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Review Article

Review on the pharmacological and health aspects of *Hylocereus* or *Pitaya*: An update

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Abstract

The need for fresh fruit and vegetables in the community is increasing, this is due to research which states that the consumption of fresh fruit and vegetables can reduce the likelihood of disease. *Hylocereus* spp or dragon fruit is a medicine plant belonging to the Cactaceae family. The distinctive morphology found in dragon fruit is the shape of the skin which corresponds to the oval body shape. Dragon fruit can grow well in dry areas. Phytochemicals in dragon fruit or pitaya include carbohydrates, protein, saponin phenolic compounds, terpenoids, oils, flavonoids, tannins, phenols, coumarin, and steroids. Meanwhile, nutritional analysis shows that the fruit contains complete nutrition, including vitamins, fat, crude fiber, and minerals. Based on previous research, dragon fruit has been proven to be used as an alternative ingredient for antimicrobial, antifungal, anti-inflammatory, anticancer, antioxidant, antulcer, antipertility, antidiabetic, hepatoprotective, hypolipidemic, neuroprotective, cardioprotective, and anti-platelet

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INTRODUCTION

Food is an important thing that can prevent chronic disease^{1,2}. Fresh fruit and vegetables are types of food that are alleged to be able to prevent various diseases³⁻⁵. One of the fresh fruits that are often consumed by people is dragon fruit^{6,7}.

Taxonomically, dragon fruit or generally known as pitaya or pitahaya is a fruit that is still in the same genus *Hylocereus* and is also a fruit group in the Cactaceae family⁸. The skin layer that is equipped with "scales" is the reason this fruit is also called dragon fruit⁹⁻¹¹. The unique thing besides the skin surface that occurs with "scales" is that in its development, there is the term "moon flower or mistress of the night" which means dragon fruit flowers only grow at night¹². Pollination at night is carried out by bats¹³. As a part of the Cactaceae family, dragon fruit is one of the fruits that are sensitive to temperature extremes, and is better in dry areas with a temperature of not more than 45°C⁹.

The distribution of dragon fruit cultivation is generally in dry areas such as the United States, Canary Islands, Australia, Thailand, Vietnam, and Southeast Asia¹². In Vietnam, dragon fruit has been cultivated for 100 years^{9,14}. Dragon fruit growth will be better when it is on soil with a very high organic matter content¹².

It is consumed as food, but the existence of dragon fruit among the people is not only fixed on the consumption of fresh fruit or in the form of juice. Sometimes dragon fruit is used for the treatment of several diseases, this is related to the content of phenolic micronutrients which function as antioxidants^{15,16}. Besides antioxidants, dragon fruit has complete nutrition in the form of vitamins, carbohydrates, fiber and betacyanin^{17,18}. Betacyanin is one of the typical substances that can be found in dragon fruit¹⁹. The function of betacyanin in dragon fruit is related to the coloring or pigmentation of dragon fruit flesh which is one of the attractions of dragon fruit. It is said to be unique because dragon fruit pigments have a variety of colors, namely red, yellow, and white²⁰, which can be seen in (Fig. 1).



Figure 1: (A) *Hylocereus undatus*, (B) *Hylocereus polyrhizus*, (C) *Hylocereus megalanthus* ²¹.

However, dragon fruit commonly known by people in Indonesia is white dragon fruit (*Hylocereus undatus*) and red dragon fruit (*Hylocereus polyrhizus*) ²². Some researchers stated that *Hylocereus undatus* originated from South America, but several other researchers stated that the origin of *Hylocereus undatus* came from Colombia or Mexico ¹². In the medical, dragon fruit has an effect as a positive anti-inflammatory, antidiabetic, anticancer, and antioxidant ¹⁷. Apart from the flesh, dragon fruit skin has benefits for human life. The thickener as well as the cosmetic coloring is one of the functions of dragon fruit peel. The antioxidant ingredients contained in the flesh of the fruit are also found in dragon fruit seeds. Not only the antioxidant content, the fat and linoleic acid content are also contained in dragon fruit seeds ¹². Besides having complete nutritional content, it turns out that dragon fruit is a type of fruit that can generate profits quickly ⁹. This is goes along with the annual harvest of dragon fruit reaching 150 tons every year ²³.

TAXONOMY

Kingdom: Plantae

Division: Spermatophyta

Class: Dicotyledonae

Ordo: Cactales

Family: Cactaceae

Genus: *Hylocereus*

Species: *Hylocereus polyrhizus*, *Hylocereus undatus*, *Hylocereus megalanthus* ²⁴.

PLANT DESCRIPTION

Pitaya (*Hylocereus spp.*) or commonly known as dragon fruit is a vine that belongs to the category of the cactus family (Cactaceae) ^{13,25}. Pitaya or dragon fruit is a cactus species that has epiphytic or terrestrial characteristics. This dragon fruit plant grows using support poles or other trees to be able to grow optimally using aerial roots, be able to get enough sun exposure, be able to get nutrients from the air and arboreal humidity. Dragon fruit plant stems have the characteristics of scandent, climbing, widening, and branching. The stem is portly and watery, has a physical shape like a triangle. Dragon fruit stems have water and nutrient reserves like cactus plants in general so that these plants can survive even in extreme environments (low humidity and infertile soil). While the flowers of this plant have a characteristic greenish yellow or slightly white color, have an aroma, are nocturnal about 20-35 cm long and 22-35 cm wide ²⁵.

For the characteristics of the dragon fruit itself, dragon fruit has an oval, thick is 4 to 9 cm, and 6 to 12 cm long and usually has a red color and has large bracteoles. Dragon fruit has a physical form that is filled with areola (protrusions) where the thorns grow, where in each areola

there are 2 to 5 spines with a size of 1-3 cm. Dragon fruit has seeds that are very small and black in the flesh. Dragon fruit usually weighs about 150 to 600 g. Dragon fruit flesh has pink, white, red, or yellow colors, and has a mixture of sour and sweet flavors. Dragon fruit is very suitable for growing in environments that have dry, tropical and subtropical climates with temperatures up to 40°C. In wet tropical climates, this dragon fruit plant will still grow well, even though it is more risky. This dragon fruit will grow on trees that have physical forms such as cacti, with a period of 30-50 days after the first flowering. This dragon fruit plant usually has a harvest cycle of 5-6 times per year ^{25,26}.

GEOGRAPHICAL DISTRIBUTION

Pitaya is cultivated in subtropical and tropical area ^{27,28}. Dragon fruit plants have been grown and cultivated in Vietnam for more than 100 years, but over time, dragon fruit cultivation has attracted the attention of farmers in various parts of the world such as Thailand, Australia, Israel, and the United States ^{9,27}. Dragon fruit plants are usually found and have been grown commercially in various countries such as Australia, the United States, Israel, Vietnam, Nicaragua, and Taiwan ⁹. However, most of these dragon fruit plants basically come from Mexico and South and Central America ²⁴. In Israel, to be precise in the Negev Desert, this dragon fruit plant can experience good growth and fruit production yields of 30% have been found ²⁴.

PHYTOCHEMISTRY

Initial phytochemical examination showed that the methanol and water extract of pitaya or dragon fruit seeds contained alkaloids, saponins, terpenoids, oils, flavonoids, tannins, phenols, carbohydrates, coumarins, and proteins ²⁹. Pitaya contains proteins, steroids, carbohydrates, alkaloids, tannins, flavonoids, and phenolic compounds ³⁰. Alkaloids that are present are cholinesterase inhibitors that can be used for Alzheimer's disease treatment like donepezil, tacrine, rivastigmine, and velnacrine. Coumarins that are present in both extracts like phenylpropanoids are antioxidant, anti-bacterial, anti-tubercular, anti-fungal, anti-viral, and anti-inflammatory. Saponins include lupane glycine, betulinic acid, and oleanolic acid can be used to treat type-2 diabetes and also chronic kidney disease. The oil of pitaya seeds contain omega-3 fatty acids, conjugated linoleic acids, phytosterols, and medium chain triglycerides that are beneficial in treating obesity and bone health. Both condensed tannins such as proanthocyanidins and anthocyanidins and hydrolyzable tannins like gallotannins and ellagitannins are present, with polyphenols being present in the peel. Pitaya peels contain higher amounts of flavonoids that have metal chelating and radical scavenging properties such as kaempferol, isorhamnetin, quercetin, and kaempferol ²⁹. Dragon fruit phytoconstituents consist of oleic acid, 1-tetracosanol, trichloroacetic acid, hexadecyl ester, octacosane, 1-hexadecyne, 2-chloroethyl linoleate, phthalic acid, 6-ethyloct-3yl-2-ethylhexyl ester, 6-

tetradecanesulfonic acid, butyl ester, tetratriacontane, heptacosane, n-hexadecanoic acid, 1,2-benzenedicarboxylic acid, mono (2 ethylhexyl) ester, (Z,Z)-9, 12-octadecadienoic

acid, 17-pentatriacontene, eicosane, γ -sitosterol. Chemical structures of phytoconstituents are compiled in Figure 2³¹.

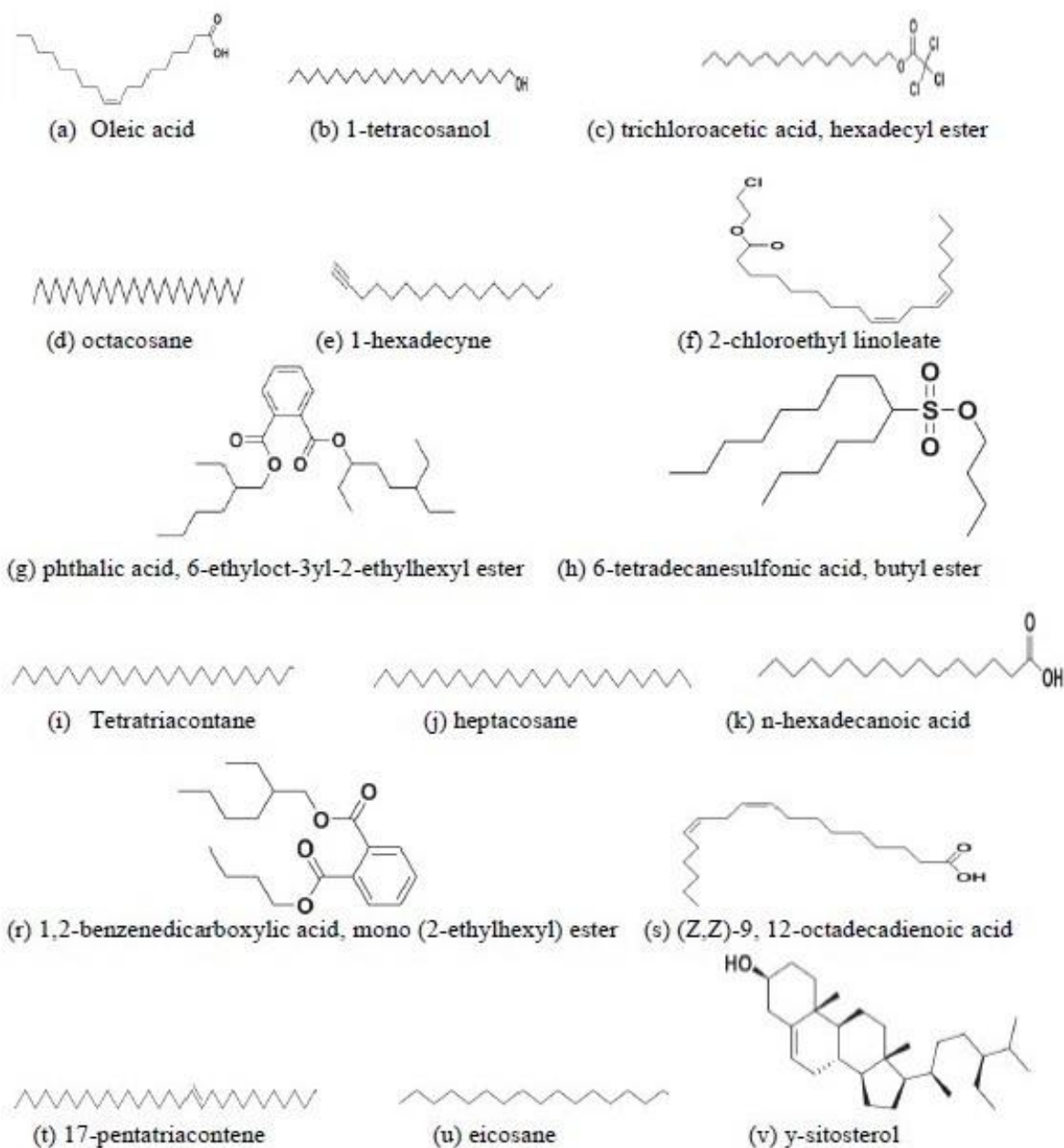


Figure 2.: Phytoconstituents from dragon fruit.³¹

NUTRITIVE VALUE

The results of the nutritional analysis showed that the average pitaya contains moisture (84-86 g/100 g), protein (0.93-1.33 g/100 g), fat (0.40-1.01 g/100 g), vitamin C (1.0-6.3 mg/100 g), vitamin A (0.0066-0.186 mg/100 g), ash (0.56 g/100 g), crude fibre (0.88-1.84 g/100 g), glucose (4.63-6.39 g/100 g), fructose (2.16-4.06 g/100 g), sorbitol 0.33 g/100 g), and carbohydrate (10.4-12.3 g/100g). Pitaya also contains several minerals such as iron (1.95-7.4 mg/100 g), potassium (181.0-321.0 mg/100 g), niacin (2.3-3.5 mg/100 g), calcium (7.6-15.6 mg/100 g), magnesium (29.5-44.3 mg/100 g), phosphorus (22.8-31.8 mg/100 g), sodium (5.0-13.5 mg/100 g), and zinc (0.26-0.42 mg/100 g)³².

TRADITIONAL USE

Pitaya has been used as traditional medication and consumption purposes in Central America, where it is also common for pitayas to be grown in family gardens³³. The leaves and flowers of pitaya were used by the ancient Mayas for medicinal use as a diuretic and healing agent³⁴. Mayas also utilizes the pitaya fruits as a diuretic, hypoglycemic, against heart disease, wound disinfectant, and tumor dissolution, and as a cure for dysentery³³. In addition, the flowers can be consumed as it is or by drinking it as a tea, the seeds possess a laxative effect, the fruit has shown an effect on gastritis, and the stalk can also be used for kidney problems³⁴.

MEDICINAL VALUES

Consumption of fruits and vegetables is necessary to prevent various diseases. This is in line with an epidemiological study in 1992 which stated that the potential for cancer in the population would be lower when the population regularly consumed fruits and vegetables³⁵. Phytochemicals are chemicals that play a biologically active role in fruits and vegetables³⁶.

One of the fresh fruits that is in great demand by the world's population is dragon fruit. One of the dragon fruit species known for its phytochemical content is the red dragon fruit (*Hylocereus polyrhizus*). Red dragon fruit contains minerals and nutrients such as vitamin B2, vitamin B3, Vitamin B1, Vitamin C, fat, carbohydrates, protein, betacyanins, polyphenols, iron, phytoalbumin, carotene, cobalamin, glucose, and phenolic³⁷. With various nutrients and minerals available, red dragon fruit has a positive effect in helping the digestive process, there are anti-diabetic, lowers blood pressure, neutralize toxins in the body, especially toxins from heavy metals, helps treat asthma as well as coughs and prevents various types of cancer especially colon cancer. Dragon fruit prevention of cancer is played by the content of phytoalbumin which has a very high antioxidant content³⁶. Iron content is also found in red dragon fruit, and iron is able to increase erythrocyte and hemoglobin levels so that it can be used as an anemia treatment, but research on anemia treatment from dragon fruit is still a clinical trial using rats¹².

Dragon fruit pulp contains flavonoids ranging from (7.21 ± 0.02 mg vs. 8.33 ± 0.11 mg of catechin equivalents/100 g of flesh and peel matters) and phenolic content of (42.4 ± 0.04 mg of gallic acid equivalents (GAE)/100 g of flesh fresh weight) and peel (39.7 ± 5.39 mg of GAE/100 g of peel fresh weight)³⁸. Both phytochemical content are very good for the body, especially as antioxidants that can act as cancer and cardiovascular disease prevention agents³⁹.

Apart from polyphenols and flavonoids, there are other phytochemicals called betacyanins and betaxanthins which are part of betalains. Studies show that the betacyanins in dragon fruit have anti-free radicals⁴⁰. As is well known, free radicals will harm the body. Being able to cause neurodegenerative disease, aging, or heart problems³⁶.

White dragon fruit (*Hylocereus undatus*) in the medical field plays a role in the wound healing process. Parts of white dragon fruit that have high effectiveness to help the wound healing process are leaves and flower water extract which have been blended in topical preparations⁴¹. In a toxicity study conducted in two groups, namely subchronic toxicity with a dragon fruit extract dose of (1250, 2500, 5000 mg/kg) and acute toxicity at the same dose showed no organ abnormalities that occurred in experimental animals³⁴.

PHARMACOLOGICAL ACTIVITY

In the treatment of different diseases, medicinal herbal plants have demonstrated pharmacological activity⁴², dragon fruit have many pharmacological activity as listed in below:

Antimicrobial activity

White dragon fruit flesh ethanolic extract was detected as around 85% of mixed oligosaccharides occur. In contrast to inulin, these oligosaccharides had greater tolerance to human salivary α -amylase. This is not digested in the stomach, but functions as prebiotics that help the stomach. *Bifidobacteria* and *Lactobacilli*, which are healthy bacteria, are increasing⁴³. Acetone extracts (70 % concentration) of

Hylocereus peel have high antimicrobial activity, particularly against *Salmonella typhi*⁴⁴.

From the disc diffusion analysis, the antibacterial activity of chloroform, hexane extract, and ethanol from the skin of white dragon fruit revealed that the inhibition region of about 7 to 9 mm was able to combat Gram-negative and Gram-positive bacteria⁴⁴. Using the micro titre process, antibacterial analysis was performed. It was the minimum inhibitory concentration (MIC) of the bacterial species *E.coli* and *Staphylococcus aureus* was found to be 50 μ l²⁹.

Antifungal activity

The presence of polyphenol antifungal activity in extracts and fractions of flesh and peels of red pitaya fruits are two yeasts, *Candida albicans*, *Rhizoctonia solani*; four molds: *Aspergillus flavus*, *Fusarium oxysporum*, *Botrytis cinerea*, *Cladosporium herbarum* which is the research panel that include laboratory control strains obtained from the American Type Culture Collection (ATCC)⁴⁵.

Anti-inflammatory activity

Anti-inflammatory action has been performed on dragon fruit. The research was carried out by mixing dragon fruit skin and flesh and separating it with vacuum distilled water, water, and drying. Then the results of this will be used for the purposes of bioassay testing against Cyclooxygenase-2 (COX-2), Acetylcholinesterase Enzymes (AChE), and 5-Lipoxygenase (5-Lipox). The results of these studies have shown that extracts derived from dragon fruit flesh showed excellent results against the three enzymes in the bioassay test and showed a stronger inhibitory power on the Acetylcholinesterase enzyme compared to other enzymes. This has shown that dragon fruit has the ability to relieve inflammatory symptoms, it can be seen from the mechanism that is directly related to cholinergic anti-inflammatory. In addition, the results shown by dragon fruit flesh on COX and Lipox enzymes also have an indication of a high potency that can cause blockages in the leukotriene and prostaglandin pathways⁴⁶. This shows that there are anti-inflammatory properties in the properties of dragon fruit. Extract from ethanol from red dragon fruit peel contains betalain which has the ability to inhibit the transcription factor NF- κ B which will result in inflammatory genes such as TNF- α and IL-1 β that will not be separated⁴⁷.

Anti-cancer activity

Various studies have shown that the flavonoids, betanin, and polyphenols in dragon fruit have an anticancer effect. The skin of dragon fruit that has been extracted with a mixture of water and ethanol solvent with a ratio of 50:50 has shown antiproliferative activity against human hepatocellular carcinoma cells in just one dose. Anticancer activity which is really precise is still being studied and cannot be known factually, however, previous research has resulted in the fact that the effect of polyphenol anticancer in dragon fruit may be mediated through factor suppression on nucleic-kappa B and by a mediated pathway. growth factor receptors, antioxidant mechanisms, anti-inflammatory, angiogenesis inhibition, cell cycle arrest and apoptosis induction, and protein kinase activation¹².

The red-fleshed contain lycopene, that is a natural antioxidant recognised to combat cancer. Antioxidants will protect cells from reactive oxygen species that can cause damaging effects and preventing any cancer-causing free radical formation³⁷. Red pitaya flesh and peel rich in polyphenols and good source of antioxidants^{37,39}. Research also shows that white dragon fruit is rich in flavonoids³⁷.

Antiulcer activity

The topical quercetin content in the skin of red dragon fruit (*Hylocereus polyrhizus*) shows antiulcer activity. It can be proven from the results of total distress in 35% of cases within 2 to 4 days and in 90% of cases within 4 to 7 days. Quercetin is useful for reducing the frequency of relapses and relieving mild symptoms⁴⁸.

Antioxidant activity

Pitaya is considered as a fruit that is low in calories but high in nutrition, water content, sugars, minerals, and antioxidants³⁴. *H. polyrhizus* or known as the red fleshed pitaya is rich in betalains which meets the trade interest for antioxidant products and also natural food colorant¹³. Pitaya seed oil holds a high potential as a source for natural antioxidants³³. Pitaya contains an abundance of phytoalbumins known for its antioxidant properties⁴⁹, not just phytoalbumins, the pulp and peel is also rich in polyphenols³⁴. Through the study from the ethanolic extract of both the peel and the flesh of *H. undatus*, it is shown that the peel contains more flavonoids than the flesh⁴⁹. The pulp of pitaya can be added to yogurt to improve the antioxidant activity³³.

Antidiabetic activity

There are several leaves and fruits that have the potential to be anti-diabetic^{50,51}, such as dragon fruit. Several studies have shown that dragon fruit has an antidiabetic activity effect²². For patients with Type II Diabetes, the use of red dragon fruit can reduce blood glucose levels. The substance that lowers blood sugar levels in red dragon fruit is glucose⁵².

In addition to glucose, dietary fiber in dragon fruit has a function to reduce the intensity of decreasing food in the intestines, thereby reducing the formation of blood glucose⁵³. The use of dried dragon fruit also has specific results as an herb for antidiabetic activity. This is also because dragon fruit dry has a blood sugar-lowering effect that can lead to diabetes¹².

For antidiabetic activity, the use of dragon fruit is not only fixed on dragon fruit flesh. Dragon fruit seeds and skin also have an antidiabetic effect. Dragon fruit seeds contain saponins that are soluble in water extracts and are useful as an antidiabetic substance, especially for people with type II diabetes²⁹. Meanwhile, dragon fruit skin contains soluble fibers that are believed to be able to regulate blood sugar levels in the body⁵³.

Diabetics will generally have wound that are difficult to heal³⁴. However, in one study, it was found that the use of *Hylocereus undatus* or white dragon fruit had the effect of accelerating the recovery process. The most effective white dragon fruit preparations used for wound healing in diabetics are topical preparations derived from flower or leaf water extracts⁴¹. The use of white dragon fruit in the wound healing process in diabetics occurs due to the presence of DNA collagent content, increased epithelialization and hydroxyproline, tensile strength and total protein³⁴.

Anti-infertility activity

An experiment showed that dragon fruit extract can maintain sperm motility and improve testicular histology. white dragon which contains gallic acid as an antioxidant which tends to increase spermatozoa quality in the form of increased motility, number, and morphology of spermatozoa in the epididymis⁵⁴.

Antiplatelet activity

Dragon fruit has antiplatelet activity because it contains ethanol and ethyl acetate extracts which have inhibitory effects in concentration-dependent manner on platelet aggregations induced by various agonists⁵⁵.

Hepatoprotective activity

The extracts of dragon fruit do have a beneficial effect on poisoned rats. Due to its high antioxidant components coming from the above-mentioned intake of CCl₄. In specific, triterpenes and flavonoids are phytochemical components that defend the liver against fat peroxidation, but with a subsequent improvement in Serum Glutamic-Pyruvic Transaminase (SGPT) and Serum Glutamic-Oxaloacetic Transaminase (SGOT), the silymarin capsule has little preventive function against liver injury. The extracts of dragon fruit are effective in protecting the liver from it has been shown to test animals against persistent damage when induced with CCl₄⁵⁶.

Cardioprotective activity

The effectiveness of polyphenols in flesh owned by *H. polyrhizus* is Anti-thrombotic effect, which increases its cardioprotective properties further⁵⁷. In one study, rats were given two thermal processing methods for this dragon fruit were selected. The results of the analysis were that the cardioprotective substances of red pitaya will be polyphenols and antioxidant material⁵⁸.

Neuroprotective activity

As mentioned previously, dragon fruit has a myriad of benefits and one of them is related to the neuroprotective activity of nerve work. The phytochemical content in dragon fruit plays an active role in neuroprotective activity, especially when preventing neurodegenerative diseases. The phytochemical content in dragon fruit which has the potential to prevent neurodegenerative diseases while also playing an active role in neuroprotector activity is essential fatty acids²⁷.

Cytoprotective activity

Pitaya is a great source of various for natural antioxidants, including ascorbic acid, betalains, and polyphenols¹². As a fiber-rich Dragon fruit, it helps in food digestion⁵⁹. Soluble fibers found in pitaya peel may help neutralize dangerous substances such as heavy metals in the digestive process and may be associated with blood sugar control in people with type II diabetes. Pitaya peel also has mucilage that can have a beneficial effect on the metabolism of cholesterol⁵³.

Hypolipidemic activity

Dragon fruit flesh extract was used to determine hypolipidemic activity in rats. The extract of dragon fruit flesh could minimize TG, total cholesterol, LDL, and total cholesterol ratio over HDL cholesterol, body weight, Lee index obesity, and could also substantially raise serum HDL cholesterol, total fecal cholesterol, and fat. From this study, it was shown that dragon fruit flesh extract had biological activities of antiobesity and hypolipidemic which could prevent atherosclerosis. Dragon fruit flesh extract consumption may not only bind cholesterol and fat from the feed but also increases the amount of cholesterol and fat in the feces⁶⁰.

Analgesic activity

Pitaya, like many other plants, contains gallic acid (3,4,5-trihydroxybenzoic acid), an organic substance that exists in

plant materials that acts as antioxidant, antibacterial, antiviral, and analgesic activities ⁶¹.

CONCLUSION

Hylocereus spp or commonly known as pitaya or dragon fruit is one of the freshest fruits which is widely consumed by the world community. Good cultivation areas for dragon fruit are in dry areas such as in Southeast Asia, America, Vietnam, Canary Island, and Thailand. Dragon fruit contains nutrients and phytochemicals that are good for the body. Various research results show that dragon fruit has activity as a preventive for several diseases that attack humans. So, based on this, dragon fruit can be classified as a fruit that can be classified as a medicinal plant which can be used as an alternative to the use of chemical-based medicinal drugs. However, this study still needs to be reviewed and validated to be more convincing that dragon fruit can be used for alternative prevention and treatment of various diseases.

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