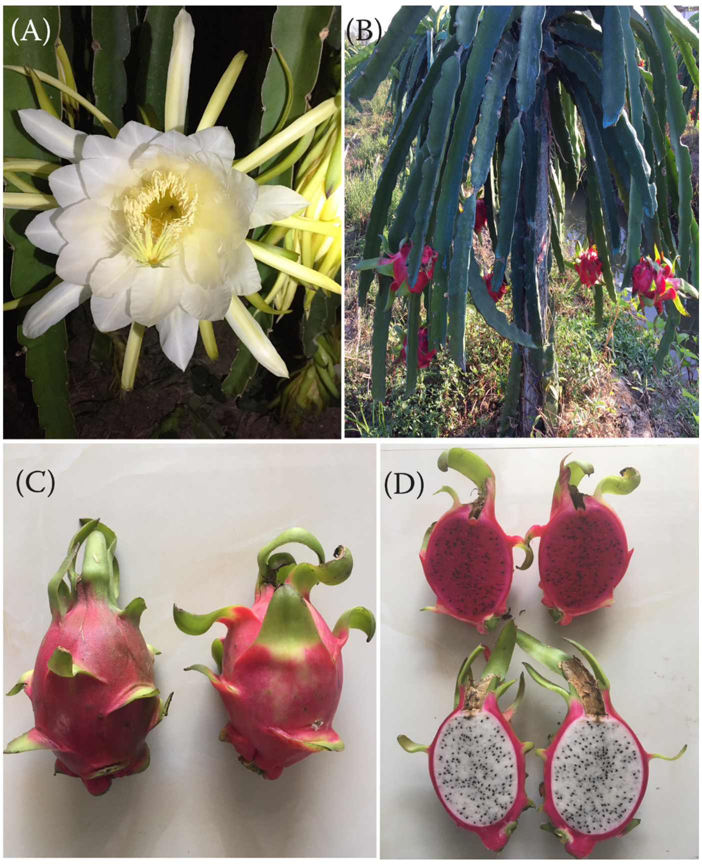

Figure 1. Flowers, stems and fruits of the pitaya of the genus *Hylocereus*: flower blooms at night (A); branched stems (B); Pitaya of *H. undatus* (left) and *H. polyrhizus* (right) (C); the oval shape with bright, red skin and green foliaceous bracts/scales resembling the skin of a dragon; red pulp and white pulp of *H. polyrhizus* and *H. undatus* (D)

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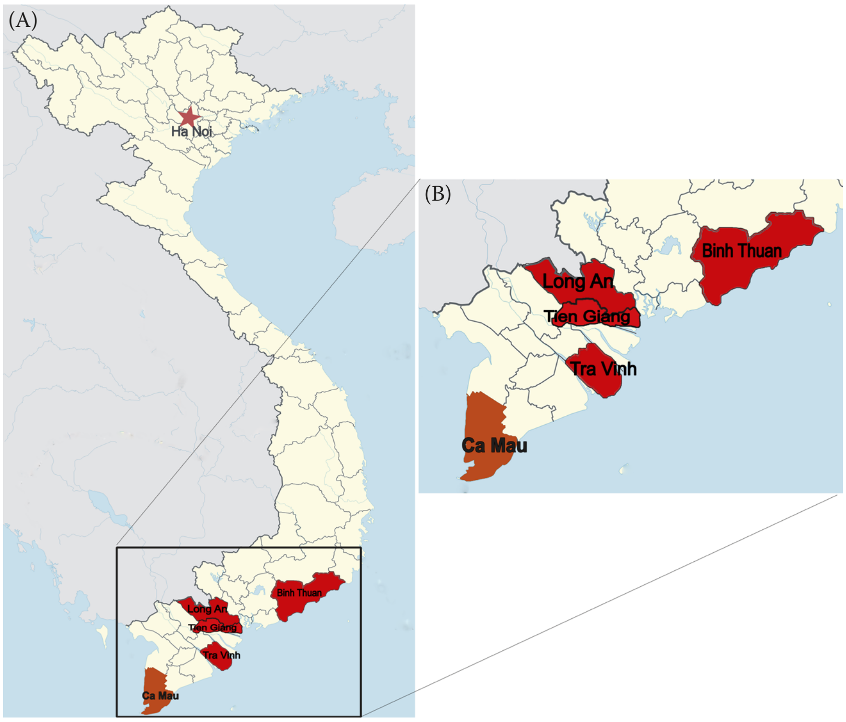

Figure 2. Maps showing the main dragon fruit cultivating areas of Vietnam in black rectangle (A), the star points to Ha Noi, the capital of Vietnam; the magnified map (B) shows the largest growing areas with the highest production of pitaya, i.e. southeast and the Mekong River Delta; Ca Mau province, in the south of the country, has mangrove areas where the dragon fruit has been successfully cultivated

ticularly for the impoverished areas of the Mekong River Delta (Hoat et al. 2018).

Dragon fruit is also considered as a medicinal plant, used in folk medicine in Asian countries, where traditional practitioners use herbal medicines to prevent and to cure diseases (Sofowora et al. 2013). The pulp and the peels have high water content, are rich in fibres and contain many nutrient elements including a high amount of vitamins, minerals, and antioxidants (Nurliyana et al. 2010; Perween et al. 2018). In recent years, the biological activity of dragon fruit has been studied and proven in several studies (Nurliyana et al. 2010; Rodriguez et al. 2016; Ismail et al. 2017; Suastuti et al. 2018; Zain et al. 2019; Juliastuti et al. 2020).

This article reviews the current knowledge of the health benefits and nutrient compositions of the dragon fruit and summarises its current production and export sales figures in Vietnam in the context of global climate change.

BOTANICAL CLASSIFICATION

Dragon fruit is a long day plant. It belongs to the genus *Hylocereus* and family Cactaceae (Morton 1987). The systematic position of dragon fruit is shown in Figure 3.

The plant is known by many names, such as dragon fruit, pitaya, pitahaya, night-blooming cereus, strawberry pear, Belle of the Night, Cinderella plant (Perween et al. 2018). In Vietnam, it is called Thanh Long (Green Dragon). From the above names, one of the most widely used is pitaya, a Haitian word meaning "scaly fruit" because it has scales or bracts on the fruit skin (Ortiz-Hernández and Carrillo-Salazar 2012).

The genus *Hylocereus* (A. Berger) Britton and Rose (1909) comprises 18 species (Anderson 2001) and it is characterised by the following typical features: *i*) climbing cacti, often epiphytic, with elongated stems normally 3-angled or 3-winged, freely branching, and branches emitting aerial roots, the areoles bearing short wool and several short spines, or rarely spineless; *ii*) flowers very large, funnel-form, usually bloom at night, limb as broad as long; *iii*) ovary and hypanthium (pericarp) bearing large leafy bracts but no spines, felt, wool, or hairs; *iv*) outer perianth-segments similar to the leafy bract on hypanthium, but longer; inner perianth segments narrow, acute or acuminate, mostly white, rarely red; *v*) stamens very many, as long as the style, or shorter; *vi*) fruit spherical to oblong, usually red and fleshy, spineless but with several broad leafy bracts, mostly large and edible; and *vii*) seeds

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Domain: Eukaryota
Kingdom: Plantae (Haeckel 1866)
Subkingdom: Tracheobionta
Superdivision: Spermatophyta (Seed plants) (Willkomm 1854)
Division: Magnoliophyta (Flowering plants) (Cronquist et al. 1966)
Class: Magnoliopsida (Dicotyledons) (Cronquist et al. 1966)
Subclass: Caryophyllidae (Takhtajan 1966)
Order: Caryophyllales (Jussieu 1789 ex Berchtold and Presl 1820)
Family: Cactaceae (Cactus family) (Jussieu 1789)
Subfamily: Cereoideae (Schumman 1898 published in Schumann 1899)
Tribe: Hylocereae (Buxbaum 1958)
Genus: *Hylocereus* (A. Berger) (Britton and Rose 1909)

Figure 3. Dragon fruit systematic position

small, black, elongate or kidney shaped (Britton and Rose 1920; Anderson 2001). The morphology of flower, stem, and fruit of *Hylocereus* spp. is shown in Figure 1.

NUTRITIONAL VALUES

Several species are included within the genus *Hylocereus*, but only a few are cultivated because of their commercial and nutritional values, such as *Hylocereus undatus*, *Hylocereus polyrhizus*, and *Hylocereus costaricensis* (Ortiz-Hernández and Carrillo-Salazar 2012; Muniz et al. 2019). The analysis of juice obtained from different species and crops of dragon fruit shows that the nutritional values are highly variable (Ruzainah et al. 2009; Ramli and Rahmat 2014; Jerônimo et al. 2015; Table 1). Thus, 100 g of fresh pulp from dragon fruit contains above 80% moisture, 0.4 to 2.2 g of protein, 8.5 to 13.0 g of carbohydrates and 6.0 g of total sugar, depending on the species and the origin. The fact that the concentrations of vitamin C obtained in the studies of Ramli and Rahmat (2014) and Jerônimo et al. (2015) were lower than one would expect from a fruit with such praised antioxidant properties was attributed by the authors to different factors: ascorbic acid is susceptible to air and light and undergoes oxidative degradation with relative ease during the preparation of juice; the concentration of ascorbic acid in fruit varies according to the type of cultivation, the stage of maturity and the conditions of cultivation; the content of vitamins and minerals is affected by the transportation and storage of the fruits, where keeping the temperature about 8 °C is the best to ensure the quality attributes of the fruit (Ramli and Rahmat 2014; Jerônimo et al. 2015). Rahmawati and Mahajoeno (2019) tested vitamin C content in three species: *H. costaricensis* (super red pulp), *H. polyrhizus* (red pulp) and *H. undatus* (white pulp), collected from four different locations: Pasuruan (East Java), Sukoharjo and Klaten (Central Java), and Bantul districts (Yogyakarta). The concentration of vitamin C oscillated from 3.3 to 6.0 mg 100 g^{-1}, depending on the species and the location; thus, the highest concentration of vitamin C content was recorded in Pasuruan super red pitaya (6.0 mg 100 g^{-1}), while the lowest concentration was found in Bantul white pitaya (3.4 mg 100 g^{-1}). Choo and Jong (2011) found that concentrations of ascorbic acid of two species *H. polyrhizus* and *H. undatus* were 36.65 and 31.05 mg 100 g^{-1} fresh pulp, respectively. Another study determined the content of ascorbic acid in *Hylocereus* sp., cv. Red Jaina (red skin with red pulp) and *Hylocereus* sp., cv. David Bowie (red skin with white pulp) of 55.8 and 13.0 mg 100 g^{-1}, respectively (Mahattanatawee et al. 2006). Consequently, the vitamin C level may vary according to species, crop, origin, maturity level of fruit, and extracting process (Mahattanatawee et al. 2006; Rahmawati and Mahajoeno 2009; Ramli and Rahmat 2014).

Another part of the pitaya, the young stem, also contains high nutritional values, including raw protein (10.0–12.1 g 100 g^{-1}), raw fibre (7.8–8.1 g 100 g^{-1}), and several minerals such as P, K, Ca, Mg, Na, Fe, Zn, in which Fe amounts to 7.5–28.8 mg kg^{-1} of dry mass (Ortiz-Hernández and Carrillo-Salazar 2012). Both the flesh and particularly the seeds of the dragon fruit have a noticeable content of fatty acids (Table 2). Jerônimo et al. (2015) analysed the flesh of the species *H. undatus* and found that the most predominant fatty acids were linoleic, oleic and palmitic acid, accounting for 50.8%, 21.5% and 12.6% of the total fatty acid content, respectively (Table 2). Similarly, Ariffin et al. (2009) analysed the oil extracted from dragon fruit seeds of red and white pitaya and found a high content of essential fatty acids, namely linoleic (~50%) and linolenic (~1%)

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Table 1. Nutritional values edible portion of different species of dragon fruit (*Hylocereus* spp.)

Component	Units (FW)	*H. polyrhizus* from Malaysia (Ramli and Rahmat 2014)	*H. polyrhizus* from Australia (Ramli and Rahmat 2014)	*H. polyrhizus* from Malaysia (Ruzainah et al. 2009)	*H. undatus* from Brazil (Jerônimo et al. 2015)
Moisture	g 100 g^{-1}	85.05	89.98	82.5–83.00	86.03
Ash	g 100 g^{-1}	0.54	1.19	nd	nd
Carbohydrate	g 100 g^{-1}	12.97	8.42	nd	10.79
Total sugar	g 100 g^{-1}	nd	nd	nd	5.92
Protein	g 100 g^{-1}	1.45	0.41	0.159–0.229	2.27
Fat	g 100 g^{-1}	nd	nd	0.21–0.61	0.16
Total dietary fibre	g 100 g^{-1}	2.65	nd	nd	nd
Crude fibre	g 100 g^{-1}	nd	nd	0.70–0.90	1.15
Energy	kcal 100 g^{-1}	62.95	35.36	nd	53.68
Iron	mg 100 g^{-1}	0.30	0.03	nd	nd
Magnesium	mg 100 g^{-1}	26.40	13.70	nd	nd
Potassium	mg 100 g^{-1}	158.29	437.35	nd	3.09
Sodium	mg 100 g^{-1}	35.63	14.30	nd	0.14
Zinc	mg 100 g^{-1}	0.40	0.09	nd	nd
Calcium	mg 100 g^{-1}	6.72	1.55	nd	nd
Phosphorus	mg 100 g^{-1}	nd	nd	nd	0.003
Vitamin A	mg 100 g^{-1}	0.085	0.89	nd	nd
Vitamin C	mg 100 g^{-1}	0.024	0.03	8.00–9.00	0.84

FW – fresh weight; nd – no data

acid, and other fatty acids such as cis-vaccenic acid (~3.0%), palmitic acid (17.5%), and oleic acid (22.7%). The benefits of mono and polyunsaturated fatty acids to human health are well-documented. For instance, these acids are known to help reducing low-density and very low-density lipoprotein fractions associated with increased serum cholesterol (Beynen and Katan 1985; Jenkins et al. 2002). In addition, linoleic and alpha-linolenic acids are necessary to maintain cell membranes, brain function and the transmission of nerve impulses under normal conditions (Glick and Fischer et al. 2013; Jerônimo et al. 2015).

PHYTOCHEMISTRY AND MEDICINAL PROPERTIES OF DRAGON FRUIT

Phytochemical compositions. Phytochemicals are defined as the bioactive, non-nutrient plant compounds (Septembre-Malaterre et al. 2018). These compounds are secondary plant metabolites, and they are associated with health benefits (Nyamai et al. 2016). In recent years, there has been increasing interest not only in the identification of the phytochemical compounds present in dragon fruit but also in the exploitation of their potential medicinal properties. Betalains, flavonoids, polyphenols, terpenoids, steroids, saponins, alkaloids, tannins, and carotenoids are bioactive compounds which can be extracted from all the parts of the pitaya (Ramli et al. 2014b; Jerônimo et al. 2015; Moo-Huchin et al. 2017; Kanchana et al. 2018; Mahdi et al. 2018). Hence, not only the edible parts of the dragon fruit, i.e. the pulp, but also the waste parts like the peels are rich in phytochemicals and thus have potential uses as herbal medicine or natural colourants (Tables 2 and 3).

Zain et al. (2019) identified 13 types of phenolic compounds from *Hylocereus polyrhizus*, using microwave-assisted extraction to get the bioactive compounds from the peel, and the full chromatogram of the peel extract obtained from UHPLC-ESI-QTRAP-MSMS analysis.

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The phenolic compounds included: quinic acid, cinnamic acid, quinic acid isomer, 3,4-dihydroxyvinylbenzene, isorhamnetin 3-O-rutinoside, myricetin rhamnohexoside, 3,30-di-O-methyl ellagic acid, isorhamnetin aglycone monomer, apigenin, jasmonic acid, oxooctadecanoic acid, 2 (3,4-dihydroxyphenyl)-7-hydroxy-5-benzene propanoic acid and protocatechuic hexoside conjugate. The results showed the richness in polyphenols and flavonoid compounds of the pitaya and pointed its value as a natural colour source with interest for the food and cosmetic industries (Table 3).

Wybraniec et al. (2007) analysed the pulps and peels of *H. ocamponis, H. undatus,* and *H. purpusii,* as well as hybrids of *H. costaricensis* × *H. polyrhizus* and *H. un-*

Table 2. Profile of fatty acids in the flesh of *Hylocererus undatus* (modified after Jerônimo et al. 2015)

Compositions of fatty acids	Red pitaya (*Hylocereus undatus*) pulp (mg 100 g^{-1})	% fatty acids
Palmitic acid (C16:0)	62.740	12.632
Palmitoleic acid (C16:1 ω-7)	1.765	0.355
Heptadecanoic acid (C17:0)	0.373	0.075
Heptadecanoic acid (C17:1 ω-7)	0.580	0.116
Oleic acid (C18:1 C ω-9)	22.066	4.442
Oleic acid (C18:1 T ω-9)	107.040	21.551
Linoleic acid (C18:2 C ω-6)	252.650	50.869
Linoleic acid (C18:2 T ω-6)	0.690	0.138
Alpha-linolenic acid (C18:3 ω-3)	4.569	0.919
α-linolenic acid (C18:3 ω-6)	0.762	0.153
Arachidic acid (C20:0)	4.587	0.923
Eicosatrienoic acid (C20:3 ω-6)	0.615	0.123
Arachidonic acid (C20:4 ω-6)	1.384	0.278
Eicosapentaenoic acid (C20:5 ω-3)	0.304	0.061
Heneicosanoic acid (C21:0)	0.610	0.122
Behenic acid (C22:0)	3.713	0.747
Docosahexaenoic acid (C22:6 ω-3)	0.608	0.122
Tricosanoic acid (C23:0)	0.351	0.070
Lignoceric acid (C24:0)	2.527	0.508
Tetracosenoic acid (C24:1 ω-9)	0.309	0.062
Stearic acid (C18:0)	27.333	5.503
Eicosamonoenoic (C20:1 ω-9)	1.091	0.219
Total saturated fatty acids (%)	102.234	20.580
Total unsaturated fatty acids (%)	394.433	79.408
Total monounsaturated fatty acid	132.851	
Total polyunsaturated fatty acids	261.582	
MUFA/SFA	1.299	
PUSA/SFA	2.558	

MUFA – monounsaturated fatty acids; SFA – saturated fatty acids; PUSA – polyunsaturated fatty acids; MUFA/SFA – ratio of monounsaturated and saturated fatty acids; PUSA/SFA – ratio of polyunsaturated and saturated fatty acids

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Table 3. Phytochemical compounds of dragon fruit

Aerial parts	Phytochemical compounds	Varietie(s)	Method	Reference
Pulp and Peel	Betacyanins, phenolics, flavonoids.	*H. polyrhizus*	colour test followed by UV-Vis	Ramli et al. (2014b)
Pulp	Carbohydrates, proteins and amino acids, alkaloids, terpenoids, steroids, glycosides, flavonoids, tannins, and phenolic compounds, saponins, oils.	*H. undatus*	NA	Kanchana et al. (2018)
Fruit	Glycosides, alkaloids, saponins, phenolic compounds, tannins, flavonoids, proteins, steroids.	*H. undatus*	colour tests	Mahdi et al. (2018)
Peel	13 phenolic compounds: quinic acid, cinnamic acid, quinic acid isomer, 3,4-dihydroxyvinylbenzene, isorhamnetin 3-O-rutinoside, myricetin rhamnohexoside, 3,30-di-O-methyl ellagic acid, isorhamnetin aglycone monomer, apigenin, jasmonic acid, oxooctadecanoic acid, 2 (3,4-dihydroxyphenyl)-7- hydroxy-5-benzene propanoic acid and protocatechuic hexoside conjugate.	*H. polyrhizus*	UHPLC-ESI-QTRAP-MSMS	Zain et al. (2019)
Pulp and Peel	Seven betacyanin compounds in pulp and 10 betacyanins in peel with betanin, phyllocactin, and hylocerenin as major compounds found in fruit peel of *H. ocamponis*. Pigments 1–10 of betacyanin profiles in *H. ocamponis* fruit peel of revealed, including: betanidin 5-*O*-β-sophoroside, betanin, 2'-Apiosyl-betanin, phyllocactin, 4'-Malonyl-betanin, hylocerenin, 2'-Apiosyl-phyllocactin, 5''-*O*-*E*-Feruloyl-2'-apiosyl-betanin, 5''-*O*-*E*-Sinapoyl-2'-apiosyl-betanin, and 5''-*O*-*E*-Feruloyl-2'-apiosyl-phyllocactin.	*H. ocamponis*, *H. undatus*, *H. purpusii*, *H. costaricensis* × *H. polyrhizus*, *and H. undatus* x *H. polyrhizus*	HPLC	Wybraniec et al. (2007)
Pulp	Four different types of carotenoids: two xanthophylls (lutein, β-cryptoxanthin), and two carotenes (lycopene, β-carotene); vitamin A.	*H. undatus*	colour test followed by UV-Vis	Moo-Huchin et al. (2017)
Pulp and Peel	Phenolics, flavonoids, betacyanins.	*H. polyrhizus*	colour test followed by UV-Vis	Wu et al. (2006)
Peel and Stem	Phenolics.	*H. undatus*	colour test followed by UV-Vis	Som et al. (2019)
Pulp and Peel	Phenolics.	*H. undatus* and *H. polyrhizus*	colour test followed by UV-Vis	Nurliyana et al. (2010)

NA – not available

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datus × *H. polyrhizus* and they recognized and identified seven (in pulps) and ten (in peels) different compounds of betacyanins (the pigments used in the food industry due to their colorant properties). They also found that the most abundant betacyanins in the peel of the species *H. ocamponis* were betanin, phyllocactin, and hylocerenin (Table 3).

Moo-Huchin et al. (2017) detected four different types of carotenoids in an edible portion of *H. undatus*, including two xanthophylls (lutein, β-cryptoxanthin), and two carotenes (lycopene, β-carotene). They found high concentrations of lutein and β-carotene (30.8 and 209.1 µg 100 g^{-1} edible portion, respectively), as well as vitamin A (34.9 µg 100 g^{-1}) (Table 3). Both vitamin A and carotenoids are considered powerful antioxidants (Palace et al. 1999).

Wu et al. (2006) analysed the pulp and peels of red pulp pitaya (*H. polyrhizus*) and found little variation in the concentrations of phenolic contents [42.4 mg gallic acid equivalents (GAE) 100 g^{-1} flesh fresh weight *vs.* 39.7 mg GAE 100 g^{-1} peel fresh weight], flavonoids (7.21 mg *vs.* 8.33 mg of catechin equivalents 100^{-1} g of flesh and peel matters), and betacyanins (10.3 mg *vs.* 13.8 mg of betanin equivalents 100 g^{-1} of fresh flesh and peel matters). While both peel and stem parts of pitaya have phenolic contents (Som et al. 2019), Nurliyana et al. (2010) after analysing *H. undatus* and *H. polyrhizus* reported higher concentrations of these compounds in the pulps (36.12 and 28.16 mg 100 g^{-1} of fresh pulps, respectively) than in the peels (3.75 and 19.72 mg 100 g^{-1} of fresh peels, respectively) (Table 3).

Antioxidant activities. Exploitation of natural antioxidant substrates in medicinal plants with preventive influences on cellular damage caused by free radicals, which are involved in many diseases like cancer, has been increasing (Young and Woodside 2001). Thus, the popularity of many plants in disease prevention could be attributed to the antioxidant (radical-scavenging) properties of their constituent phenolic compounds (such as flavonoids, phenolic acids, stilbenes, lignans and tannins), alkaloids, and vitamin C (Pietta 2000; Nyamai et al. 2016; Gan et al. 2017; Pehlivan 2017; San Miguel-Chávez 2017). Several studies link the scavenging activity of antioxidants with the content of total phenolic compounds (Bertoncelj et al. 2007; Wu and Ng 2008). Phenolic compounds, like phenolic acid (e.g. gallic acid) and polyphenol (e.g. flavonoids), are highly correlated with antioxidant activity (Nurliyana et al. 2010), and some of them have been proven *in vitro* to be more effective antioxidants than vitamin C and vitamin E (α-tocopherol) (Rice-Evans et al. 1997; Table 3).

The antioxidant properties of the dragon fruit are widely acknowledged and the antioxidant activity of different species, as well as the antioxidant content of different parts of the plant (e.g. pulp, peel, stem, foliage), have been subjected of many detailed studies (Wu et al. 2006; Nurliyana et al. 2010; Choo and Yong 2011; Ramli et al. 2014b; Jerônimo et al. 2015; Moo-Huchin et al. 2017; Mahdi et al. 2018; Zain et al. 2019). Most studies have been focused on two species of the genus *Hylocereus*, which stand out in cultivation and distribution: *H. polyrhizus* and *H. undatus*. Two of the most widely used methods to evaluate antioxidant activities are 2, 2'-diphenyl-β-picrylhydrazyl (DPPH) (Brand-Williams et al. 1995) and 2, 2'-azino-bis (3-ethylbenzothiazoline-6-sulphonic acid) ($ABTS^{\pm}$) (Re et al. 1999). Both are spectrophotometric techniques based on quenching of stable coloured radicals (DPPH or $ABTS^{+}$) which determine the radical scavenging ability of antioxidants even when present in complex biological mixtures (e.g. plant or food extracts).

Nurliyana et al. (2010) used DPPH assays to test the radical scavenging activity of pulps and peels of *H. polyrhizus* and *H. undatus* and found that for both species the peels contained higher radical scavenging activity than the pulps. Moreover, the antiradical activity for peels of both species was higher than that of the positive control, a potent synthetic antioxidant named butylated hydroxyanisole (BHA), at approximate concentrations of sample from 0.8 to 1.0 mg mL^{-1}. IC_{50} [defined as the concentration of an inhibitor where the response (or binding) is reduced by half] values for the peels of *H. polyrhizus* and *H. undatus* were 0.30 and 0.40 mg mL^{-1}, respectively, higher than BHA (0.15 mg mL^{-1}). In the case of pulps of both species, they showed low percentage of radical scavenging activities over the measured extract concentrations, suggesting that their IC_{50} values could be higher than 1.0 mg mL^{-1}. Interestingly, the total phenolic content (TPC) assay demonstrated that peels of both *Hylocereus* species contained higher phenolic content than the pulps.

In a further study with red pitaya (*H. undatus*), Jerônimo et al. (2015) obtained similar results like Nurliyana et al. (2010) regarding the higher antioxidant activity of the peel compared to the pulp. Thus, the antioxidant activity of the pitaya peel (445.2 mg mL^{-1}) was greater than in the pitaya pulp (1 266.3 mg mL^{-1}). The highest concentration of compounds with antioxidant activity in the fruit peels, usually discarded, supports its value as leftovers rich in fibre, nutrients, and bioactive compounds.

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The DPPH assay performed by Choo and Yong (2011) on the ethanol extracts from pulp and fruit (peel and pulp) of *H. polyrhizus* and *H. undatus* showed EC_{50} values of 9.93 and 11.34 mg mL^{-1} for the pulp and fruit of *H. polyrhizus*, respectively, and of 9.91 and 14.61 mg mL^{-1} for the pulp and fruit of *H. undatus*, respectively [EC_{50} is defined as the concentration of a drug that gives half-maximal response]. Within the same species of *Hylocereus*, the fruits (peels and pulps) showed a higher phenolic content than the pulps, which was also related to a higher antiradical power. However, when the authors compared the antiradical power of the two species of *Hylocereus*, they found that: *i*) it was not proportional to the total phenolic content in the pulps, i.e. the total phenolic content of *H. undatus* pulp was higher than that of *H. polyrhizus*, and *ii*) both species showed no significant difference in the ascorbic acid content. These results indicate the importance of ascorbic acid as an antioxidant and suggest a synergistic relationship between the ascorbic acid and the phenolics in the radical scavenging activity. The variation in the concentration of phenolic compounds and ascorbic acid in fruit is associated with the type of cultivation, the maturation stage, and the conditions of cultivation, among others (Choo and Yong 2011; Jerônimo et al. 2015).

While most research on dragon fruit focuses on the radical scavenging activity of pulps and peels, limited research is carried out on the antioxidant capacity of other parts of the plant. Among these studies, Som et al. (2019) tested chloroform and methanol extracts of foliage and peel of white flesh dragon fruit (*H. undatus*) for higher total phenolic content (TPC) and antioxidant activity. Their results showed that methanol solvent was more efficient than chloroform solvent to extract phenolic content since the former can extract both polar and non-polar compounds, while the latter can extract only non-polar compounds. According to their results, peels had higher TPC than foliage regardless of the solvent used, but in any case, reaching higher concentrations after methanol extraction [48.15 mg of gallic acid (GAE) 100 g^{-1} peel extract and 18.89 mg GAE 100 g^{-1} peel extract for methanol and chloroform, respectively, *vs.* 30.30 mg GAE 100 g^{-1} foliage extract and 5.92 mg GAE 100 g^{-1} foliage extract for methanol and chloroform, respectively]. However, the DPPH assay showed that the antioxidant activity of chloroform extractions was higher compared to methanol extractions. According to the authors, the discrepancies between the results of TPC and DPPH assays could be attributed to reversible reactions between DPPH and some phenols, and to the slow rate of reaction between DPPH radicals and the substrate olecules. Although chloroform extracts of peels had higher antioxidant activity than those of foliage, and although there were no previous studies on the antioxidant value of dragon fruit foliage, Som et al. (2019) concluded that foliage has indeed the potential as a natural antioxidant alternative to the toxicity associated to many synthetic antioxidants.

Wu et al. (2006) measured for the first time the phenolic content and antioxidant activity of peel and flesh of red pitaya (*H. polyrhizus*) in order to determine the value of this species as a source of antioxidants and its potential role in the prevention of degenerative diseases related to oxidative stress, such as cancer. Acetone extracts from *H. polyrhizus* flesh and peel were analysed for antioxidant activity using DPPH and $ABTS^+$ radical scavenging assays. The effective concentrations determined by DPPH for flesh and peel were 22.4 and 118.0 μmol vitamin C equivalents g^{-1} dried extract, respectively, and the values of EC_{50} for $ABTS^+$ were 28.3 and 175.0 μmol Trolox equivalents antioxidant capacity (TEAC) g^{-1} dried extract, respectively. The authors concluded that the effect of flesh and peel on antioxidant activity could be related to the types of polyphenolics they contained. Moreover, the higher the number of hydrogen-donating groups (e.g. –OH, –NH, –SH) in the molecular structure, the higher the antioxidant activity. In this sense, although the pitaya peel is usually wasted, its slightly higher polyphenolic and betanin contents make it a better antioxidant than the flesh, and it should be considered a valuable compound against cancer cell proliferation.

Antioxidant activities of supercritical carbon dioxide extracts of *H. undatus* and *H. polyrhizus* peels were evaluated by DPPH radical scavenging assay, compared to the vitamin C standard. The EC_{50} values of *H. undatus* and *H. polyrhizus* peel were 0.91 and 0.83 mg mL^{-1}, respectively (Luo et al. 2014).

Moo-Huchin et al. (2017) performed a study to determine the carotenoid composition and antioxidant activities of carotenoid extracts from tropical fruits from Yucatan (Mexico) including dragon fruit (*H. undatus*). The total carotenoid content of 19 different tropical fruits expressed as mg of β-carotene 100 g^{-1} of edible portion ranged from 0.70 to 36.41 mg 100 g^{-1}. Among the fruits evaluated, the highest carotenoid content was found in the Mamey sapote fruit with 36.41 mg 100 g^{-1}, while the dragon fruit contained only 0.86 mg 100 g^{-1}, followed by the green sugar apple with 0.70 mg 100 g^{-1}. However, the DPPH method

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revealed that the antioxidant activity of the dragon fruit was higher than that of several other analysed fruits, despite having lower total carotenoid content compared to other fruits. The study identified and quantified by HPLC four carotenoids in the fruits, including two xanthophylls (lutein and β-cryptoxanthin) and two carotenes (lycopene and β-carotene). The contents of lutein, β-cryptoxanthin, lycopene, and β-carotene found in dragon fruit were 30.8, 0.6, 3.2, and 209.1 mg 100 g^{-1}, respectively, which were in the mid-range of concentrations detected in the other fruits evaluated in this study. According to Moo-Huchin et al. (2017), the presence of carotenoid contents in tropical fruits like pitaya, with significant levels of vitamin A precursors such as β-cryptoxanthin and β-carotene, highlights the benefits of including tropical fruits in the diet, not only because of their antioxidant activity but also as a supplement of vitamin A, whose deficiency particularly affects developing tropical countries.

Esquivel et al. (2007) studied the phenolic compound profiles of six representatives of the genus *Hylocereus*, including five Costa Rican genotypes of purple pitaya (*Hylocereus* sp.), namely 'Lisa', 'Rosa', 'San Ignacio', 'Orejona' and 'Nacional', and *H. polyrhizus* fruits. Their results showed that the genotypes presented different individual phenolic compound profiles, and the antioxidant capacity of these fruits was mostly based on betalains, followed by their biosynthetic precursors, while non-betalainic phenolic compounds had a minor antioxidant role.

Abd Manan et al. (2019) determined the total phenolic content, total flavonoid content, and antioxidant capacity of water extract from *H. polyrhizus* pulp. The total phenolic content was tested using the Folin-Ciocalteu (F-C) assay (Folin and Ciocalteu 1927), the total flavonoid content was determined by the spectrophotometric method (modified after Stankovic et al. 2011), and the antioxidant activity was measured by four different procedures, such as DPPH, $ABTS^+$, Ferric Ion Antioxidant Power (FRAP) (modified after Benzie and Strain 1996), and phosphomolybdate assay (based on Prieto et al. 1999 and modified after Ahmed et al. 2015). The free radical scavenging activities of various dilution factors of water extract of *H. polyrhizus* pulp ranged from 61.61% to 73.38% using DPPH, and 38.69% to 92.66% after $ABTS^+$. The higher the concentration of the extract, the higher the antioxidant activity. The antioxidant capacity, determined by FRAP and phosphomolybdate assays, was 132.17 μmol Fe^{2+} equivalents 100 mL^{-1} of juice and 28.94 mg ascorbic acid equivalents (AAE) 100 mL^{-1} of juice, respectively. The four used methods showed a strong positive correlation between total phenolic and total flavonoid content of the water extract of pulp and antioxidant activities. Moreover, according to Abd Manan et al. (2019), pharmaceutical and nutraceutical industries could benefit from their results, since they support the use of water as a natural, biodegradable and non-toxic solvent for the extraction of profitable bioactive plant compounds, e.g., polar and readily soluble in water antioxidants such as flavonoids and polyphenols.

Several studies support the benefits of the consumption of dragon fruit in the control and management of oxidative stress related diseases. Diabetic infected rats treated with water extract of the fruit pulp of *H. undatus* were able to control oxidative stress through a decrease in malondialdehyde (a marker of oxidative stress) levels, and an increase in superoxide dismutase (antioxidant enzyme) and total antioxidant capacity (Swarup et al. 2010). Harahap and Amelia (2019) reported that rats treated with white flesh dragon fruit extract (*H. undatus*) and subjected to heavy physical exercise showed a lower lactic acid level and creatine kinase (CK) activity, compared to untreated rats under heavy physical exercise. High levels of lactic acid can lead to a release of much more free radicals, and high CK activity may be considered a biomarker for muscle tissue damage. Doses of 200 and 300 mg of red fruit extract kg^{-1} body weight effectively reduced the level of acid lactic and the CK activity. Thus, the experiments conducted in rats demonstrated that free radicals released during heavy physical exercise were inhibited in the presence of antioxidants from dragon fruit extract.

In short, dragon fruit has strong antioxidant properties as proven in numerous studies both *in vitro* and *in vivo*. The high antioxidant contents of phenolics, flavonoids, betalain, and ascorbic acid are responsible for these activities. The pitaya exhibits a high potential as a natural agent to drive away aging-associated diseases, mostly related to oxidative stress due to imbalance between antioxidants and free radicals, such as cancer, diabetes, atherosclerosis, hypertension, Alzheimer's disease, Parkinson's disease, and inflammation.

Antidiabetic properties. Diabetes mellitus is one of the most common systemic diseases in the world, linked to hyperglucemia as the result of a malfunction of the pancreas in the production of insulin and/or to the inadequate sensitivity of cells to the action of insulin (American Diabetes Association 2009).

In the folk medicine of many countries, diabetic treatments have traditionally included plants such as neem (*Azadirachta indica*), ivy gourd (*Coccinia indica*), bit-

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ter gourd (*Momordica charantia*), jamblon (*Syzygium cumini*), aloe vera (*Aloe barbadensis Miller*), and chicory *(Cichorium intybus)* (Ocvirk et al. 2013; Kooti et al. 2016; Adinortey et al. 2019). In general, medicinal plants show antidiabetic effects through biochemical mechanisms such as recovery of pancreatic β-cell function, improvement of insulin sensitivity by receptors, stimulation of insulin secretion, inhibition of liver gluconeogenesis, enhanced glucose absorption, and inhibition of glucose-6-phosphatase, β-amylase, and β-glucosidase activities (Adinortey et al. 2019).

The antidiabetic capacity of dragon fruit has been the subject of numerous studies. Omidizadeh et al. (2014) investigated the anti-insulin resistant activity from red pitaya (*Hylocereus polyrhizus*) in insulin resistant rats induced by fructose supplement. The results of this study showed that pitaya lessened insulin resistance, suggesting that antioxidant and soluble dietary fibre contents of red pulp pitaya are responsible for its anti-insulin resistant capacity.

Swarup et al. (2010) observed that the aqueous extract of the fruit pulp of *H. undatus* at doses of 250 and 500 mg kg^{-1} body weight decreased fasting blood glucose levels in streptozotocin-induced diabetic rats, although not to normal levels. Such lowering effect was limited and could not be increased with higher doses of pulp extract.

The effect of red pitaya (*H. polyrhizus)* consumption on blood glucose level and lipid profile of type 2 diabetic patients was assessed in a study of Abd Hadi et al. (2012). The experiment was conducted during a seven-week period divided into three phases: one pre-treatment week (phase 1), four weeks of treatment (phase 2) and two post-treatment weeks (phase 3). During phase two, patients were treated with 400 g and 600 g of pitaya per day, without interrupting their medication. Fasting blood samples and anthropometric measurements were monitored throughout the study to test the effect of pitaya on blood glucose, triglyceride, and cholesterol [total, low-density lipoprotein (LDL-) and high-density lipoprotein (HDL-)] levels, as well as Body Mass Index (BMI). The results showed that while the consumption of 400 g of fruit was more effective in lowering triglyceride levels, the treatment with 600 g was more effective in decreasing blood glucose, total and LDL-cholesterol levels, and increasing the HDL-cholesterol level. Body weight and total body fat did not present any significant differences between both treatments.

The beneficial effects of red and white dragon fruit in diabetes prevention were also investigated by Poolsup et al. (2017) through a systematic review and meta-analysis of more than 401 studies, including publications in medical journals but also unpublished academic research, which compared the effect of dragon fruit with placebo or no treatment in prediabetes or type 2 diabetes subjects. There is a general trend to observe a greater reduction of blood glucose with higher doses of pitaya, but Poolsup et al. (2017) concluded that due to restricted available data and poor quality of clinical evidence, further well-controlled clinical trials are yet required to further evaluate the clinical benefits of this fruit in prediabetes and type 2 diabetes patients.

Antiviral and antimicrobial activity. Physiological and biochemical basis of plant resistance to attacks by different pathogens (i.e. virus, fungi, or bacteria) is related to secondary metabolites that plants synthesised after a microbial infection (García-Mateos and Pérez-Leal 2003; Montes-Belmont 2009; Hernández-Alvarado et al. 2018; Mickymaray 2019). Different criteria can be used for the classification of secondary metabolites involved in plant immunity, i.e. core structure, common precursors, and mechanisms of action. According to the mode of biosynthesis and accumulation of defence-related phytochemicals, one of the most frequently used criteria, defensive metabolites produced and stored constitutively in plant tissue are named phytoanticipins (e.g. saponins, glucosinolates, cyanogenic glucosides, and benzoxazinone glucosides) whereas those synthesized *de novo* in response to infection are termed phytoalexins (e.g. camalexin, phenylalanine-derived phytoalexins like resveratrol, isoflavonoids like glyceollins, or terpenoids) (Müller and Börger 1940; Van Etten and Bateman 1971; Paxton 1981; Piasecka et al. 2015). The benefits of the consumption of plants against a wide range of pathogenic microorganisms are associated with different bioactive compounds, including secondary metabolites with greater antimicrobial properties like flavonoids (flavones, flavonols, flavanols, isoflavones, anthocyanidins), terpenoids (sesquiterpene lactones, diterpenes, triterpenes, polyterpenes), steroids, phenolic acids (hydroxybenzoic, hydroxycinnamic acids), stilbenes, lignans, quinones, tannins, coumarins (simple coumarins, furanocoumarins, pyranocoumarins), alkaloids, glycosides, saponins, lectins, and polypeptides, which exhibit a great antimicrobial potential (Iwu et al. 1999; Chanda et al. 2010; Naseer et al. 2012; Fadipe et al. 2013; Umer et al. 2013; Tahera et al. 2014, Mickymaray 2019). The antimicrobial activity of the plant extracts and their bioactive compounds involves different mechanisms such as to promote microbial cell wall disruption and lysis, induce generation of oxygen species production to kill microbes, prevent biofilm formation of bacteria,

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inhibit cell wall construction, inhibit several enzymes related to the replication of microbial DNA, inhibit energy synthesis of microbes, and inhibit bacterial toxins to the host (Mickymaray 2019).

The antiviral activity of betacyanin, a red-violet pigment belonging to the betalains, from red pulp pitaya (*H. polyrhizus)* against dengue virus type 2 (DENV-2) has been recently studied by Chang et al. (2020). To obtain betacyanins, the authors extracted the pulp of red pitaya using methanol. Vero cells were infected with DENV-2, incubated with different concentrations of betacyanin for 48 h at 37 °C, and then the percentage of virus yield inhibition was studied. The results demonstrated a dose-dependent virucidal effect of betacyanin against DENV-2 after virus adsorption to the host cells, with an IC_{50} of 126.7 μg mL^{-1} and 95.0% of virus inhibition at the maximum non-toxic betacyanin concentration (379.5 μg mL^{-1}). An extract concentration below 2.5 mg mL^{-1}, i.e. content of betacyanins below 379.5 μg mL^{-1}, was determined as non-cytotoxic to Vero cells.

The biological functions, i.e. antimicrobial, antioxidant and anticancer capacities, and major bioactive compounds of methanolic stem extract of pitaya (*H. polyrhizus*) were evaluated by Ismail et al. (2017) applying agar cup plate (500 μg stem extract per cup) and disk diffusion (100 μg stem extract per dish) methods. The 95% methanol extract showed strong broad-spectrum antimicrobial activity against five pathogenic strains, including Gram-positive and Gram-negative bacteria (*S. aureus* and *Pseudomonas aeruginosa*, respectively), yeast (*Candida albicans*) and moulds (*Aspergillus niger* and *Fusarium oxysporum*) expressed by inhibition zones as 29.0, 29.0, 29.5, 17.5, and 29.5 mm by cup agar method (100 μL/cup), and 9.5, 11.0, 10.0, 8.0, and 16.5 mm by disk diffusion method (20 μL/disk) against *S. aureus*, *P. aeruginosa*, *C. albicans*, *A. niger* and *F. oxysporum*, respectively. The strong antimicrobial activity of methanol pitaya stem extract could be related to the synergistic action of its oxygenated terpenes like 5-cedranone, eucalyptol, and α-terpineol (Hammer et al. 2003; Ismail et al. 2017).

In another study about the potential application of pitaya peels as a natural source of antibacterial agents, Nurmahani et al. (2012) used disc diffusion and broth micro-dilution methods to evaluate the antibacterial properties of ethanol, chloroform, and hexane extracts from *H. polyrhizus* (red flesh pitaya) and *H. undatus* (white flesh pitaya) against nine pathogens, i.e. *Bacillus cereus*, *S. aureus*, *Listeria monocytogenes*, *Enterococcus faecalis*, *Salmonella typhimurium*, *E. coli*, *Klebsiella pneumoniae*, *Yersinia enterocolitica*, and *Campylobacter jejuni*. Their results showed that all the extracts tested exhibited inhibition zones of about 7–9 mm against certain bacteria, indicating a broad-spectrum activity against both Gram-positive and Gram-negative bacteria. The chloroform extract of the peel of both pitaya species had the most powerful antibacterial activity compared with ethanol and hexane extracts, with *H. polyrhizus* peel being greater than *H. undatus* peel. Chloroform extract of *H. polyrhizus* was the most potent antibacterial extract, successfully inhibiting the growth of all bacteria at 1.25 mg mL^{-1}. Nevertheless, although all the bacteria were to some extent sensitive to the different extracts tested, with minimum inhibitory concentrations for the different extracts ranging from 1.25 mg mL^{-1} to 10 mg mL^{-1}, the chloroform extract of red flesh pitaya peel stands out as a good source of natural antibacterial agent against both Gram-positive and Gram-negative bacteria. The authors highlighted the potential value of pitaya peel, usually discarded as domestic waste, as an underestimated source of antibacterial agents.

The study of Khalili et al. (2012) analysed the antibacterial activity of methanol peel and flesh extracts from red flesh pitaya, white flesh pitaya, and papaya against pathogenic food microorganisms, including *Staphylococcus epidermidis*, *S. aureus*, *Enterococcus faecalis, L. monocytogenes*, *Salmonella enterica* Typhi, *Serratia marcescens*, *Shigella flexneri*, *Klebsiella* sp., *Pseudomonas aeruginosa*, and *E. coli*.

The antimicrobial activity of the methanolic extracts against each pathogenic bacterium was evaluated by the agar diffusion assay. In short, the method consisted in inoculating and spreading 100 μL of a suspension containing 10^8 CFU mL^{-1} of bacteria on nutrient agar plates and distributing sterile disks (6 mm diameter) impregnated with 30 μL of extract solutions (100 mg mL^{-1}), and of the positive controls penicillin G (10 μg per disc) and gentamicin (10 μg per disc) used as standards to determine the sensitivity of each bacterial species tested. The inoculated plates were incubated at 37 °C for 24 h, and the antibacterial activity of each compound was evaluated by measuring in millimetres (mm) the diameter of the inhibition zone associated with each impregnated disk. High antibacterial activities were associated with inhibition zones of at least 14 mm (including the diameter of the disc). While white pitaya and papaya flesh and peel extracts did not inhibit the growth of several of the tested bacteria, they showed some activity (inhibition zones less than 11 mm) mostly against Gram-positive bacteria. On the other hand, the methanolic red pitaya flesh extract produced inhibition zones

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with diameters larger than 14 mm, i.e. high antimicrobial activity, against all the Gram-positive bacteria tested and all the Gram-negative bacteria except *S. flexneri* (12.50 ± 0.90 mm). These inhibition zones created by the methanolic fruit extracts were larger in some cases than those generated by the standard antibiotics. The results of Khalili et al. (2012) showed the potential of fruit extracts as a source for the production of drugs, since they demonstrated antimicrobial activity against a broad spectrum of bacteria, including those strains which developed resistance to frontline antimicrobial drugs (e.g. *E. coli*).

A recent study of Zain et al. (2019) also tested the antibacterial activity of the pitaya (*H. polyrhizus*) peel extract and found a small antibacterial effect on the Gram-positive and Gram-negative bacteria, *S. aureus* and *E. coli*, respectively. The authors concluded that despite the small antibacterial effect of the pitaya peel extract, the results were consistent with previous works which considered that it was yet sufficient to support its use as a natural colour source and antibacterial agent in food and cosmetic products (Majhenič et al. 2007; Guo et al. 2011; Mback et al. 2016).

It is stated that betacyanins, phenolics, fatty acids, alkaloids, glycosides, tannins, terpenes and α-terpineol might be responsible for the antimicrobial activity of dragon fruit (Khalili et al. 2012; Nurmahani et al. 2012; Ismail et al. 2017).

Anticancer activity. The antiproliferative potential of dragon fruit is related to its content of *strong antioxidants such as polyphenol, anthocyanin, betalains,* steroids and triterpenoids **(**Wu et al. 2006; Luo et al. 2014; Guimarães et al. 2017). Among these compounds, aside from antimicrobial and antiviral properties, betalains can also inhibit the lipid peroxidation, cyclooxygenase (COX-1 and COX-2) enzymes and proliferation of human tumour cells (Strack et al. 2003; Reddy et al. 2005; Afandi et al. 2017).

Supercritical carbon dioxide extracts of pitaya peels from *H. polyrhizus* and *H. undatus* possess antioxidant and cytotoxic activities, as demonstrated by Luo et al. (2014). The extracts of both pitaya species showed cytotoxic activity against three types of cells, i.e. PC3 (human prostate cancer cell line), Bcap-37 (human breast cancer cell line), and MGC-803 (human gastric cancer cell line) with IC_{50} values ranging from 0.61 to 0.73 mg mL^{-1}. Luo et al. (2014) also identified β-amyrin, β-sitosterol, and stigmast-4-en-3-one as the compounds responsible for the cytotoxic activities.

Guimarães et al. (2017) studied the protective effect of *H. polyrhizus* pulp extract against breast cancer. They observed a decrease in cell proliferation in MCF-7 (ER^+) cell line treated with pulp extract (500 to 1 000 μg mL^{-1}). The cell cycle analysis showed that the pulp extract caused an increase in G_0/G_1 phase followed by a decrease in G_2/M phase. Moreover, the extract induced apoptosis in MCF-7 cells and suppression of $BRCA_1$, $BRCA_2$, PRAB (progesterone receptor isoform A and B), and Er*α* (estrogenic receptor α) gene expressions.

Wu et al. (2006) also proved the antiproliferative activity of pitaya extract against B16F10 melanoma cell line. This study revealed that the antiproliferative activity of the peel extract on B16F10 melanoma cancer cells was stronger than that of the pulp extract.

Wound healing activity. Wound healing is a complex process consisting of several stages aimed at restoring the integrity of damaged tissues, and involving different cell populations, the extracellular matrix, and the action of soluble mediators such as growth factors and cytokines. Wound management constitutes a daily challenge in clinical pathology and it often fails without an appropriate physiological, endocrine, and nutritional support (Velnar et al. 2009).

Tsai et al. (2019) used ethanol-water extracts from different parts of *Hylocereus polyrhizus*, such as peel, stem, and flower to perform an in vitro test of their wound healing properties. NIH-3T3 fibroblast cell line was used to test cell migration ability in the scratch assay. The result showed that the stem and flower of dragon fruit extracts in 95% aqueous ethanol at the concentration of 1 000 μg mL^{-1} promoted the migration of fibroblasts after 24 h which play a crucial role in the wound healing process. In this study, the extracts from the stem, peel, and flower in 95% aqueous ethanol of the dragon fruit had high activity in DNA damage protection. The powerful antioxidants present in the dragon fruit extracts include phenolic and flavonoid contents involved, inter alia, in DNA protection and wound healing activities, properties with potential applications in the pharmaceutical, cosmetic, and food industries.

Perez et al. (2005) studied the wound healing properties of aqueous extracts of leaves, rind, pulp, and flowers of *H. undatus* in wounded streptozotocin-diabetic rats. Excision and incision wounds were inflicted on the back of each rat, and they were treated with different concentrations (0.05%, 0.1%, 0.2%, 0.4%, and 0.5%) of aqueous extracts (200 μL per wound), which were applied topically twice daily for seven days. Both types of wounds were observed daily for the aspect and evolution of the scratch and scar (including the number of days

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required for the scar to fall off). Additionally, for incision wounds, the tensile strength after removing the sutures on day seven was measured on day ten. The results showed that the topical application of pitaya extracts contributed significantly to wound healing, and *H. undatus* did not have any hypoglycaemic activity. However, the healing activity was significant only for the aqueous extracts of flowers and leaves, while the extracts of pulp and peel showed lower wound healing activity and the rind extract produced a weak cicatrising effect. The flower extract of *H. undatus* had the most marked effect on wounded areas. Perez et al. (2005) concluded that the topical application of *H. undatus* extracts in streptozotocin-diabetic rats increased hydroxyproline (related to enhanced collagen synthesis), tensile strength, total proteins and DNA collagen content, leading to better epithelisation and facilitating the healing process.

A study conducted by Juliastuti et al. (2020) provided further evidence of the benefits of dragon fruit in wound healing processes, through the formation of collagen fibre density. The authors observed that treatment with *H. polyrhizus* peel ethanol extract at a 30% concentration increased the density of collagen fibres after tooth extraction in Wistar rats compared to the control.

Anti-hyperlipidaemic and anti-obesity activities. Dyslipidaemia is a complex disease and major risk factor for adverse cardiovascular events, as it is known to promote atherosclerosis (Pol et al. 2018).

With the aim of evaluating the effect of red dragon fruit peel powder (*H. polyrhizus*) on the blood lipid levels, Hernawati et al. (2018) fed different groups of hyperlipidaemic Balb-C male mice with different doses of pitaya peel powder, ranging from 50 to 200 mg kg^{-1} body weight (BW) during 30 days. After the treatment, blood samples of each group were analysed for total cholesterol levels, triglycerides, and low-density lipoprotein cholesterol (LDL-c) and the results showed that all these parameters decreased along with increasing doses of red dragon fruit peel powder. Hernawati et al. (2018) pointed that pitaya peel powder supplemented in foods would contribute to preventing hyperlipidaemia thanks to the benefits associated with its composition: *i*) a high content of crude fibre in the peel (69.30% total dietary fibre, divided into 56.50% insoluble food fibre and 14.82%. soluble food fibre) helps to lower the energy intake since it traps cholesterol and bile acids in the small intestine, it can increase insulin sensitivity, and it also increases satiety; *ii*) a high content of antioxidants, phenol and particularly tocotrienol (vitamin E) reduces liver cholesterol levels and plasma total cholesterol and LDL-cholesterol concentrations.

The study of Suastuti et al. (2018) on the anti-obesity and hypolipidaemic activity of methanol flesh extract of *H. costaricensis* showed that obese rats fed the flesh extract at a dose of 100 mg kg^{-1} BW decreased significantly their body weight, Lee obesity index, organ weight, visceral fat weight, total cholesterol, low-density lipoprotein, triglycerides, very low-density lipoprotein, and total cholesterol/high-density lipoprotein (HDL) ratio. In contrast, the concentration of HDL-cholesterol, faecal fat and cholesterol increased in these rats.

Sudha et al. (2017) evaluated in vitro the antioxidant, antidiabetic, and anti-lipase activities of white pitaya (*H. undatus*) juice extract. The phytochemical screening of the white dragon fruit revealed the presence of bioactive compounds with antioxidant, antidiabetic, and anti-lipase activities, such as triterpenoid, alkaloid, flavonoid, and saponin, with great value and potential uses.

In short, bioactive compounds in dragon fruit extracts, including crude fibre, phenolic, polyphenol, and flavonoid content, contribute to the decrease of serum lipid profile, since these antioxidants are able to inhibit the absorption of cholesterol in the intestine, facilitating its excretion through the faeces (Hernawati et al. 2018; Suastuti et al. 2018).

Hepatoprotective activity. A recent study of Parmar et al. (2019) evaluated possible hepatoprotective properties of methanolic extract of dragon fruit against acetaminophen-induced liver injury in rats. The animals were treated for three days, 30 min prior to acetaminophen ingestion (3 g kg^{-1} day^{-1}, p.o.), with different doses of methanolic extract of pitaya (300 and 500 mg kg^{-1}, p.o.) and silymarin (200 mg kg^{-1}, p.o.), a standardised extract obtained from seeds of Silybum marianum widely used in the treatment of liver diseases of varying origins, used in the study for comparative purposes. At the end of the last treatment, blood was collected and analysed for various serum enzymes, and the rats were sacrificed for histological studies. The results obtained by Parmar et al. (2019) supported the antioxidant and hepatoprotective potential of pitaya, both at enzymatic and histological levels: the enzyme levels of alanine and aspartate aminotransferase, alkaline phosphatase, total and direct bilirubin, lactate dehydrogenase, gamma-glutamyl transferase and total protein, as well as oxidative stress parameters such as levels of malondialdehyde, reduced glutathione and activity of superoxide dismutase and catalase were found to be restored towards normalisation by the extract of dragon fruit comparable to silymarin. Moreo-

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ver, dragon fruit was found non-toxic even at the highest dose of 5 g kg^{-1}.

Cauilan (2019) evaluated the protective effect of the oral administration of crude and ethanolic *H. polyrhizus* fruit extracts (2 500 mg kg^{-1} BW), compared to the standard treatment with silymarin, in rats with carbon tetrachloride (CCl4) induced hepatic damage. Hepatoprotective activity was detected by significant decreases in serum glutamic-pyruvic transaminase and serum glutamic-oxaloacetic transaminase levels among rats administered with *H. polyrhizus* extracts, compared to both the control group (without dragon fruit extract) and the silymarin treated group. This study suggested that the hepatoprotective activity of pitaya could be related to its rich composition of antioxidants such as triterpenes, flavonoids, glycosides, tannins, saponin, and alkaloids.

Cardiovascular protective activity. Cardiovascular disease is the leading cause of death in men and women in developed countries and accounts for up to a third of all deaths worldwide. Increased arterial stiffness is associated with an increased risk of cardiovascular events. Lifestyle change and/or an appropriate treatment can reverse the arterial stiffness associated with some medical conditions. The therapeutic and preventive potential of pitaya against oxidative stress-related diseases, mostly related to its bioactive compounds such as antioxidants, has attracted the interest of several studies. Omidizadeh et al. (2011) corroborated the hypothesis that polyphenols and antioxidant content would be the cardioprotective compounds of red pitaya. They also warned that the key to food processing being able to preserve the nutritional value and cardioprotective benefits of the tropical fruits is the selection of the right thermal processing methods.

Swarup et al. (2010) proved that nutritional supplementation with water pulp extract from *H. undatus* pitaya to streptozotocin-induced diabetic rats significantly decreased the aortic stiffness, measured as pulse wave velocity. Ramli et al. (2014a) proved that diastolic stiffness of the heart was reduced after the supplement of pitaya juice in high-carbohydrate and high-fat diet-induced metabolic syndrome rats.

Anti-inflammatory activity. Because of its composition, including compounds such as betalains and squalene, Dragon fruit has antioxidant and anti-inflammatory properties. Rodriguez et al. (2016) reported anti-inflammatory activity of maltodextrin encapsulated and non-encapsulated betalains from *H. polyrhizus* peel extract. Betalains are unstable and sensitive to degradative factors such as temperature, pH, oxygen, or light, but their bioactivity can be extended by encapsulation through the addition of a protective and impermeable layer (Jackman and Smith 1996; Mulinacci and Innocenti 2012; Rodriguez et al. 2016). Betalains inhibited sodium dodecyl sulphate (SDS)-induced vascular irritation of duck embryo chorioallantoic membrane (CAM). Encapsulated betalains by maltodextrin-gum Arabic or maltodextrin-pectin matrices exhibited five- to six-fold higher anti-inflammatory activity compared to non-encapsulated betalains. The strong anti-inflammatory activity of betalains from *H. polyrhizus* peels may be attributed to their strong antioxidant activity. Free radicals may be main pro-inflammatory mediators; thus, removal of the mediators leads to alleviation of the inflammatory response (Rodriguez et al. 2016).

Eldeen et al. (2020) investigated the anti-inflammatory properties of flesh and peel of *H. undatus* and identified its main bioactive compounds. They found betalains, which are known to have high radical scavenging activity, and they reported for the first time the presence of squalene (a polyunsaturated hydrocarbon with a formula of C30H50 and formed by six isoprene units) in the flesh of the fruit as the dominant constituent (13.2%). According to their results, squalene exhibited inhibitory activity against three pro-inflammatory enzymes, i.e. 5-lipoxygenase, cyclooxygenase-2, and acetylcholinesterase, with EC50 values ranging between 46 and 47 µg mL^{-1}. The study of Eldeen et al. (2020) showed the potential of pitaya for the management of neuronal and inflammatory conditions through different mechanisms including leukotrienes, prostaglandins, and cholinergic pathways.

Anti-anaemia activity. Pitaya contains essential nutrients, including precursors required for the erythropoiesis, such as iron (Fe), vitamins C, E, B12, thiamine, and riboflavin (Tenore et al. 2012). Rahmawati et al. (2019) conducted a study to evaluate the effect of dragon fruit on postpartum mothers, who are considered susceptible to anaemia. Postpartum mothers were supplied with 400 cc of *H. polyrhizus* fruit juice (obtained from 500 g of pitaya) for 14 days. The results showed that levels of haemoglobin, haematocrit, and erythrocytes increased significantly in the treatment group, compared to the control group. According to Rahmawati et al. (2019), the high content of vitamin C in the dragon fruit is responsible for its anti-anaemia activity, as it facilitates the absorption of iron needed in the production of blood and non-heme iron.

Prebiotic potential. Prebiotics are non-digestible oligosaccharides that stimulate the growth of normal flora in the colon and provide protective effects against intestinal diseases, such as colon cancer (Gibson et al. 2004;

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Khuituan et al. 2019). White and red-flesh dragon fruit contains, as major carbohydrates, glucose, fructose, and some oligosaccharides (total concentrations of 86.2 and 89.6 g kg^{-1}, respectively) (Wichienchot et al. 2010). The fruit of *Hylocereus undatus* contains a high amount of mixed oligosaccharides (75% of dry matter with a predominant degree of polymerisation 2, 3, 4, and 5) (Pansai et al. 2020). The percentage of mixed oligosaccharide content in *H. undatus* ethanolic flesh extract was quantified as 85% (Choo et al. 2016). Pansai et al. (2020) evaluated the properties of dragon fruit as potential prebiotics and immune capacity stimulant and found that dragon fruit oligosaccharides (DFO) increased faecal bifidobacteria and lactobacilli but decreased bacteroides and clostridia. Additionally, the study showed that DFO also have immune response boosting properties by increasing concentrations of immunoglobulin A and G.

Wichienchot et al. (2010) investigated the dragon fruit as a potential source of high-yielding oligosaccharides for commercial prebiotic production. They found the optimal extraction conditions for pitaya flesh in 80% (w/v) ethanol, solvent to flesh ratio of 2 : 1 at ambient temperature (ca. 28 °C). Their results showed that oligosaccharides from dragon fruit have several functional properties which make them suitable as ingredients in functional food and nutraceutical products. These properties include reduced calorie intake and insulinaemia, compared to digestible carbohydrates, and particularly prebiotic properties, such as resistance to acid conditions in the human stomach, partial resistance to human salivary α-amylase and the capability to stimulate the growth of lactobacilli and bifidobacteria.

The use of dragon fruit as a dietary supplement has further benefits associated with its mixed oligosaccharide content, including the increase of colonic smooth muscle contractions without morphological change, bulk-forming facilitation, and laxative stimulation to increase faecal output and intestinal motility (Khuituan et al. 2019).

DRAGON FRUIT IN VIETNAM

Productions and exports of dragon fruits in Vietnam. At the present time, two species of dragon fruit, *Hylocereus undatus* (white flesh) and *H. polyrhizus* (red flesh), are widely cultivated in 63/65 provinces/cities of Vietnam, occupying about 95% and 5% of the total cultivated area, respectively (Hoat et al. 2018). The total growing area of dragon fruit in Vietnam expanded quickly from 5 512 ha in 2000 to 55 419 ha in 2018, with total output production of 1 074 242 t and export values of about USD 1.1 billion. Moreover, according to the Vietnamese General Department of Customs, dragon fruit accounts for 32% of the total export value of vegetables and fruits of Vietnam (Hien 2019). Pitaya is currently cultivated all around the country, although most growing areas are located in the southeast and the Mekong River Delta (Figure 2). Three provinces concentrate most of the production and are specialised in large-scale cultivation, i.e. Binh Thuan, Tien Giang, and Long An, in decreasing order of crop extension and production. Thus, Binh Thuan province has the largest area of pitaya in Vietnam accounting for about 52.28% of the total cultivated area and 55.11% of the production. Long An is the second largest area, with 20.35% of cultivated area and 24.51% of the production. At the third place, Tien Giang province contributes with 14.48% of cultivated area and 15.04% of the production (Hoat et al. 2018; Hien 2019).

Vietnam leads the world in this exotic tropical fresh fruit exports, with 80–85% of the output production being exported to over 40 countries and territories, while only the remaining 15–20% of the production is consumed in domestic markets. The main key markets are China, Thailand, Indonesia, Malaysia, Singapore, the Netherlands, Spain, Germany, the United Kingdom, Australia, Canada, and the United States (Hoat et al. 2018; Hien 2019). According to the Ministry of Industry and Trade of Vietnam, 80% of dragon fruit produced in Vietnam is exported to China and 99% of dragon fruit on the Chinese market is imported from Vietnam (The Asia Foundation 2019). However, this situation is slowly changing, as China has been gradually increasing the growing areas of dragon fruit and exploiting potential export markets for this fruit has become necessary for the Vietnamese economy. A survey of the Centre for the Promotion of Imports (CBI) from developing countries (CBI 2019) revealed that Europe is a potentially big market to export dragon fruit. However, expanding to the European market requires high-quality standards, where the collaboration and awareness of all the actors involved in the control of the pitaya production processes are necessary for the acquisition of both international and national standard certificates for the good agricultural practices (GAP), such as Global GAP and Viet GAP, which guarantee clean and safe products for health and environment.

The state of cultivations of dragon fruit at Mekong River Delta. The Mekong River Delta (in the southwestern region in Vietnam) has typical climate conditions of a tropical country, including two seasons, i.e. wet and dry. Under climate change conditions, lack

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of water and increase of salinity levels in the dry season have been raising serious problems in the region (Eastham et al. 2008). Although dragon fruit is commonly known as a salt sensitive plant (Mizrahi et al. 1997; Cavalcante et al. 2008), it tolerates salinities up to 6.4‰ (10.0 dS m^{-1}) depending on the plant vegetative stage (Bárcenas-Abogado et al. 2002; Cavalcante et al. 2008). In addition, dragon fruit has high drought resistance (Nie et al. 2015; Wang et al. 2019). At the Vietnamese province of Ca Mau (Figures 2 and 4), local farmers experimentally planted dragon fruit in a mangrove area, using a white mangrove tree (*Avicennia marina*) as a trellis. Interestingly, dragon fruits improved their tolerant capacity and grew well under these salinity conditions (Figure 4). Currently, although the crop yield is not as productive as that of dragon fruit from other regions in the country where it grows under "normal" soil conditions, the harvested fruits achieved a good reputation among local consumers (Binh-Nguyen 2020).

Two of the three provinces with the largest planting areas of dragon fruit, and therefore concentrating most of the production in Vietnam, are located in the Mekong Delta region, i.e. Long An and Tien Giang. When considered together, they contribute to almost all the growing areas of pitaya in the Mekong Delta (Hoat et al. 2018; Figure 5). Tra Vinh province, also located in the Mekong Delta and smaller than Long An and Tien Giang provinces, has been strongly investing and developing new plantations of dragon fruit (Hoat et al. 2018; Figure 5). Tra Vinh is the poorest coastal province in the Mekong River Delta, with over 80% of the population dependent on the agricultural sector and about 30% of the Khmer people population (World Bank Group 1999). Hence, finding the way towards a sustainable agriculture development, in the context of the serious lack of fresh water and saline infiltration, is a key duty for the local governments of the Mekong Delta region. The map of the expansion of the areas dedicated to the cultivation of dragon fruit in the three biggest production provinces of the Mekong Delta since 2010 shows a remarkable hectare increase in all the provinces (Figure 5). This growth trend, however, is slightly different over the time in each province. Thus, while Long An experienced the greatest growth in the area (ha) dedicated to pitaya in the periods 2010–2013 and 2013–2016, with increases up to 3.0 and 2.5 times, respectively, Tien Giang and Tra Vinh exhibited an increase of about 1.5 to nearly 2.0 times in these years. In the period 2016–2019, the growth trend of areas dedicated to pitaya cultivation was maintained in the three provinces, but while Tien Giang and Long An showed a rise of only 2.0 and 1.5 times, respectively, Tra Vinh increased 4.0 times the cultivation areas.

The commitment of Vietnam to the production of dragon fruit is clearly shown by the remarkable increase in cultivated areas, particularly in the Mekong River Delta. The exports of this product have brought

Figure 4. Dragon fruit grown clung to the white mangrove trees in the mangrove area of Ca Mau province, Vietnam

Arrows show white mangrove trees [*Avicennia marina* (Forssk.) Vierh.]; arrowheads point to dragon fruit clung to the tree (adapted from Binh-Nguyen 2020)

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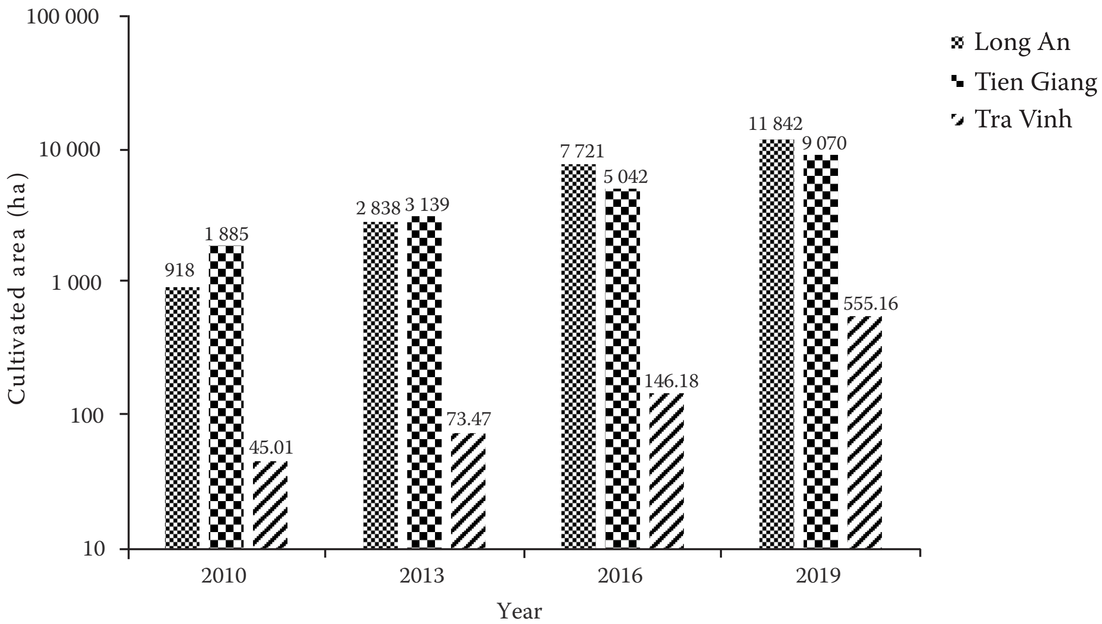

Figure 5. Increase in the growing areas dedicated to dragon fruit in the major producing provinces of the Mekong Delta region from 2010 to 2019 (unpublished data from Tra Vinh Statistical Office, Vietnam)

great benefits for Vietnamese agriculture, proving its value in the sustainable development of the country, especially in the southwestern region.

CONCLUSION

Due to its nutritional and medical properties, the dragon fruit brings numerous benefits to human health, mostly for the control and management of the oxidative stress. All the different parts of the pitaya (i.e. stems, flowers, peels, and pulps) contain bioactive compounds involved in a wide range of beneficial biological activities, including, antioxidant, antimicrobial, and anticancer capacities. These include betalains, flavonoids, polyphenols, terpenoids and steroids, saponins, alkaloids, tannins, and carotenoids, which have been proven as effective, healthier, safer and sustainable alternatives to synthetic drugs for the treatment and prevention of many diseases such as diabetes, cancer, obesity, hyperlipidaemia and pathogenic agents such as viruses, bacteria, and fungi. Besides the pharmaceutical value of its compounds, the pitaya is also a natural source of colourants with potential uses in the food and cosmetic industries.

The dragon fruit, due to its ecological characteristics, benefits to human health, and the commercial value has become a cost-effective product for the Vietnamese economy and a driving force in the sustainable development of the country, particularly in the promotion of sustainable use of ecosystems and biodiversity of the southwestern region, more sensitive to the effects of climate change. The high adaptability and tolerance of the pitaya to a wide range of severe environmental conditions explains the success of the experimental planting model of this climbing cactus in the mangrove areas (high salinity environment) of the Mekong Delta region. Further studies are yet needed to understand the adaptive mechanisms underlying saline tolerance of the dragon fruit and to select genotypes capable of growing under the increasingly severe conditions caused by global climate change.

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