

Anti-Inflammatory, Antioxidant, and Other Health Effects of Dragon Fruit

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Abstract: Dragonfruit (*Hylocereus* genus) has the potential for the prevention of diseases associated with inflammatory and oxidative processes. We aimed to comprehensively review dragon fruit health effects, economic importance, and possible use in delivery systems. PubMed, Embase, and Google Scholar were searched, and PRISMA (Preferred Reporting Items for a Systematic Review and Meta-Analysis) guidelines were followed. Studies have shown that pitaya can exert several benefits in conditions such as diabetes, dyslipidemia, metabolic syndrome, cardiovascular diseases, and cancer due to the presence of bioactive compounds that may include vitamins, potassium, betacyanin, p-coumaric acid, vanillic acid, and gallic acid. Moreover, pitaya has the potential to be used in food and nutraceutical products as functional ingredients, natural colorants, ecologically correct and active packaging, edible films, preparation of photoprotective products, and additives. Besides the importance of dragon fruit as a source of bioactive compounds, the bioavailability is low. The development of delivery systems such as gold nanoparticles with these compounds can be an alternative to reach target tissues.

Keywords: dragon fruit, pitaya, *Hylocereus*, antioxidant, anti-inflammatory, health effects, delivery system

I. INTRODUCTION

Due to the profound changes in lifestyle resulting from modern life, there has been a progressive increase in non-communicable chronic diseases.

Among them, cardiovascular diseases (CVD) are among the most deadly diseases in the world (32% of all global deaths) in western countries. Besides mortality, these conditions are associated with the leading cause of disabilities. Therefore, preventive measures are crucial to reduce the risk factors. Fruit and vegetables are essential compounds of a healthy diet, and their consumption in adequate amounts can diminish the risk of obesity, diabetes, CVD, and some types of cancer. Estimates from the World Health Organization (WHO) indicate that inadequate consumption of fruit and vegetables is among the top ten risk factors for the global burden of diseases worldwide [1,2,3],4. Over the years, countless fruits have been associated with the prevention of non-communicable chronic diseases, and pitaya has also been considered [5],6. The dragon fruit of pitaya is a rustic fruit belonging to the Cactaceae family, the genus *Hylocereus*. It is known as dragon fruit due to the presence of bright red skin with overlapping green fins covering the fruit. Other common names given to this fruit are pitahaya, dragon pearl fruit, night-blooming cereus, strawberry pear, and Cinderella plant. Depending on the species, its fruits may have different characteristics, such as shape, presence of thorns, skin, and pulp color, reflecting high genetic variability [5,6,7]. The health-promoting potential of pitaya fruit is due to the presence of bioactive compounds related to numerous benefits such as anti-diabetic, anti-inflammatory, antioxidant, anti-cancer, and antimicrobial. As a result of these beneficial actions, the consumption of this fruit has increased in different regions worldwide [7,8]. Dragonfruit is becoming popular in many countries and is consumed raw



or can be added to drinks, jelly, and candies. In addition, the pigments can be used as a coloring agent in the pharmaceutical and food industries [9]. Three varieties that are distinguished by color of the skin and flesh are mainly cultivated: *Hylocereus undatus* (possessing white flesh and red skin), *H. polyrhizus* (with red skin and red flesh), and *H. megalanthus* (yellow skin and white flesh) [6,10]. The fruit has an oval shape, and the pulp has a sweet and sour taste. The seeds are very small and black-colored [11,12]. Figure 1 and Figure 2 show the plant, the flower, and the fruit of *Hylocereus* spp.



Figure 1





Figure 2.

The fruit of *Hp. olyrhizus*(A), *H. undatus*(B), and *H.megalanthus*(C).

In addition, there are some studies showing dragon fruit's effects, but there is still a need for detailed scientific investigations to show the benefits this plant can bring to consumers. Moreover, dragon fruit can open a new window for developing multi-targeting drugs to prevent and treat several diseases and can be used for several technological applications in the food and pharmaceutical industries. For these reasons, we aimed to comprehensively review dragon fruit's health effects, its economic importance, and its possible use in delivery systems. To the best of our knowledge, this is the first review considering the species *H. undatus*, *H. polyrhizus* and *H. megalanthus* and their role in health and technological applications.

II. MATERIALS AND METHODS

2.1. Focused Question

The focal question for this review was: what are the effects of the genus *Hylocereus* fruit on health?

2.2. Language

We used only studies published in English language.



2.3. Databases

For this review, we consulted the following databases: PubMed, EMBASE, Google Scholar, and COCHRANE.

2.4. Study Selection

In this review, we included Randomized Controlled Trials (RCTs) that studied the effects of the genus *Hylocereus* on human health. Moreover, in vitro and in vivo studies were considered. The MeSH terms applied were pitaya or dragon fruit or *Hylocereus* or *H. undatus* or *H. polyrhizus* or *H. megalanthus* and health or glycemia or blood pressure or cholesterol or lipids or body mass index or obesity or body weight or cardiovascular diseases. The inclusion criteria were RCTs, placebo-controlled studies, quasi-experimental studies, and in vivo and in vitro models. Only full texts were added. The exclusion criteria were articles performed in languages other than English, Spanish, and Portuguese, poster presentations, editorials, and case reports. Review texts helped in the discussion section.

2.5. Data Extraction

We did not restrict a period for the search for trials. The search for human, animal, and in vitro studies followed Preferred Reporting Items for a Systematic Review and Meta-Analysis (PRISMA) guidelines.

2.6. Quality Assessment

To perform a quality assessment, the evaluation of the presence of risk of bias in the RCTs (detection, selection of the study, and reporting biases) was performed according to The Cochrane Handbook for Systematic Reviews of Interventions [14]. Additionally, the evaluation of the presence of risk of bias in the included animal studies (detection, selection of the study, and reporting biases) was performed according to the Systematic Review Centre for Laboratory animal Experimentation RoB tool (SYRCLE'S guidelines) [15].

2.7. Evaluation of Economic Importance and Technological Applications

Other studies, such as research studies, reviews, and metanalysis, were evaluated to help describe the possible technological applications of pitaya and the economic importance of this plant.

III. RESULTS

Many studies have shown that dragon fruit can benefit numerous health problems and work as an analgesic, antioxidant, anti-diabetic, anti-cancer, cardio-protective, liver protective, and neuroprotective. However, only five clinical trials were found and included. All of them were performed with *Hylocereus*. Three of them were performed in Malaysia [16,17,18], one was performed in Indonesia [19], and one in the United Kingdom [20]. The primary outcomes were improved glycemia, lipid profile, and antioxidant status [16,17,18], flow-mediated dilation, and arterial stiffness [20]. In vitro studies showed anti-glycation, anti-diabetes, anti-viral, anti-plasmodium, hepatoprotective, immunomodulatory, and osteogenic effects. In vivo studies have also shown the effects of the genus *Hylocereus* on animal models (Table 1). Lira et al. [21] demonstrated the anxiolytic effects of pitaya in zebrafish. Anand Swarup et al. [22] demonstrated that pitaya's pulp extracts have potent actions against arterial stiffness, reducing blood pressure and controlling pulse wave velocities. Holanda et al. [23] investigated the effects of *Hylocereus* on the lipid and glycemic profile of rats. Silva et al. [24] investigated the use of red pitaya in glycemia. Yeh et al. [25] and Ramli et al. [26] showed that pitaya affects the liver's health, reducing liver lipids content and enhancing the enzymatic potential of the hepatocytes against liver injuries. Ramli et al. [27] and Song et al. [28] demonstrated more profoundly the metabolic effects of pitaya, principally in enhancing lipid metabolism, diminishing obesity, and augmenting the gut microbiota content of Akkermansia. Macias-Ceja et al. [29] demonstrated that pitaya could exert anti-inflammatory actions in rats' gastrointestinal systems, principally regulating pro-inflammatory pathways and diminishing the chance of rats developing colitis.



Lastly, Perez et al. [30] demonstrated that many extracts of pitaya could exert wound-healing effects against diabetic-induced wounds principally by enhancing tensile strength, hydroxyproline, DNA, total proteins, collagen content, and epithelization. The evaluation of the bias of the animal studies

IV. DISCUSSION

4.1. Bioactive Compounds of Hylocereus Species

The phytochemical compounds found in dragon fruit mainly belong to phenols, flavonoids, sterols, fatty acids, and tocopherol. Among the numerous bioactive compounds found in the pulp and peel, it is possible to highlight the presence of ascorbic acid, tocopherol, thiamin, niacin, and riboflavin, minerals like calcium, magnesium, potassium, phosphorous, betacyanin, β -carotene, lycopene, p-coumaric acid, protocatechuic acid, vanillic acid, gallic acid, syringic acid, and p-hydroxybenzoic acid. The properties of these phytochemicals Tahre analysis performed on *H. undatus* pulp with different solvents indicated the presence of carbohydrates, tannins, saponins, anthocyanins, quinones, glycosides, terpenoids, triterpenoids, phenols, acids, and steroids in aqueous extract. In the methanolic extract, carbohydrates, tannins, saponins, flavonoids, alkaloids, anthocyanins, cardiac glycosides, terpenoids, triterpenoids, phenols, acids, and steroids were identified. Extraction with hexane showed carbohydrates, saponins, anthocyanin, quinones, phenols, and acids. Carbohydrates, saponins, alkaloids, cardiac glycosides, triterpenoids, phenols, and coumarins were extracted in chloroform, as well as carbohydrates, tannins, saponins, flavonoids, alkaloids, anthocyanin, cardiac glycosides, terpenoid acids, triterpenoids and steroids in ethyl acetate .

4.2. Healthy Benefits of Hylocereus Species

Dragon fruit has been used as a medicinal food since ancient times by Mayas—using the fruit and the flowers as hypoglycemic, wound disinfectant and diuretic, for dysentery, tumor dissolution, and as a healing agent. Moreover, the flowers and the seeds can be used as beverages for gastritis, as laxatives, and to improve kidney function. These properties are derived from the multi-bioactive compounds found in this plant, mainly in the fruit. Furthermore, it shows no toxicity since a study with dragon fruit extract at a dose of 1250 to 5000 mg/kg did not produce interferences or abnormalities in the organs of animal models Below it is possible to find some effects of pitaya fruit.

As the results found in the use of pitaya pulp or its bioactive compounds can exert anxiolytic, antioxidant, and anti-inflammatory effects in animal models.

Improvements in hepatic steatosis and reduction of liver injury are also observed, in addition to balancing the intestinal microbiota. These results in animal studies allow us to say they can also be observed in humans.

4.2.1. Antioxidant Effects by Species

Hylocereus polyrhizus is rich in betalains and other bioactive compounds such as vitamins and phenolic compounds that exert relevant antioxidant properties and, for these reasons, are related to the prevention of several human diseases. The oil results from the seeds, and the peel is also an essential source of antioxidant compounds. The peel of *H. undatus* possesses more flavonoids than the flesh .

The antioxidant properties of dragon fruit extract were investigated. Total antioxidant status was reduced in pre-diabetic and normocholesterolemic subjects that consumed red pitaya. Arapand and Amelia showed that fruit extract could minimize oxidative damage production in animals submitted to physical exercises. Other authors have shown that the pulp extract can decrease oxidative damage in STZ-induced diabetes in rats .

Putri et al. showed that the intake of red dragon fruit could reduce malondialdehyde levels in diabetic rats and, for these reasons, is associated with reducing the oxidative stress related to this disease. shows the main antioxidant effects associated with the *Hylocereus* species.



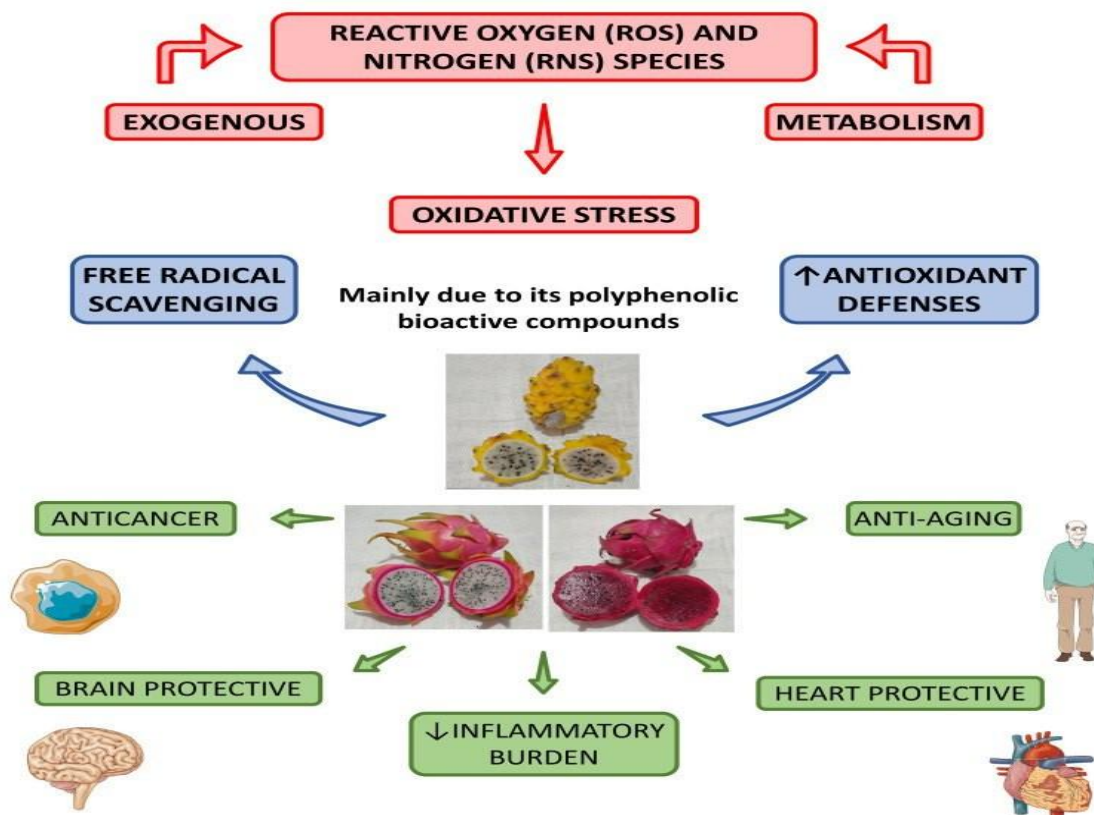


Figure3.

Main antioxidant effects of Hylocereus species and their health effects. ↑ —increase; ↓ — decrease.

4.2.2. Anti-Inflammatory Effects

Besides the antioxidant actions, dragon fruit can also exert anti-inflammatory actions. Saenjume et al. [45] found anthocyanins (cyanidin 3-glucoside, delphinidin 3-glucoside, and pelargonidin 3-glucoside) in the pulp and peel of pitaya red. The authors found that the pulp enriched with the first anthocyanin (cyanidin 3-glucoside) inhibited the synthesis of reactive oxygen and nitrogen species, cyclooxygenase-2 (COX-2), and inducible nitric oxide synthase (iNOS), in in vitro models and without resulting in cytotoxicity.

Another study showed that the dragon flesh and peel extract and the isolated squalene led to the inhibition of pro-inflammatory enzymes such as cyclooxygenase-2, lipoxygenase, and acetylcholinesterase and concluded that this fruit could produce a significant potential for the control and management of inflammatory processes through different pathways that may include, prostaglandin, leukotriene, and cholinergic pathways [73].

Amim et al. [74] found different effects (anti-inflammatory, antioxidant and anti-bacterial actions) in the extracts of *Hylocereus polyrhizus* and *H. undatus* (the aqueous extract of *H. polyrhizus* showed most significant effects than *H. undatus*). The authors found that the aqueous extract of these species resulted in more protective anti-inflammatory and antioxidant activities compared to the ethyl acetate and ethanolic extracts.

Al-Radadi et al. [75] found significant anti-inflammatory, anti-diabetic, anti-Alzheimer, and cytotoxic effects of gold nanoparticles using pH. *Hylocereus* species. Figure4 shows the most prominent anti-inflammatory effects associated with the *Hylocereus* species.



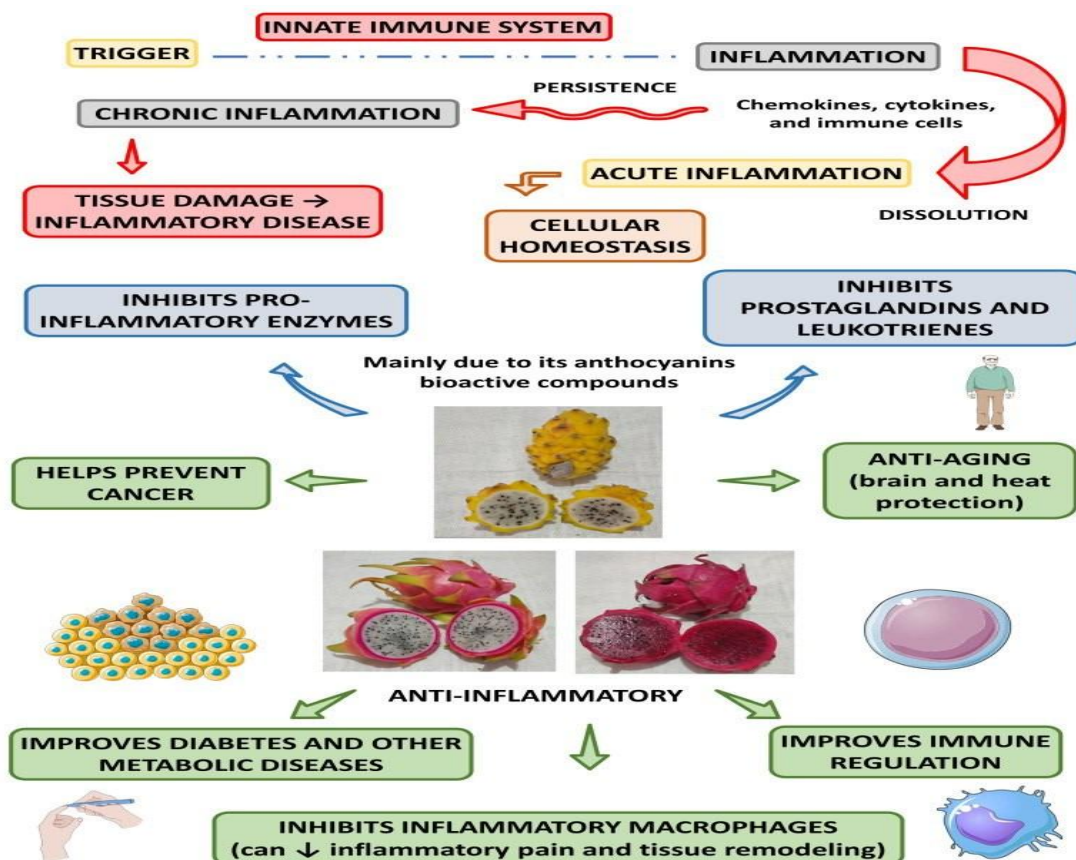


Figure4.

Main anti-inflammatory effects of *Hylocereus* species and their health effects. ↓ —decrease.

4.2.3. Prebiotic Effects

The main carbohydrates in white and red flesh dragon fruit are glucose, fructose, and oligosaccharides. The mixed oligosaccharides are resistant to hydrolysis by human α -amylase and artificial human gastric juice (about 34.88% and 4.04%, respectively). Moreover, the mixed oligosaccharides can also stimulate the growth of lactobacilli and bifidobacterial, thus showing prebiotic properties [76]. Dasaesamoh et al. [77] showed that the fecal fermentation of pitaya oligosaccharides increased the populations of Bifidobacteria and Lactobacillus and reduced the populations of Bacteroides and Clostridium. Moreover, ethanolic fermentation resulted in a positive prebiotic effect. Lactic acid, acetic acid, propionic, and butyric acids were produced at substantial concentrations.

4.2.4. Antimicrobial Effects

In a study to investigate the antimicrobial effect of red pitaya pTeelms,ak et al. [78] found that the extract has efficient in vivo and in vitro effects against several microorganisms, such as *Escherichia coli* and *P. aeruginosa*. Sushmitha et al. [79] investigated the effects of *H. datus* seeds in Gram-negative and Gram-positive bacterial species and found that the minimum inhibitory concentration is 50 μ L for *Staphylococcus aureus* and *Escherichia coli*. Tenore et al. [80] also found antimicrobial activity for hexane, chloroform, and ethanol extract of the skin of *H. undatus* and showed inhibition of the growth of Gram-negative and Gram-positive bacteria.



Extract of the peel and fruit of the red dragon fruit can also exert anti-fungal actions against *Rhizoctonia solani*, *Candida albicans*, *Aspergillus flavus*, *Botrytis cinerea*, *Fusarium oxysporum*, and *Cladosporium herbarum* [80].

4.2.5. Anti-Cancer Effects

Some studies have shown the anti-cancer potential of dragon fruit. Duiivta. karant et al. [81] aimed to evaluate the ability of this fruit to produce nanoparticles and found they can significantly inhibit the growth of MCF-7 breast cancer cells. Another study showed that the fecal fermentation of pitaya oligosaccharides augmented the populations of *Lactobacillus* and decreased the populations of *Bacteroides* and *Clostridium*, and resulted in the production of lactic acid, acetic acid, propionic and butyric acids that can inhibit Caco-2 cells and has a potential for risk reduction in colon cancer [77].

In a very interesting study, Padmavathy et al. [37] demonstrated that methanol extracts of *H. undatus* have promising anti-cancer effects against human liver cancer (HepG-2) cells.

Wu et al. [82] investigated the anti-proliferative effect of red pitaya on B16F10 melanoma cells. They showed that the peel has stronger inhibition of the growth of these cancer cells than the flesh. The authors concluded that both peel and flesh are rich in polyphenols and good sources of antioxidants, and for these reasons, the peel can inhibit the growth of melanoma cells.

The anti-cancer activities promoted by pitaya are related to several bioactive compounds such as phenolic acids, flavonoids, and betacyanin [83,84].

Figure 5 shows the most pronounced anti-cancer effects associated with the *Hyllocereus* species.

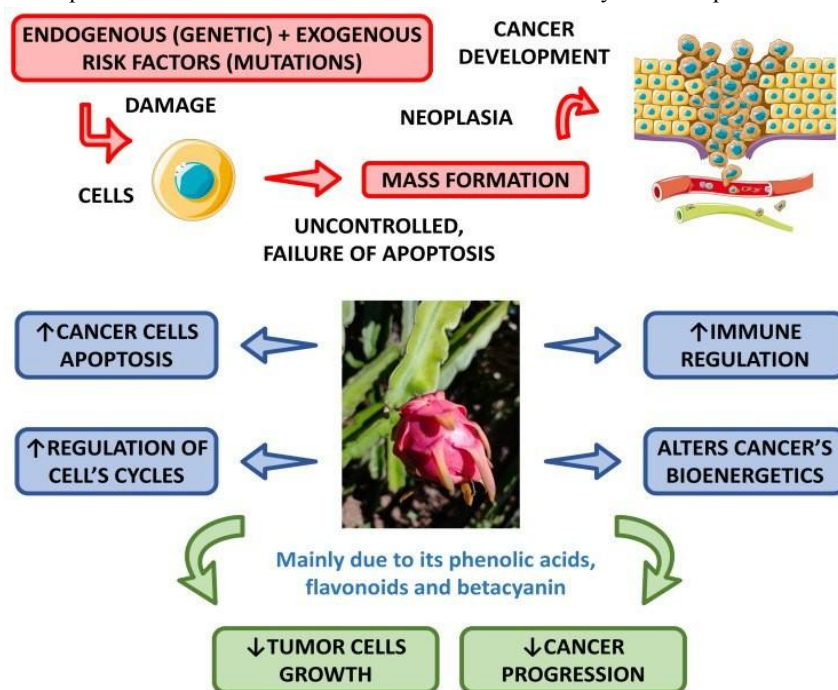


Figure 5.

Main anti-cancer effects of *Hylocereus* species. ↑ —increase; ↓ —decrease.

4.2.6. Anti-Diabetic Effects

Many studies have demonstrated that the consumption of red pitaya can reduce glycemia in humans [16,17,18]. In a systematic review and meta-analysis, Iso et al. [8] found that dragon fruit can be used to prevent diabetes.



The study of Putri et al. [72] showed that pitaya associated with metformin could significantly decrease glycemia and HOMA-IR (homeostasis model assessment-Insulin Resistance) in type 2 diabetic rats. The authors suggested that red dragon fruit could be used as an alternative to metformin due to its effectiveness in decreasing HOMA-IR (and thus, insulin resistance) and malondialdehyde levels. Moreover, the consumption of red pitaya promoted a hypoglycemic effect in dyslipidemic C57BL/6 mice, contributing to reducing the risk of insulin resistance [85].

Fadlilah and Sucipto [19] found that pitaya (pHo. lyrhizu) effectively reduces fasting blood sugar levels in students who consume high calories daily.

Marietta et al. [86] investigated the effects of red pitaya skin extract on glycemia and lipid profile of diabetic and dyslipidemic male Wistar rats and found no significant reduction in glycemia.

4.2.7. Anti-Lipidemic Effects

The use of red pitaya can improve lipid profile, decrease total cholesterol, LDL-c, and triglycerides, and increase HDL-c levels in normocholesterolemic subjects, pre-diabetic, and type 2 diabetic patients [16,17,18].

The consumption of red pitaya also showed benefits in lipid levels in dyslipidemic C57BL/6 mice, contributing to reducing cardiovascular diseases [85].

The study of Marietta et al. [86] evaluated the effects of the consumption of red pitaya skin extract on the lipid profile of male Wistar rats with diabetes and dyslipidemia and did not find a significant reduction in the lipid profile of these animals.

Setiawan et al. [87] investigated the effects of Hpo. lyrhizus peel powder on male Balb-c mice. Their results showed decreased triglycerides, total cholesterol levels, and LDL-c. Moreover, they observed an increase in HDL-c levels. The authors concluded that the use of the peel of this fruit could improve the blood lipid of mice with hyperlipidemia.

Figure 6 shows the most relevant anti-lipidemic and anti-diabetic effects associated with the *Hylocereus* species and how these effects are associated with atherosclerosis.



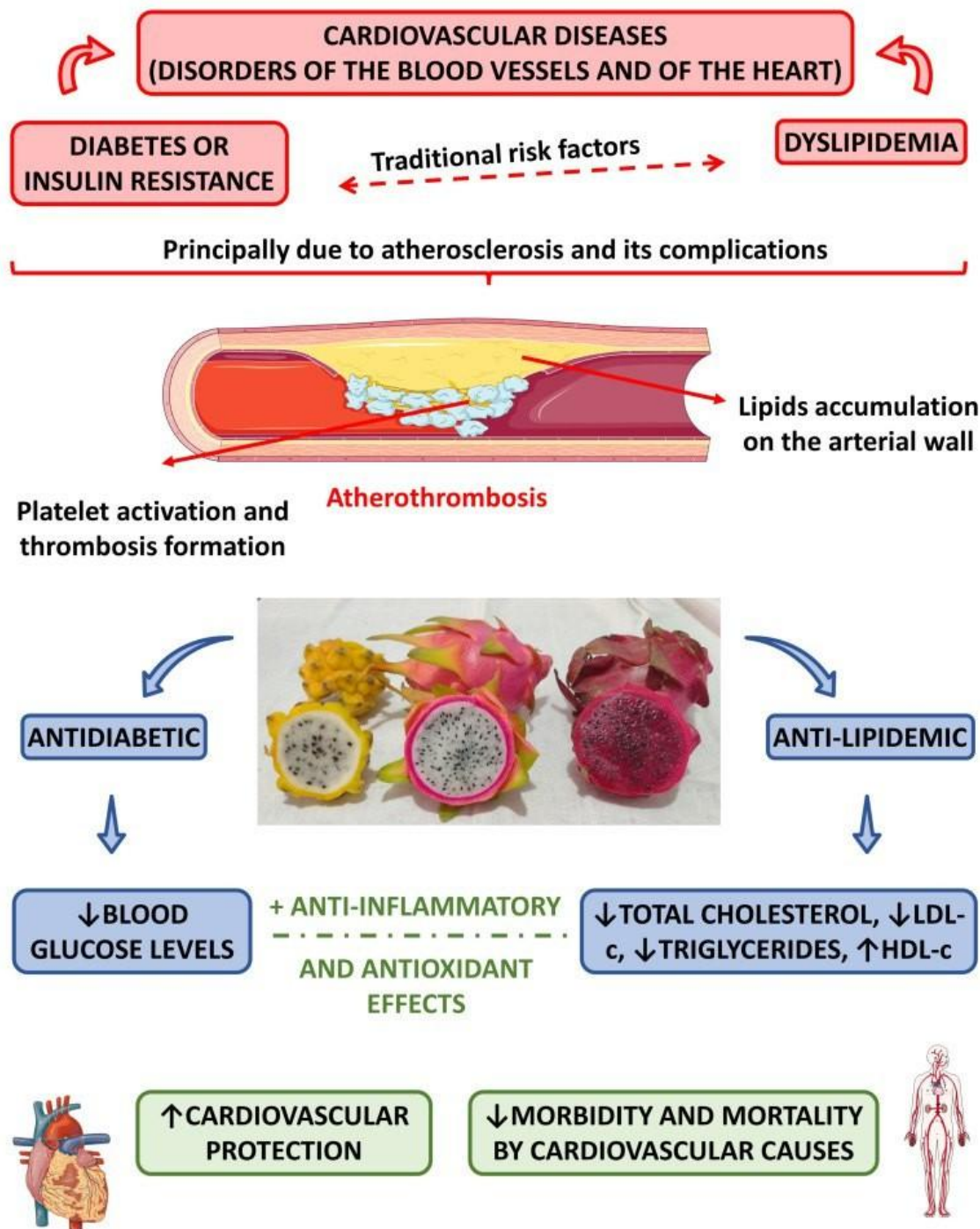


Figure6

Cardiovascular protective effects of the Hylocereus species. ↑—increase; ↓—decrease; HDL-c—high-density lipoprotein cholesterol; LDL-c—low-density lipoprotein cholesterol.



4.3. Technological Applications and Economic Importance

With the opening of trade, the world fruit market has become more competitive and open to novelties, such as native and exotic fruits, mainly due to media disclosures about the benefits of fruit consumption, highlighting them as healthy, balanced, functional and diversified—with the colors, shapes, smell, and flavors, which aroused the desire for native and exotic fruits. The pitayas are within the exotic fruits group and have aroused consumers' interest. Due to their high commercial and tolerance to water stress, they also aroused the interest of fruit growers in their planting and cultivation [96,97,98,99]

In the exotic fruit market, pitaya has stood out in Brazil and other parts of the world since it has agronomic and economic potential due to its rusticity. Commercial value is high since production, transport, and distribution costs require specialized logistics and quality control [100,101,102]

Each part of dragon fruit (pulp, rind, seeds, flower buds, dried flowers) has tremendous nutritional value in terms of antioxidants, fiber, vitamin C, and minerals, especially calcium and phosphorus, nutritional attributes that caught researchers' attention so that it can be used and processed in different products. The fruit peel has the potential as an anti-bacterial agent, natural dye, and antioxidant, in addition to the nutritional benefits of ripe fruit. The young stem and fresh flower buds are also edible and can be used as a vegetable. The dried flowers were considered to make a tea rich in antioxidants. The fruit pulp can be used to produce juice, wine, jam, and other products. The skin is used for the extraction of natural colorings as well as a source of pectin, and the seeds are mainly used to extract the oil, which contains about 50% essential fatty acids. In addition, seeds are an ingredient in many food products, such as syrups, ice creams, candies, and yogurts [5,103].

Pitaya skins are rich in betacyanins, which contribute greatly to the fruit's abundant red appearance. The main betacyanin compounds are betanin, betanidin, phylococyanin, isophylococyanin and hydroxybetanidin. Due to the numerous bioactive compounds that can be recovered, the use of food products as functional ingredients or natural colorings would help improve the overall added value of pitaya and reduce the environmental impact. Unlike anthocyanins, betacyanins can maintain desirable pH stability in the range of 3 to 7, but betacyanins can have stronger antioxidant activities, which suggests great potential to be applied in the food and nutraceutical industries. [94,103,104] Betacyanins, in particular, cover a class of natural red-violet coloring pigments with chemical and biological properties for broad-ranging applications in the food, cosmetic, and pharmaceutical industries [50,105]. A study by Belluciet al. [106] found that red pitaya extract can be considered a natural additive to improve color and sensory acceptance of meat products.

Betacyanins can be applied as a natural dye to improve color property. On the other hand, the dietary fiber in dragon fruit peel can be used to replace partial fat in products such as ice cream. In one study, *Hylocichla* peel was introduced as a fat substitute to formulate high-fiber, low-calorie ice cream [107,108].

Another use of dragon fruit in the industry is the development of environmentally friendly, active packaging and edible films to extend the shelf life of food products, with the recovery of betacyanins and other phenolic compounds [109,110]. Betacyanins can be recovered to be used as active packaging or as an edible coating [109,111].

Tamagno et al. [112] suggest using microencapsulated pitaya (*H. undatus*) pulp extract as a food supplement to minimize the effects of copper poisoning and to avoid oxidative damage caused by metals.

According to Hübner [113], adding dragon fruit pulp and ginger in the secondary fermentation process produced beers with superior antioxidant capacity compared to the control beer, suggesting an alternative flavor, aroma, and antioxidant compounds in this style of beer.

The results of a study performed by Vijayakumar et al. [114] demonstrated that *H. polyrhizus* bark extract is a potent antioxidant with photoprotective properties. In addition, the phenolic compounds and flavonoids helped the overall antioxidant properties, the high sun protection factor value, and broad-spectrum UVA and UVB photoprotection.

Moreover, a study using red pitaya extract showed that it presents substantial blood biocompatibility and physiological stability. The green production of gold nanoparticles with fruit extract can be an alternative to chemical production and is important for biological and medical applications [75].



4.4. Delivery Systems for Hylocereus Compounds

With the increased incidence of chronic degenerative diseases, consumers are increasingly interested in nutritional, healthy, and safe food. For these reasons, the demand for natural products has increased substantially. For example, the search for pigments to substitute artificial colorants or additives in food products has been a desired target. Moreover, natural compounds may also be associated with anti-inflammatory and antioxidant actions that would meet the need for prevention and, or, as adjuvants in treating many chronic conditions [115,116,117,118,119,120]. On the other hand, bioactive compounds may not have the necessary bioavailability to reach target tissues in the body and rapidly undergo degradation under many types of storage, processing, or the gastrointestinal environment, due to oxygen, temperature, pH, light, and enzyme exposure. The possible effectiveness of bioactive compounds depends on their bioavailability, and, for these reasons, this is an obstacle to overcome [121,122].

The need to study drug delivery systems aims to maximize therapeutic efficacy or minimize side effects by impacting the absorption, distribution, metabolism, and elimination of a drug compound [123]. The elaboration of an edible delivery system for active bio compounds is challenging due to the differences in solubility, bioavailability, and potential for novel food and pharmaceutical applications. One of the challenges is that all materials involved must have quality control to be used in food and sufficient chemical and physical stability to withstand the conditions to which they will be subjected (such as changes in temperature, solubility, pH, etc.) [43,124,125].

Betacyanins in the *Hylocereus* species are natural water-soluble nitrogenous pigments and red-violet. Together with yellow betaxanthins, they constitute betalains. However, as with other bioactive compounds, betacyanins exhibit a short shelf-life and low bioavailability (some studies show that betanin bioavailability is lower than 1% of the ingested amount). Betanin bioavailability was found to be around 0.5–0.9% among human volunteers [126]. In another study, the authors demonstrated that only 0.21M plasma concentration is retained after ingestion of 500 g of the pulp of cactus pear fruit, resulting in 16 mg of betanin and a bioavailability near 0.68% [127]. Choo et al. [43] showed that betacyanins bioaccessibility in fermented red dragon fruit drink and pressed red dragon fruit juice undergoes reduced loss (around 25%) in the gastric-like environment and higher loss during intestinal digestion. After intestinal digestion, fermented red dragon fruit drink retained around 46.0% of betanin and the fruit juice retained approximately 44.0% (concentration of betanin of 17.1 mM and 12.4 mM, respectively). The findings of this study suggested that betacyanins are bioaccessible; however, fermentation can augment bioavailability. A study performed by Sawick et al. [128] revealed that betacyanins suffered intensive degradation when fermented juice prepared with red beet was administered via gavage to rats and absorbed from the stomach. Nineteen betacyanins (eight were native compounds, and 11 were metabolites) were found in the physiological fluids of the rats. Peak amounts were found in the portal vein 15 and 30 s after administration of the extract (respectively, 0.8 and 12.3 μ M for 5 mg and 20 mg betacyanins). Elimination (excretion) of these compounds in urine peaked after 15 and 30 s (0.1 and 3.3 μ mol/h after 5 and 20 mg), respectively. In another animal study, Krant et al. [129] showed that betanin underwent metabolization mainly in the stomach wall (74%), followed by the colon (60%), and in a small percentage, in the small intestine (35%). Only a tiny percentage underwent liver metabolization, and about 2.7% was eliminated in urine and feces [75]. Furthermore, the presence of these compounds is influenced by external factors, such as food source, food matrix (type of product, structure, composition, processing, and viscosity), processing (pH, viscosity, fermentation, and Brix), water activity, temperature, oxygen, light, pH, mechanisms of absorption, and catalytic enzymes [126,127,130,131,132,133,134,135].

The preparation of nanoliposome phospholipids augmented the stability of betanin and resulted in higher 2,2-diphenyl-1-picrylhydrazyl radical-scavenging capacity in gummy candies than those containing free betanin [132]. Encapsulated betanin (w/o/w double emulsions) showed higher encapsulation efficiency and emulsion stability [134]. In the hydrophilic form, betacyanin from red dragon fruit extract is a high-value bioactive component with a plethora of applications as functional food or nutraceuticals. Harimurteit et al. [130] developed a red dragon fruit extract encapsulated product in water-in-oil-in-water-in-oil-in-water emulsions as a delivery system ensuring antioxidant activities. In another study, betanin microencapsulation



added of potatosuccinylatedstarch increased the stability of stored yogurt [136]. Although the applications of nanoparticles for distribution, labelling, and heating have grown, their biological importance has been highlighted by the increase in their use and respect for the environment [137]. As a result, the manufacture of nanoparticles using plants or bio compounds has grown substantially. Tiny-sized gold nanoparticles with biostability are essential and could be employed in several biomedical applications. In a study, the authors produced gold nanoparticles (25.31 nm) using *H. polyrhizus* extract (pulp/seed oil extract), aiming to function as a reducing and stabilizing agent. Due to its substantial physiological stability and blood biocompatibility, green production of gold nanoparticles with red pitaya fruit extract is an alternative to chemical production and can be helpful for medical and biological applications. The authors used the nanoparticles in various biological assays, including anti-inflammatory, antioxidant, anti-diabetic, and anti-Alzheimer assays, and performed cytotoxic investigations. The anti-diabetic effects were shown by different concentrations of the nanoparticles (50 to 200 mg/mL), significantly inhibiting the alpha-amylase enzyme. The maximum anti-inflammatory action was obtained at 400 mg/mL with the inhibition of COX-1 ($50.51 \pm 1.32\%$) and COX-2 ($58.74 \pm 0.76\%$). The antioxidant effects were investigated at 100, 200, 300, 400, and 500 mg/mL of extract and pulp/seed oil. The antioxidant effects increased with the increase in concentrations. In the anti-Alzheimer investigation, Acetylcholinesterase and Butyrylcholinesterase were evaluated at different concentrations. Nanoparticles produced significant results at 400 mg/mL (inhibition of $69.11 \pm 1.12\%$ against Acetylcholinesterase and $64.78 \pm 0.71\%$ against butyrylcholinesterase). The inhibition actions were dose-dependent. In addition, nanoparticles exhibited a dose-dependent cytotoxic action against HepG2, HCT-116, and MCF-7 cell lines, showing as a viable anti-cancer therapy and an option for colon and breast cancer treatment. This study showed that these nanoparticles could be used as vectors for biomedical applications that may include medication and gene delivery or as a biosensor where they will be in contact with blood [75].

The fruit extract of *H. undatus* can also be used to produce nanoparticles, as shown by Rizvi et al. [138]. These authors worked on the green synthesis of iron oxide nanoparticles made from fruit extract of this species and observed efficient photocatalytic actions towards azo dyes. These results bring to light the possibility of using the genus *Hylocereus* to produce nanoparticles that can be used for pharmaceutical purposes or in the food industry.

4.5. Waste Generated by Dragon Fruit Chain

Fruit and vegetable waste are severe environmental problems and are considered pollutants. They can significantly damage the aquatic and non-aquatic environment, resulting in severe inconvenience to animal and human organisms. For these reasons, the removal of this waste is highly urgent. The skin of the red pitaya is a residue from the pulp extraction or processing of the fruit's juice and represents 33% of its weight. The volume of pitaya peel discarded worldwide is around 0.8 to 4 tons of fresh matter per hectare, making this fruit a source of waste that can be reused [80,139]. Bakar et al. [140] characterized the red pitaya skin and found high levels of dietary fiber (69.3%), most of which were insoluble but still with a good concentration of soluble fiber and considerable amounts of pectin (10.79%). Thus, applying pitaya peel flour can be a good alternative as a fiber or fat substitute in several products, enriching them nutritionally and sensorially [108]. Studies also suggest that pitaya peel pectin can be used as a functional and natural additive in low-viscosity beverages and foods [141,142].

Pitaya seeds possess an oil that is a mild laxative that reduces total and LDL-c levels in humans by inhibiting cholesterol absorption in the intestine. The oil has a high level of functional lipids and can be used as a new source of essential oil [143].

V. CONCLUSIONS

Studies show that pitaya has beneficial potential for human health, having antioxidant, anti-inflammatory, antilipemic, anti-diabetic, anti-bacterial, anti-fungal, and anti-cancer effects. The consumption of this fruit can act on oxidative stress and anti-inflammatory processes and control or reduce the occurrence of conditions such as diabetes, dyslipidemia, metabolic syndrome, cardiovascular diseases, and cancer. Pitaya has great economic



importance due to its excellent nutritional value, and the possible use of peels, rich in betacyanins, can be applied as a natural dye.

On the other hand, dietary fiber from fruit peels can be used to replace partial fat in products such as ice cream. The great potential for using pitaya in the food, cosmetics, and pharmaceutical industries can be demonstrated in the development of ecologically correct and active packaging, edible films, preparation of photoprotective products, natural additives for meat products, beer production, in addition to compounds that can act as natural cytotoxic agents in the therapeutic approach of various types of cancer. Besides the importance of dragon fruit as a source of bioactive compounds, the bioavailability is low. The development of delivery systems such as gold nanoparticles with these compounds can be an alternative to reach target tissues.

The analysis of the studies included in this review shows us that dragon fruit has immense potential to improve numerous aspects of human health since it can reduce and treat risk factors for metabolic diseases in studies carried out with human beings and can present cytotoxicity in cancer cells. In addition, it has the potential to improve numerous technological aspects of food production and quality in terms of adding antioxidants and dietary fiber.

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