Review Article

A brief review on *Opuntia humifusa* Raf.: Phytochemical and pharmacological aspects

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Abstract

The present review is an attempt to highlight the various ethnobotanical and traditional uses as well as phytochemical and pharmacological reports on *Opuntia humifusa.* Raf a typical prickly pear type of plant belongs to the family Cactaceae. The plant is widely distributed throughout the tropical and arid regions of India. It has nutritional as well dense medicinal values it was proved for its edible and therapeutic *Opuntia humifusa.* Raf applications. The presence of potent phytochemicals like flavonoids, polyphenol- kaempferol, rutin, ascorbic acid, Vanillic acid, p-coumaric acid, ferulic acid, syringic acid, 4-hydroxybenzoic acid, protocatechuic acid, salicylic acid, caffeic acid, gallic acid, etc., compelled the plant to use to its maximum utility. The isolated phytoconstituents of plants such as flavonoids, polyphenol, and ascorbic acid proved for its antioxidant property and also, the plant possesses other components particularly calcium, minerals, amino acids, etc. The different parts of plants were preclinically tried and conformed to the potency of the therapeutic strategy of a plant. The important pharmacological properties especially anticancer, antifungal, antihypertensive, antiulcer, antimicrobial, antiatherosclerosis, hepatoprotective, type-2 diabetes, and coronary heart diseases have been proved the plant as traditionally and medicinally important. hence the present review was focused to collect and summaries the overall brief information on various parts of the plant *Opuntia humifusa.*raf based on chemical constituents, ayurvedic, modern usage, and its biological activities.

***Keywords*:** Therapeutically*, Opuntia humifusa*, antioxidant, phytoconstituents, flavonoids

Introduction

The *Opuntia humifusa* Raf is originally cactus featured plant that grows near the ground surface of tropical and arid parts the world (Kim et al., 2006). The various parts of plant abundantly filled with nutritionally edible components and classically used for its known biological properties. Due its chemical compositions the plant is therapeutically practiced to treat both local, chronic diseases acting as boon for mankind. The plant exhibits various phenolic derivatives, antioxidants like ascorbic acid, gallic acid Vanillic acid, p-coumaric acid, ferulic acid, syringic acid, 4-hydroxybenzoic acid, protocatechuic acid, salicylic acid, caffeic acid, gallic acid and also possesses pigmented carotenoids such as flavonoids, polyphenol- kaempferol, rutin, betalains. Opuntia aerial and underground parts have beneficial properties.

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O. humifusa possess aerial and subsurface parts of plants consisting of spines cladodes, flowers, fruits Glochids etc (Christiana et al., 2018). According to previous research reports, the Cactaceae family reported with 130 different genera and about 1500 various species, all of which are well adapted to the arid lands and a variety of climates and have become common for all the locations around the world (Alice et al., 2015). *O. humifusa* extract has been widely used for topical-cosmetic, biomedical, and as well as food-additive applications because to its excellent characteristics *O. humifusa* is well known for their high moisture, vitamins, minerals, antioxidant anti-inflammatory, hypoglycemic, anticancer, antifungal dermatitis, gastric ulcer, Antihypertension, antimicrobial, and anti-diabetes (Kyungmi et al., 2017; Ah-Ram Han et al., 2018). The *O. humifusa* extracts were found to effectively alter the expression of inflammatory cytokines. According to a recent study of *O. humuifusa* plant reported with reduces the risk of disease like stroke, coronary heart disease, and obesity (Ah-Ram Han et al., 2010; Park et al., 2010).

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Geographical Distribution

It is widely distributed in semi-arid countries throughout the world. It has been cultivated for a long time; it can be cultivated during a winter even with the temperature reaching below 20^0C usually grows near the surface of ground. Some arid growth locations like Karnataka, Rajasthan, Tamilnadu. This biodiversity determines the component profile of each species as well as other factors such as growth locations prevailing climatic conditions and soil conditions (Jae Youl Cho et al., 2006; Christiana et al., 2018).

Identification of *Opuntia humifusa* plant

The prickly pear grows to a height of 6 feet or more and has the largest pad with white spines, measuring 8 to 16 inches long. It can be found all over world especially near the desert regions. Plains prickly pear is a short, spreading variety native to the Rolling and High Plains regions.

Morphological Characters of *Opuntia humifusa*

In general, *O. humifusa*. is a low, decumbent plant although it can reach heights of 30 to 40 cm during the growing season when the cladodes are turgid. Depending on the amount of suitable habitat, it develops small to enormous populations (>5 hectares).

Cladodes

Cladodes are lime to dark green in colour, and as they mature, they become cross-wrinkled. During the winter months or when there is a water shortage. Cladode sizes vary widely depending on the environment. The length, width, and height range from 3.1 to 8.5 (17.7) cm, 2.0 to 5.2 (9.0) cm, and 4 to 10 cm, respectively. The thickness is 19 mm. Obovate, ovate, orbicular, and elliptical are some of the shapes available. The major chemical constituents found in cladodes are Gallic acid, Coumaric acid, 3,4-dihydroxybenzoic, 4-hydroxybenzoic acid, Ferulic, Salicylic, Vanillic Syringic, Synaptic acids, Protocatechuic acid, etc. Phenolic acids - Gallic acid, Coumaric acid, 3,4-dihydroxybenzoic, 4-hydroxybenzoic acid, Ferulic, Salicylic, Vanillic Syringic, Synaptic acids, Narcissin Terpenoid volatiles (Taxonomic revision of the *Opuntia humifusa* complex (Opuntieae: Cactaceae) of the eastern United).

Spines

Spines are yellowish or cream in colour when juvenile, mottled with reds and browns in rings around the base, then turn a mild to bright white hue with yellowish tips as they mature. As the spines age, they turn a light or dark grey colour with yellowish, brownish, or black tips. They measure 5-7.1mm in length and 0.7-1.3mm in diameter, and are heavily retrorsely barbed as juveniles, with the barbs decreasing away with age. Each areole of *O.humifusa* can have up to two spines. (Taxonomic revision of the *Opuntia humifusa* complex (Opuntieae: Cactaceae) of the eastern United.2) The spines are made up of exterior chalky coating. The spines appear light cream, light yellow, or even colourless when this is rubbed off (e.g., after a hurricane). Depending on the age of the cladode from which it is created and the areole from which it is produced, spines can be upright, spreading, or some what collapsed. Spines can become deflexed and appressed to the cladode if another cladode or flower is formed from the same areole. (Taxonomic revision of the *Opuntia humifusa* complex (Opuntieae: Cactaceae) of the eastern United.2)

Glochids

Glochids come in a variety of colours, including pale yellow, brown, and even colourless. As a result of exposure to external stimuli, glochids darken with age (sunlight). The glochids of plants growing in a greenhouse were virtually blackened by a terrestrial alga. This has also been proved in natural populations. There will almost probably be glochid colour misinterpretations as a result of this. Glochids can grow to be up to 6 mm in length (Ecology of eastern prickly pear cactus (*Opuntia humifusa)* in oak openings preserve).

Flowers

The inner tepals of this type are completely yellow. On the outside, the tepals are green. The filaments of the stamens are yellowish or creamy in colour. The anthers are a bright golden colour Chemical compounds such as Gallic acid can be found in the plant *O. humifusa*. Kaempferol 3-O-Rutinoside, Quercetin 3-O-Rutinoside, Quercetin 7-O-Rutinoside, Glucoside, Isorhamnetin 3-O-Robinobioside, Isorhamnetin 3-O-Galactoside, Isorhamnetin 3-O-Rutinoside, Isorhamnet 3-O-rhamnosyl 7-O-rutinoside isorhamnetin 3-O-arabinoside of kaempferol (Ecology of eastern prickly pear cactus (*Opuntia humifusa)* in oak openings preserve).

Fruits

The fruits are juicy, elliptical in shape, and edible this fruit is developed into reddish pink colour and it is around 7cm in length. According to the study the total amounts of vitamin C and polyphenol in *O. humifusa* fruits were found to be much higher than in other plant parts comparatively root, cladodes, and seeds. The fruit encompass Betanin, isobetanin, betanidin, isobetanidin, and phyllocactin are among the betalains found in cactus pear fruits, as well as minerals, amino acids, flavonoids, and phenolic acids (ferulic acid, syringic acid, and caffeic acid). Flavonoids Rutin Isorhamnetin Myricetin Quercetin Kaempferol Luteolin Glycosides of isorhamnetin Glucosides of kaempferol (Park et al., 2011).

Root

Cactus pear is a shallow-rooted crop with a fleshy root

system that can spread horizontally from 4 to 8 meters away from the mother plant after a few years. Flavonoids are found in the root. Glycosides Tannins, Coumarins Polysaccharides Fatty acids are a type of fatty acid. *O. humifusa* is high in nutrients (betalains, vitamins, minerals, phenolic compounds, flavonoid compounds, and polysaccharides). Vanillic acid, p-coumaric acid, ferulic acid, syringic acid, 4-hydroxybenzoic acid, protocatechuic acid, salicylic acid, caffeic acid, gallic acid, and sinapic acid are among the phenolic acids found there, while flavonoid compounds such as rutin, narcissi, kaempferol, and quercetin are among the flavonoid compounds. Based on the excellent characteristics of *O. humifusa* (for example high moisturization, high antioxidant activity, anti-inflammation and anti-diabetes) various ailments, including arteriosclerosis, gastritis, diabetes mellitus, and hyperglycemia, had been successfully treated with *O. humifusa* (Cho et al., 2009).

Therapeutic uses

O.humifusa can withstand extreme cold (-20°C) and hard climatic conditions. Nutrient-dense environments and contains a wide range of minerals, including in addition to calcium, mineral matter, and amino acids, Flavonoids, polyphenols, vitamin C, and tocopherol (which is related to vitamin E) are all antioxidants (Kwon, 2005).

Opuntia Shown to be effective against geriatric illnesses, diabetes, Hypertension, arthritis, gastritis, and constipation are all symptoms of hypertension. Moreover, Opuntia has also been proven to help with improvement. Appetite stimulation and bowel movement stimulation (Lee, 2005).

Against the free radical diphenyl-1-picryl hydrazyl, *O. humifusa* showed antioxidant and scavenging action (DPPH). Furthermore, the *O. humifusa* extracts were found to effectively alter the expression of inflammatory cytokines (Youl Cho et al., 2006; Pritchard et al., 1986).

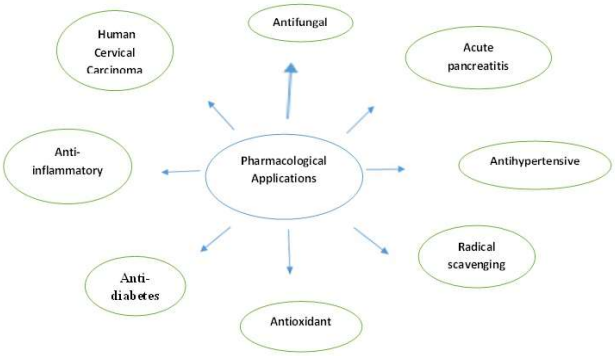

Figure 1. Reported Pharmacological Activities of *Opuntia humifusa*

The vulnerability to oxidative damage is determined by cellular antioxidant status, which is frequently altered in response to oxidative stress. As a result, there has recently been a surge in interest in the role and application of natural antioxidants in the prevention of oxidative damage in diabetes (Pritchard et al., 1986). *O. humifusa* extracts work well. Reduced-matrix transcription factor, which is linked to microphthalmia was suppressed. MMP-1 (metalloproteinase-1) and c-Jun N-terminal kinases (JNK) phosphorylation. As components in a variety of functional cosmetics, they can help with whitening and wrinkle reduction (Park et al., 2017). Further studies proved the skincare application potential of *O. humifusa* by controlling UVB-induced hyaluronic acid synthesis to aid in the suppression of water loss and erythema development (Zhao et al., 2012).

Pharmacological Activities.

Table 1. The reported pharmacological activities of various parts of *Opuntia humifusa* Ref.

Sl.no	Parts of plant used	Inducers	Pharmacological Activity Proved	Type of Animal Used	References
01	Cladode	Biostir AD- Dermatitis	Dermatitis	Mice	Jin-A Lee et al., (2015)
02	Fruit	UVB Radiation	Inflammation and Proliferation in Hairless	Mouse	Jin-A Lee et al., (2015)
03	Stems	streptozotocin	lower blood glucose and cholesterol levels in diabetes	Rats	Sahng-Wook Hahma et al., (2011)
04	Stem	water-soluble polysaccharides	high-fat-diet-fed	Mice	Eun-In Yang et al., (2018)
05	Leaves	Microwave-Assisted	Human Keratinocyte Skin Cell		Ju-Young Moon et al., (2020)
06	Seeds	ovariectomy	Treatment on the Mass, Quality, and the Turnover of Bone in Ovariectomized	Rats	Jieun Park et al., (2011)
07	Stem	Ameliorated Cerulein	Acute Pancreatitis	Rats	Sun Bok Choi et al., (2013)
08	Stems	Endophytic fungi	antifungal activity		Alice F. Silva-Hughes et al., 2015)
09	Leaves	Ethanol	Gastric ulcer	Mouse	Chi-YeolYoo et al., (2021)
10	Leaves	DPPH radical	Radical scavenging	Cell culture	Jae Youl Cho et al., (2005)
11	Roots	Endophyte	Arbuscular mycorrhizal fungal	Mycorrhizal fungal	Deotare PW et al., (2014)
12	Roots	DPPH radical	Antioxidant and Inflammatory Mediators	Rats	Kim Ye Jin et al., (2014)

Figure 2. Different parts of *Opuntia humifusa* Raf. Plants figures

Anticancer Properties of Extracts from *Opuntia humifusa* Against Human Cervical Carcinoma Cells

In this study, the antioxidant content of *O. humifies* was determined. The stem of *O. humifies* has a higher level of b-carotene than the rest of the plant. High diets of carotenoid-rich vegetables and fruits, as well as high blood levels of carotenoids, have been linked in epidemiological studies. b-carotene is linked to a lower risk of some diseases like cancer (Cai et al., 2004).

The antioxidant and anticancer properties of extracts from medicinal plants and herbs are linked to the presence of phenolic substances such as phenolic acids, quinines, flavonoids, and tannins (Dinicola et al., 2013). Fruit and vegetable seed extracts are commonly utilized as anticancer and antioxidant treatments (Birasuren et al., 2013). Many investigations have recently revealed that the cactus has antiproliferative effect against a variety of cancers. Extracts of *O. humifies* were found to suppress the proliferation of human cervical cancer HeLa cells by stopping the cell cycle at the G1 phase by upregulating and down regulating cyclin D1 and Cdk4 in this study (Garcia-Solis et al., 2009). The growth arrest that occurs when cultured cells are treated with polyphenolic substances like genistein (Chan et al., 2003) curcumin (Das, Chaudhuri et al., 2002) and tea catechins coincides with the decreased proliferation found in HeLa cells treated with *O. humifies* extracts (Bhesh et al., 2017).

Opuntia humifusa aqueous extract alleviates ethanol-induced gastric ulcer in a mouse model *Opuntia humifusa*

Aqueous extract alleviates ethanol-induced gastric ulcer in a mouse model Gastric ulcer on ethanol-induced animal model, the gastroprotective properties of *O. humifies* aqueous extract were investigated. Polyphenolics, flavonoids, and dietary fibers are found in greater amounts in this plant than in any other subtropical plant. The anti-ulcer properties of *O. humifies*, on the other hand, are unknown. As a result, we used an ulcer model to test the gastroprotective efficacy of this plant extract. *O. humifies* extracts have anti-inflammatory (Hahm et al., 2009; Ahn et al., 2014) anti-diabetic, anti-aging, skin whitening, anticancer, and antioxidant properties (Hahm et al., 2011).

***Opuntia humifusa* Ameliorated Cerulein-Induced Acute Pancreatitis:** In this work, the protective benefits of *O. Humifusa* were shown in a mouse model of cerulein-induced Acute Pancreatitis. Our findings show that *O. Humifusa* reduces pancreatic damage and the resulting lung harm. The activity of serum amylase, lipase, cytokine, and MPO was lowered both before and after *O. Humifusa* therapy. And also discovered that the inhibitory effects of *O. Humifusa* on acute pancreatitis are mostly due to a decrease in pancreatic cell death (Huang et al., 2005).

Opuntia humifusa stems lower blood glucose and cholesterol levels in streptozotocin-induced diabetic rats

In the Diabetics mellitus (DM) groups, STZ-induced diabetes resulted in a rise in blood glucose levels and a reduction in insulin levels. The blood glucose levels of the *O. humifusa* stems groups were considerably lower than those of the DM controls after the rats were given *O. humifusa* for 7 weeks. Furthermore, comparable to other high-fiber–containing foods, *O. humifusa* dietary fibre content and maybe other carbohydrate components may explain for its glucose-lowering impact (Cho et al., 2001; Platt and Bailey, 1982). Insulin non-starch carbohydrate in the diet was linked to a markedly low glucose response (Coskun et al., 2005). Flavonoids have been linked to an increase in beta cell mass, with flavonoids either preventing apoptosis or boosting beta cell proliferation. In terms of beta cell actions in vivo, the flavonoid-rich portion of Egyptian moru alba root has been shown to protect against STZ-induced damage. Similar effects were reported in diabetic rats fed *O. humifusa* in this investigation. In rats

with STZ-induced diabetes, administration of *O. humifusa* resulted in a drop in serum glucose levels and a modest rise in serum insulin concentrations. Flavonoids such as quercetin and its derivatives are abundant in the stems of *O. humifusa*. Vitamin C and E deficiency has been found in diabetes individuals and experimental animals in several investigations (Butterworth et al., 2005 ; Eklund Långvik et al., 2005).

Treatment on the Mass, Quality, and the Turnover of Bone in Ovariectomized Rats

The current research shows that regular oral treatment of *O. humifusa* stem extract can prevent bone loss in rats caused by ovarian hormone deprivation. In Ovariectomized rats, it increased bone mass, quality, and mechanical strength. The high concentration of polyphenolic chemicals found in *O. humifusa* appears to be responsible for these benefits. As a result, it might be a competitor for the development of innovative herbal techniques to treating osteoporosis in postmenopausal women (Alves et al., 2005 ; Yen Hsieh 2002 ; Ahn et al., 2017).

Biological activities of water-soluble polysaccharides (WSP) from *O. humifusa* stem in high-fat-diet-fed mice

Finally, high molecular weight water soluble acidic heteropolysaccharides, most likely arabinogalactans, were isolated from the stems of *O. humifusa*. They were mostly constituted of arabinose, galactose, and uronic acid. In high fat diet fed mice, the biological activity of the polysaccharide indicated their benefits in avoiding cardiovascular illnesses, diabetes, gastrointestinal ulcer, immunological function, and constipation improvement. These findings show that the WSP of *O. humifusa* stem has the potential to be exploited for pharmacological and therapeutic purposes (Campanile et al.,1994).

Cactus cladodes (*Opuntia humifusa*) extract minimizes the effects of UV irradiation on keratinocytes and hairless mice

In photo damaged human keratinocytes, *O. humifusa* extract has been shown to greatly increase HAS (Hyaluronic acid synthase) expression, which regulates HA (hyaluronidase) production. The protective effect of *O. humifusa* was attributed to increased HAS transcript expression and reduced HYAL (hyaluronidase) transcript expression, not to skin cell proliferation stimulation. In hairless mice exposed with UV, *O. humifusa* extracts treatments prevented trans epidermal water loss and erythema formation, it appears that *O. humifusa* extracts protects the skin against photodamage caused by UVB rays. As a result, *O. humifusa* extracts has the potential to be employed in cosmetics (Hashizume et al.,1997; Alam et al.,2020).

Discussion and Conclusion

The present review on plant demonstrates that daily oral administration of *O. humifusa* extract is effective in preventing in various diseases. *O. humifusa* includes an abundance of antioxidant components that have great therapeutic and cosmetic applications. The cladode of *O. humifusa* appear to have the potential to be used as a functional food item in the future. *O. humifusa* is a good source of dietary fibre and contain nutritional components. These findings might indicate that *O. humifusa* is a viable drug with therapeutic benefits. the results of this study show that *O. humifusa* may be regarded a functional food for the development of bone strength. Other unidentified components yet to be revel.

The *O. humifusa* has been used from many decades in Ayurveda because of its pharmacological importance. *O. humifusa* have lots of pharmacological properties i.e., antimicrobial, antifungal, anticancer antidiabetic, antioxidant, radical scavenging and anti-inflammatory (ascorbic acid, Vanillic acid, p-coumaric acid, ferulic acid, syringic acid, 4-hydroxybenzoic acid, protocatechuic acid, salicylic acid, caffeic acid, gallic acid). It can also be used to treat breast cancer very effectively. *O. humifusa* have been recommended for the treatment of diarrhea, skin diseases and high fat diet. *O. humifusa* disclose the strong medicinal properties of the plant. The use of *O. humifusa* aqueous extract as a safe and effective technique for controlling and treating stomach ulcers is highlighted by the above-mentioned findings. therefore, they seem to be interesting for investigation of new pharmaceuticals.

In terms of phytochemical constituents and pharmacology, a vast reservoir of selected species remains untapped, and this is the research gap for future studies. Further research into *Opuntia humifusa* plant and their phytochemical constituents is required to fully understand the molecular mechanisms of their action in vivo and in vitro, as well as to ensure that plant extracts are safe for human consumption.

Conflict of interest

The authors have no conflicts of interest regarding this exploration**.**

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References

Ammar I, Bardaa S, Mzid M, Sahnoun Z, Rebaii T, Attia H.2015. Antioxidant, antibacterial and in vivo dermal wound healing effects of Opuntia flower extracts. International Journal of Biological Macromolecules, 81:483-90.

Bhesh Raj Sharma, Park CM, Choi JW, Rhyu DY. 2017. Anti-nociceptive and anti-inflammatory effects of the

methanolic extract of *Opuntia humifusa* stem. Avicenna Journal of Phytomed, 7(4):366-375.

Birasuren B, Kim NY, Jeon HL, Kim MR. 2013. Evaluation of the antioxidant capacity and phenolic content of *Agriophyllum pungens* seed extracts from Mongolia. Preventive Nutritional and Food Science, 18:188–195.

Cai Y, Luo Q, Sun M, Corke H. 2004. Antioxidant activity and phenolic compounds of 112 traditional Chinese medicinal plants associated with anticancer. Life Science ,74:2157–2184.

Chan MM, Fong D, Soprano KJ, Holmes WF, Heverling H. 2003. Inhibition of growth and sensitization to cisplatin-mediated killing of ovarian cancer cells by polyphenolic chemopreventive agents. Journal Cell Physiology, 194:63–70.

Cho IK, Jin SW, Kim YD. 2009. Analysis of components in the parts of *Opuntia ficus indica* from Shinan, Korea. Korean Journal of Food Preservative, 16:742-746.

Cho JY, Park S-C, Kim T-W, Kim K-S, Song J-C, Kim S-K. 2006. Radical scavenging and anti-inflammatory activity of extracts from *Opuntia humifusa* Raf. Journal of Pharmacy Pharmacology, 58(1):113–9.

Choi SB, Bae G-S, Park K-C, Jo I-J, Seo S-H, Song K. 2014. *Opuntia humifusa* ameliorated cerulein-induced acute pancreatitis. Pancreas, 43(1):118–27.

Christiana Eleojo Aruwa, Stephen O. Amoo, Tukayi Kudanga. 2018. Opuntia (Cactaceae) plant compounds, biological activities and prospects – A comprehensive review. Food Research International, (112).

Coskun O, Kanter M, Korkmaz A, Oter S. 2005. Quercetin, a flavonoid antioxidant, prevents and protects streptozotocin-induced oxidative stress and beta-cell damage in rat pancreas. Pharmacology Research, 51:117-23.

Das M, Chaudhuri T, Goswami SK, Murmu N, Gomes A, Mitra S, et al., 2002. Studies with black tea and its constituents on leukemic cells and cell lines. Journal of Experimental Clinical and Cancer Research, 21:563–568.

Dinicola S, Mariggio MA, Morabito C, Guarnieri S, Cucina A, Pasqualato A, D'Anselmi F, et al., 2013. Grape seed extract triggers apoptosis in Caco-2 human colon cancer cells through reactive oxygen species and calcium increase extracellular signal-regulated kinase involvement. British Journal of Nutrition, 110:797–809.

Eklund PC, Langvik OK, Warna JP, Salmi TO, Willfor SM, Sjoholm RE. 2005. Chemical studies on antioxidant mechanisms and free radical scavenging properties of lignans. Organic and Biomolecular Chemistry, 3336-3347.

Feugang JM, Ye F, Zhang DY, Yu Y, Zhong M, Zhang S . 2010. Cactus pear extracts induce reactive oxygen species production and apoptosis in ovarian cancer cells. Nutritional Cancer, 62:692–699.

Frey RS, Singletary KW. 2003. Genistein activates p38 mitogen-activated protein kinase, inactivates ERK1/ERK2 and decreases Cdc25C expression in immortalized human mammary epithelial cells. Journal of Nutrition, 133:226–231.

Garcia-Solis P, Yahia EM, Morales-Tlalpan V, Diaz-Munoz M. 2009. Screening of antiproliferative effect of aqueous extracts of plant foods consumed in Mexico on the breast cancer cell line MCF-7. International Journal of Food Science Nutritional, 60 Supplements 6:32–46.

Grigelmo-Miguel N, Martin-Belloso O. 1999. Comparison of dietary fiber from byproducts of processing fruits and greens from cereals. LWT Food Science and Technology, 32:503-508.

Guevara-Figueroa, T, Jiménez-Islas, H, Reyes-Escogido, Mortensen, AG Laursen et al., 2010. Proximate composition, phenolic acids, and flavonoids characterization of commercial and wild nopal (Opuntia spp.). Journal of Food Composition and Analysis, 23:525–532.

Ha, M.-J, You, S.-H, Ha, M.-J, You, S.-H. 2016. Bioactive characteristics of extracts of *opuntia humifusa* fruit as functional cosmetic ingredients. Asian Journal of Beauty and Cosmetology, 14:463–472.

Han, AR, Lim, TG, Song, YR, Jang, M, Rhee . 2018. Inhibitory effect of *opuntia humifusa* fruit water extract on solar ultraviolet-induced MMP-1 expression. International Journal of Molecular Science, 19, 2503.

Han, SH, Park, K, Kim, EY, Ahn, SH, Lee, HS, Suh.2017. Cactus (*Opuntia humifusa*) water extract ameliorates loperamide- induced constipation in rats. BMC Complementary and Alternative Medicine, 17, 49.

Hahm SW, Park J, Son YS. 2010. *Opuntia humifusa* partitioned extracts inhibits the growth of U87MG human glioblastoma cells. Plant Foods Human Nutrition, 65(3):247-52.

Hahm SW, Park JE, Son YS. 2011.*Opuntia humifusa* stem lower blood glucose and cholesterol levels in streptozotocin-induced diabetic rats. Nutritional Research, 31: 479-487.

Jo MS, Lee S, Yu JS, Baek SC, Cho YC, Kim KH. 2020. Megastigmane derivatives from the cladodes of *Opuntia humifusa* and their nitric oxide inhibitory activities in macrophages. Journal of Natural Products,

83(3):684–92.

Jung BM, Han KA, Shin TS. 2011. Food components of different parts of cheonnyuncho *(Opuntia humifusa*) harvested from Yeosu, Jeonnam in Korea. Journal of Korean Social and Food Science Nutrition, 40: 1271-1278.

Kim YJ, Park CI, KIM SJ, Ahn EM. 2014. Antioxidant and inflammatory mediators' regulation effects of the roots of *Opuntia humifusa*. Asian Pacific Journal of Tropical Biomedicine, 57: 1-5.

Kim DH, Yang BK, Jeong SC, Park JB, Cho SP, Das S. 2001. Production of a hypoglycemic extracellular polysaccharide from the submerged culture of the mushroom, Phellinus linteus. Biotechnology Lett, 23:513-7.

Kwon DK, Song YJ. 2005. Effect of *Opuntia humifusa* supplementation on endurance exercise performance in rats fed a high-fat diet. Korean Journal of Exercise and Nutrition, 9: 183-18.

Lee JA, Jung BG, Kim TH, Lee SG, Park YS, Lee BJ. 2013. Dietary feeding of *Opuntia humifusa* inhibits UVB radiation-induced carcinogenesis by reducing inflammation and proliferation in hairless mouse model. Photochemical Photobiological, 89(5):1208–15.

Lee KS, Oh CS, Lee KY. 2005. Antioxidative effect of the fractions extracted from a cactus Cheonnyuncho (*Opuntia humifusa*). Korean Journal of Food Science Technology, 37(3):474-8.

Lee JN, Lee CH, Kim YS. 2015. Protective effects of *Opuntia humifusa* cladode extracts against biostir AD-induced atopic dermatitis in NC/Nga mice. Food Science Biotechnology 24(3):1123–30.

Lee SH, Yoo CY, Son HU, Fanar A, Choi HJ, Alam M. 2020. *Opuntia humifusa* aqueous extract alleviates ethanol-induced gastric ulcer in a mouse model. Asian Pacific and Journal Tropical Biomedical,10(9):403.

Lee WTK, Leung SSF, Leung DMY, Wang SH, Xu YC, Zeng WP. 1997. Bone mineral acquisition in low calcium intake children follow the withdrawal of calcium supplement. Acta Paediatrica nurturing the child, 86: 570-576.

Lo HC, Tsai FA, Wasser SP, Yang JG, Huang BM. 2005. Effects of ingested fruiting bodies, submerged culture biomass, and acidic polysaccharide glucoronoxylomannan of Tremella mesenterica Retz: Fr on glycemic responses in normal and diabetic rats. Life Science, 78:1957-66.

Moon JY, Ngoc LTN, Chae M, Van Tran V, Lee YC. 2020. Effects of microwave-assisted *Opuntia humifusa* extract in inhibiting the impacts of particulate matter on human keratinocyte skin cell. Antioxidant, 9(4):271.

Nazirogilu M, Butterworth P. 2005. Protective effects of moderate exercise with dietary vitamin C and E on blood antioxidative defense mechanism in rats with streptozotocin-induced diabetes. Canadian Journal of Applied Physiology, 30(2):172-85.

Park J, Hahm SW, Son YS. 2011. Effects of Cheonnyuncho (*Opuntia humifusa*) seeds treatment on the mass, quality, and the turnover of bone in ovariectomized rats. Food Science Biotechnology, 20(6):1517–24.

Park, K, Choi, H.-Song, Y .H, Jung, E.Y, Suh, H.J. 2017. Cactus cladodes (*Opuntia humifusa*) extract minimizes the effects of UV irradiation on keratinocytes and hairless mice. Pharmaceutical Biology, 55: 1032–1040.

Platt PR, Bailey CJ. 1982. Role of dietary factors in the hyperinsulinemia of genetically/obese hyperglycaemic (ob /ob) mice. Journal of Nutrition, 112: 2212-6.

Sahng Wook, Jieun Park, Yong-Suk Son. 2011. *Opuntia humifusa* stems lower blood glucose and cholesterol levels in streptozotocin-induced diabetic rats. Nutritional Research 31, 479–487.

Sánchez-Castillo C, Dewey P, Aguirre A, Lara J, Vaca R, Leon P. 1998. The mineral content of Mexican fruits and vegetables. Journal of Food Composition and Analysis, 11: 340-356.

Sara Bensadon, Deisy HH, Sonia G, Sayago-Ayerdi et al., 2010. By-Products of *Opuntia ficus-indica* as a Source of Antioxidant Dietary Fiber. Plant Foods for Human Nutrition, 65:210–6.

Seong G, Lee S, Min YW, Jang YS, Park SY, Kim CH. 2020. Effect of a Symbiotic Containing Lactobacillus paracasei and *Opuntia humifusa* on a Murine Model of Irritable Bowel Syndrome. Biomolecules and Nutrient, 12(10):3205.

Silva-Hughes AF, Wedge DE, Cantrell CL, Carvalho CR, Pan Z, Moraes RM. 2015. Diversity and antifungal activity of the endophytic fungi associated with the native medicinal cactus *Opuntia humifusa* (Cactaceae) from the United States. Microbiology and Research, 175:67-77.

Slattery ML, Benson J, Curtin K, Ma KN, Schaeffer D, Potter JD. 2000. Carotenoids and colon cancer. American Journal of *Clinical Nutrition*, 71(2),575–582,

Taxonomic revision of the *Opuntia humifusa* complex (Opuntieae: Cactaceae) of the eastern United. 2.

Teixeira S, Siquet C, Alves C, Boal I, Marques MP, Borges F. 2005. Reis S. Structure–property studies on the antioxidant activity of flavonoids present in diet. Free Radical Biology & Medicine 39, 1099 -1108.

Yang EI, Lee CH, Che DN, Jang SI, Kim YS.2019. Biological activities of water-soluble polysaccharides from *Opuntia humifusa* stem in high-fat-diet-fed mice. Journal of Food and Biochemistry ,43(4): 12806.

Yoon JA, Hahm SW, Son YS. 2009. Nutrients contents in different parts of prickly pear (*Opuntia humifusa*) and possible anti-breast cancer effect. Korean Journal of Food Nutrients, 22: 485-491.

Yen GC, Hsieh CL.2002. Inhibitory effects of Du-zhong (Eucommia ulmoides Oliv.) against low-density lipoprotein oxidative modification. Food Chemistry,77: 449-456.

Zhao LY, Huang W, Yuan QX, Cheng J, Huang ZC, Ouyang LJ. 2012. Hypolipidemic effects and mechanisms of the main component of *Opuntia dillenii* Haw. polysaccharides in high-fat emulsion-induced hyperlipidaemic rats. Food Chemistry, 134:964–971.

Zhong, XK, Jin, Lai, FY, Lin, QS, Jiang, JG. 2010. Chemical analysis and antioxidant activities in vitro of polysaccharide extracted from *Opuntia ficus indica* Mill. Cultivated in china. Carbohydrates and Polymers,82, 722–727.