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OPUNTIA FICUS-INDICA: ESCALATING FROM FARM TO PHARMACOLOGICAL ACTIONS

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ABSTRACT: Medicinal plants are a reservoir of biologically active compounds with therapeutic properties, and in that context, *Opuntia ficus indica* and other *Opuntia* species are of immense importance because of their nutraceutical and pharmaceutical values along with their anti-inflammatory effects, hypoglycemic, anti-hyperlipidemic effects, anti-atherogenic and anti-spermatogenic potential. The cactus *Opuntia* is a xerophytic plant grown in more than thirty countries, including Mexico, South America, South Africa and India. All parts of the plant, including pear, roots, cladodes, seeds and juice, have these pharmacological properties, which have been attributed to the presence of high content of phenolic acids, flavonoids such as quercetin, kaempferol, anthocyanin and ascorbate *etc.*, and pigments such as carotenoids, betalains, tannins *etc.* Other reported phytochemical components such as biopeptides, phytoalbumins, minerals such as vitamin B1, B2, B3 and Vitamin C, soluble fibers also add to the medicinal properties of *Opuntia spp.* presence of these bioactive has made *Opuntia* a high potential plant that can be investigated for commercial production and consumption as a nutraceutical. The present review provides an up-to-date report on phytochemical composition, distribution, and habitat-cultivation conditions, various pharmacological and nutraceutical properties of *Opuntia*. The contribution of this herb to medicinal activities has been demonstrated by numerous studies carried out *in-vitro* and *in-vivo* and it can be considered as an important medicinal plant that has enormous potential which has not yet been fully evaluated.

INTRODUCTION: Phytopharmaceuticals have been important sources of traditional medicines as well as modern drugs. These have been harnessed since long for the prevention and cure of diverse ailments. The use of phytopharmaceutical substances to control diseases as an age-old practice has steered the drug discovery regime to identify and validate these phytopharmaceutical candidates for a safe and effective alternative approach towards creating healthy individuals.

Natural products extracted from plants especially from the Cactaceae family, have been widely used in folk medicine and in pharmaceutical and nutraceutical industries. One of the most important genera in this family is *Opuntia*, with more than 200- 300 species, mainly growing wild in arid and semi-arid regions ^{1,2}.

Opuntia ficus-indica (L.) Miller is a tree-like cactus belonging to the Cactaceae family. Although indigenous to Mexico, this plant is distributed in different parts of the world, including India. The cactus is majorly cultivated for its sweet and juicy fruit (prickly pear), having rich in nutritional benefits ² and has vast potential for commercial processing in semi-parched districts of the world for the pharmaceutical industry and nutraceutical

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industry due to its active nutrients and multiple properties of bioactive compounds³⁻⁵. This review provides a complete and updated account of various active compounds and the biological and medical benefits of wild and domesticated *Opuntia* spp. in chronic diseases, along with the probable mechanisms. The review aims to explore the food and functional potential of this fruit as a nutraceutical with immense health benefits to mankind.

Habitat: The cactus *Opuntia* (genus *Opuntia*, subfamily *Opuntioideae*, family Cactaceae) is a xerophyte representing about 200 – 300 species and is mainly growing in arid (less than 250 mm annual precipitation) and semi-arid (250 – 450 mm annual precipitation) zones. Due to their remarkable genetic variability, *Opuntia* plants show a high ecological adaptivity and can therefore be encountered in places of almost all climatic conditions^{8,11}.

Botany: The *Opuntia* cacti represent the most distinguishing species of succulent plants because of its shallow root system that allows rapid water uptake along with a thick, waxy cuticle that prevents unrestricted water loss and crassulacean acid metabolism (CAM), an alternative photosynthetic pathway that allows plants to uptake atmospheric carbon di oxide at night when water loss is reduced. These plants are acknowledged as supreme crops for arid regimes because they are exceptionally efficient at producing biomass under insufficient water conditions. The subfamily *Opuntioideae* is further classified based on short,

sharp, barbed, deciduous spines called glochids^{2,6}. The fruit of this plant is oval or elongated berry fruit, consisting of thick fleshy skin or rind surrounding a juicy pulp having varying degrees of edibility, flavor and sweetness, which contains many hard-coated seeds. The skin and pulp colour, pulp texture, sugar content, and juice acidity of cactus fruits are directly related to the presence, intensity, and activity of nutritional and functional compounds⁷.

Production: *Opuntia* plants are grown in more than 30 countries on about 100 000 ha^{2, 11, 12} among others Mexico, the Mediterranean (Egypt, Italy, Greece, Spain, Turkey), California, South America (Argentina, Brazil, Chile, Columbia, Peru), the Middle East (Israel, Jordan), North Africa (Algeria, Morocco, Tunisia), South Africa, and India^{2, 11, 13, 14}. Commercial cultivation of *Opuntia* is done in Italy, Spain, Mexico, Brazil, Chile, Argentina and California. As a CAM plant, *Opuntia* spp. is distinguished by an increased water use efficiency of 4 - 10 mmol CO₂ per mol H₂O. Through succulence, the capacity to store high quantities of water, the plant may pull through despite extreme environmental conditions^{2, 15}. The harvesting is done from April to August when the plant reaches a weight of 90 – 100 g and a length of 15 – 20 cm^{2, 16-18}. *Opuntia* plants give rise to edible stems known as pads, vegetables, cladodes, nopales, or pencas. The soft young part of the cactus stem, young cladode or “nopalitos”, is more commonly consumed as vegetable in salads, while the cactus pear fruit is consumed as a fresh fruit.



FIG. 1: *OPUNTIA* CLONES INTRODUCED IN INDIA FROM TEXAS, USA (1987)¹⁴

Opuntia: Introduction in India: As shown in Fig. 1 and 2, thirty-three *Opuntia* clones were introduced in India in 1987 at the Nimbkar Agricultural Research Institute at Phalton, India, through an Indo-US collaborative research program from Texas A&M University. Subsequently, five promising clones (1270, 1271, 1280, 1287, and 1308) having low water requirements were introduced at Karnal. As cactus pear can grow well with low inputs and pre-requirements and even under wasteland conditions, great potential was

found for its adoption and cultivation as a commercial crop in arid regions of India such as Bikaner. It was also cultivated as four exotic varieties of cactus-pear fruiting types (1271, 1280), and vegetable type (1308 and Nopalea) in Agra. Similarly, this plant was introduced in rain-fed Bundelkhand region (Central India) as a surrogate source of forage, as a bio fence, and as a source of food for the economically weaker human and animal population settled in this ecologically poor environment¹⁹.

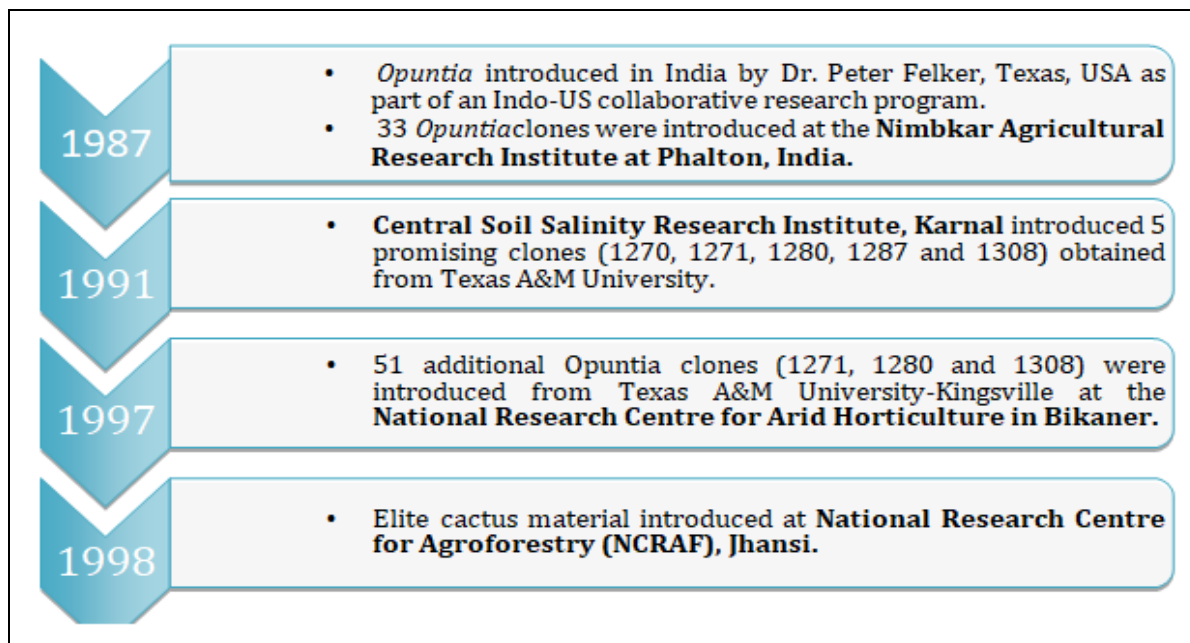


FIG. 2: TIMELINE OF *OPUNTIA* CLONES INTRODUCED IN INDIA

Composition and Nutritional Characteristics of *Opuntia Ficus Indica*: The cactus pear is an oval or elongated berry fruit (typically 100-200g), consisting of thick fleshy skin or rind (30-40 percent of total fruit weight) surrounding a juicy pulp (60-70 percent of total fruit weight), which contains many hard-coated seeds (5-10 percent of the pulp weight)²⁰. In general, the prickly pear fruit contains approximately 85% water, 15% sugar, 0.3% ash, and less than 1% protein, as shown in Fig. 3^{21, 24, 25}. According to the United States Department of Agriculture and based on the amount of daily value (DV) provided in a 100 g serving, the fruit has a moderate content of essential nutrients, as shown in Fig. 4. The dietary fiber is 14% DV, and vitamin C content is 23% DV. Among minerals, magnesium has a 21% DV. The other constituents in fresh fruit pulp are carbohydrates (9.57%), fiber (3.6%), and lipids (0.51%). The nutritionally important vitamin

content in 100g of fresh fruit pulp was Niacin (Vitamin B3) (Trace amounts), Riboflavin (Vitamin B2) (0.06%), Thiamine (Vitamin B1) (0.014%), Vitamin E (111–115µg) and Vitamin K1 (53µg). The mineral content in prickly pear fruit pulp was found to be as Calcium (56 mg/100g), Iron (0.30 mg/100g), Magnesium (85 mg/100g), Phosphorous (24 mg/100g), Potassium (220 mg/100g), Selenium (0.6 mg/100g), Sodium (5 mg/100g) and Zinc (0.18 mg/100g)”^{21, 22}. However, the quantities and concentrations of the nutritional components of the fruit vary with the cultivation site, climate and fruit variety²¹⁻²³. The seeds of cactus fruits contain significant amounts of proteins and lipid, the latter composed of about 75 percent linoleic acid. In fruits of different *Opuntia* species, seed protein content varies from 3 to 10 percent dry weight and seed lipid content varies from 6 to 13 percent dry weight²⁰.

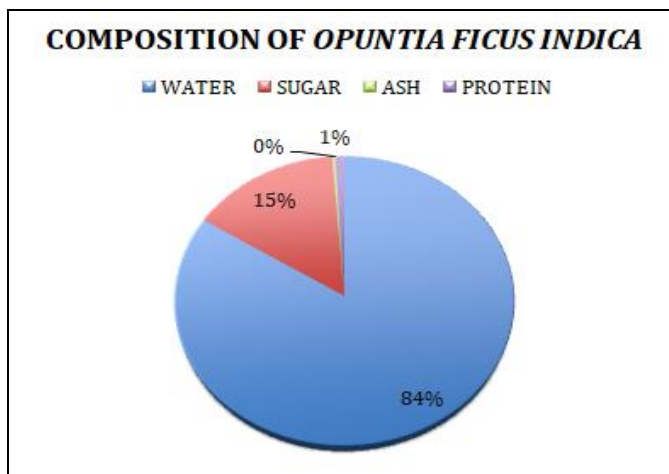


FIG. 3: PIE CHART REPRESENTING BASIC COMPOSITION OF *OPUNTIA FICUS INDICA* BASED ON AMOUNT OF DAILY VALUE PROVIDED IN 100G SERVING ACCORDING TO THE UNITED STATES DEPARTMENT OF AGRICULTURE

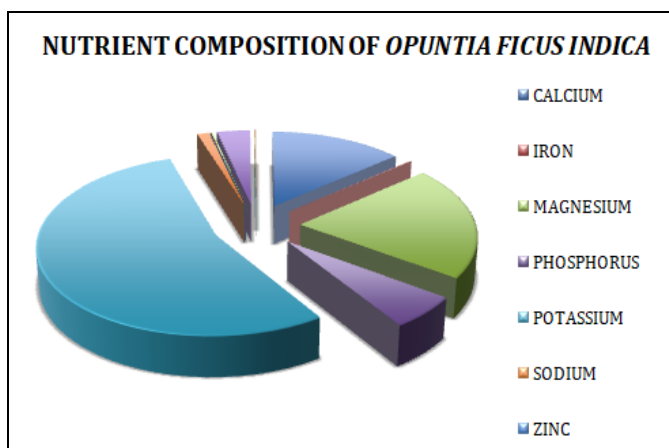


FIG. 4: PIE CHART REPRESENTING NUTRIENT COMPOSITION OF *OPUNTIA FICUS INDICA* IN mg/100g ACCORDING TO UNITED STATES DEPARTMENT OF AGRICULTURE

Pharmacological Properties of *Opuntia* Species:

Opuntia ficus indica is used for its pharmaceutical, nutraceutical, and cosmeceutical properties in tea, jam, juice, oil, as shown in Fig. 5 and 6. It is applied as an herbal remedy for many wide ranges of health problems in different countries. For instance, in the sub-Saharan traditional medicine pharmacopeia, cactus flowers and fruits are used as anti-ulcer genic or antidiarrheal agents; flowers being also administered as an oral anti-hemorrhoid medication and cladode sap as a treatment for whooping cough. On the other hand, indigenous populations consume large amounts of either fresh or dried fruits as food. In these populations, cactus cladodes, fruits and flowers are featured for their interesting contents of antioxidants, pectin polysaccharides and fibers³⁴ *Opuntia* has high values of antioxidant compounds such as polyphenols, flavonoids, betaxanthin, and betacyanin^{1, 26}. Hence, most parts of the cactus plant (pulp, peel, seeds, and cladode) have shown notable antioxidant activities^{1, 27-29}. Moreover, cactus pear fruit extract has presented with activities such as anti-ulcer genic, antioxidant, anticancer, neuroprotective, hepatoprotective and anti-proliferative activities^{2, 27, 30-33}. Prickly pear has also been used for the treatment of gastritis, hyperglycemia, arteriosclerosis, diabetes, and prostate hypertrophy, as shown in Fig. 5^{35, 36}. Further sections review the various pharmacological activities of this fruit and its possible applications as a functional food with medicinal properties.

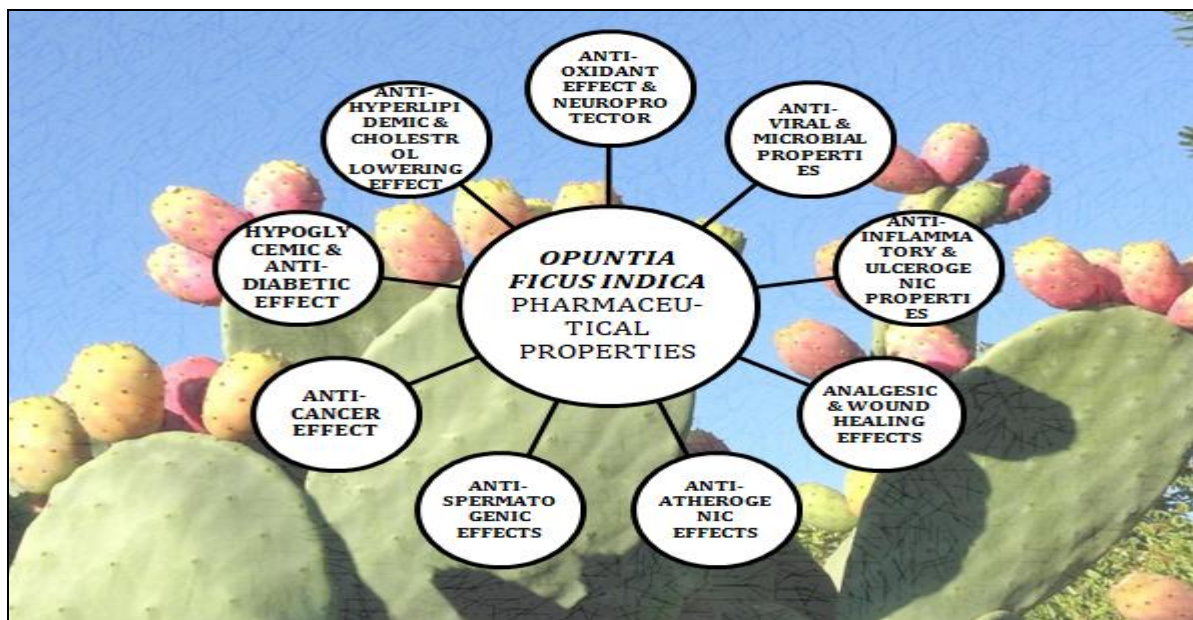


FIG. 5: VARIOUS PHARMACEUTICAL PROPERTIES OF *OPUNTIA FICUS INDICA*

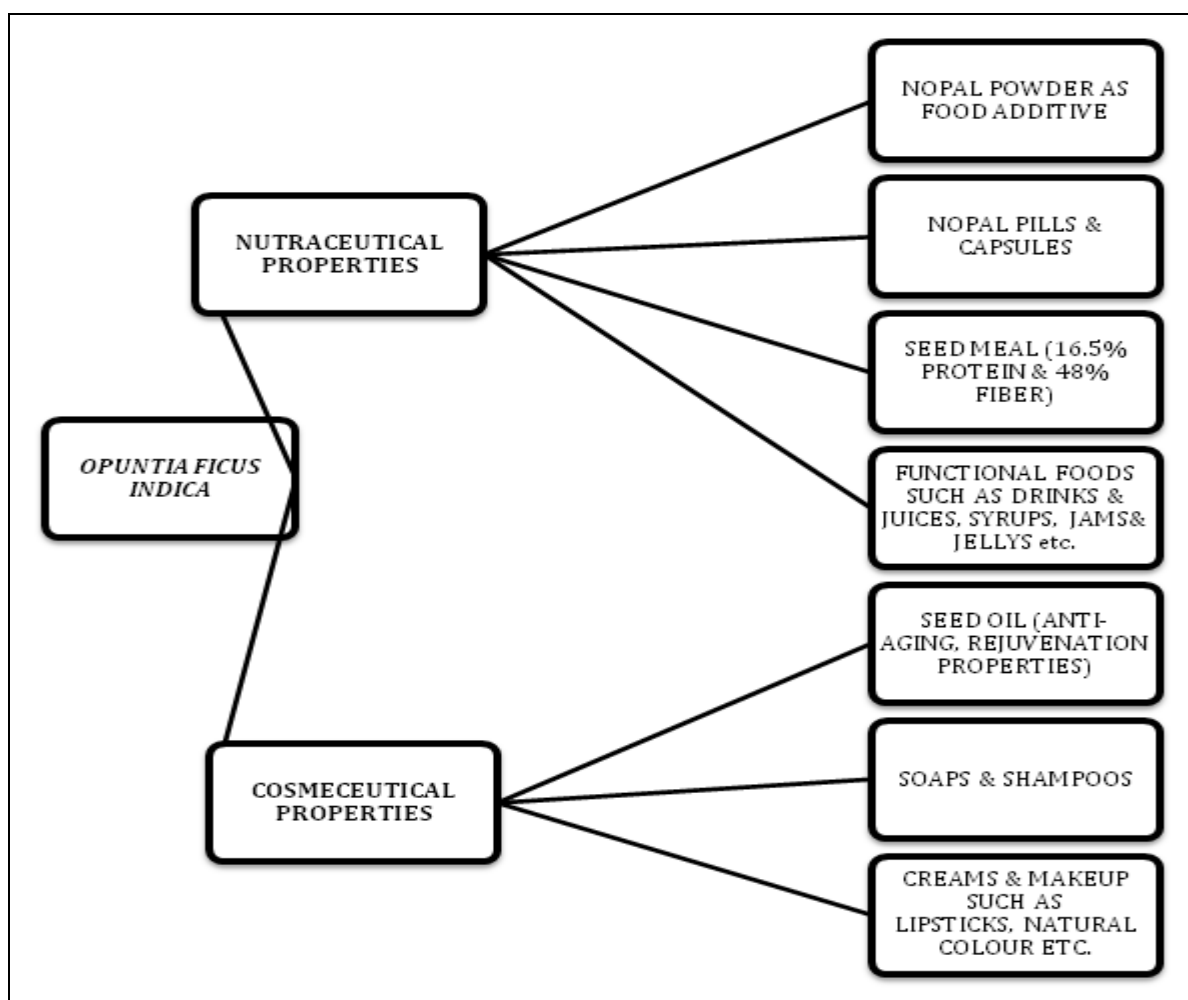


FIG. 6: VARIOUS NUTRACEUTICAL AND COSMECEUTICAL PROPERTIES OF *OPUNTIA FICUS INDICA*

Anti-Oxidant Capacity: The recent advances in the knowledge of free radicals and reactive oxygen species (ROS) in biology have led to a medical revolution that promises a new age of health and disease management and the search for effective, nontoxic natural compounds with antioxidative activity has intensified in recent years. A positive correlation has been found in numerous studies between a plant-based diet and decreased risk of diseases such as cancer, neurodegenerative and cardiovascular ailments especially caused by high oxidative stress. The antioxidant action is one of many characteristics by which fruit and vegetable substances might show their beneficial health effects^{37, 38, 44-46}. The presence of several antioxidants (ascorbic acid, carotenoids, reduced glutathione, cysteine, taurine, and flavonoids such as quercetin, kaempferol, and isorhamnetin) has been reported from fruits and vegetables of different varieties and categories of cactus prickly pear^{37-39, 41, 47}. These characteristics are due to the ability of antioxidants to neutralize reactive oxygen

species such as singlet oxygen, hydrogen peroxide or H_2O_2 , or suppress the xanthine/xanthine oxidase system, all of which may lead to oxidative injury, *i.e.*, lipid peroxidation. These have been validated by various phytochemical investigations, metabolome analysis and *in-vitro* and *in-vivo* studies^{37, 39, 40, 42, 46-50}.

Reports and previous studies have indicated the dose-dependent protective effect of *Opuntia ficus-indica* fruit extract on erythrocytes against lipid oxidation induced *in-vitro* by ethanol^{51, 52}. The same extract was also found to be active in protecting plasmid DNA against the strand breakage induced by hydroxyl radicals. Phytochemical investigations of the ethanol extract revealed the presence of high number of phenolic compounds namely quercetin, (+)-dihydroquercetin, and quercetin-3-methyl ether which may be responsible for antioxidant activity. These quercetin derivated are well recognized as free radical scavengers capable of preventing

neuronal cell damage caused by H_2O_2 and xanthine/xanthine oxidase^{2, 50}. Restoration of scavenging activity in a dose-dependent manner to near normal level has also been reported in ethanol fed rats provided with prickly pear^{51, 53}. The

normalization of scavenging activity by prickly pear juice supplement could be because of the natural antioxidants, which could modify the internal imbalance between oxidant species and the antioxidant defense system⁵¹.

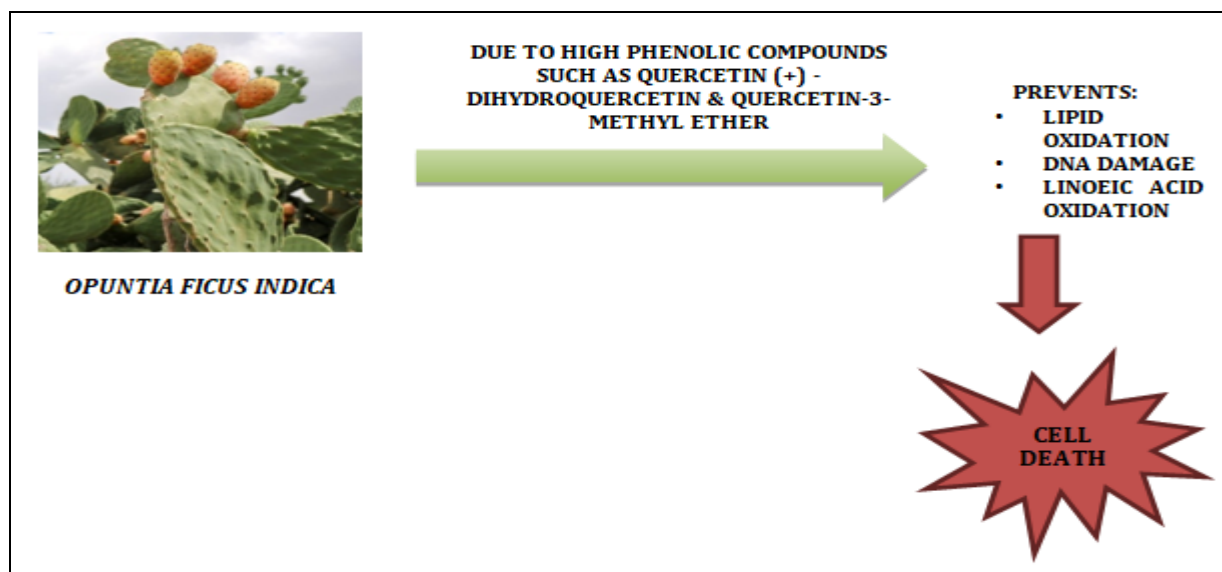


FIG. 7: PHYTOCHEMICAL INVESTIGATIONS REVEALED THAT *OPUNTIA FICUS INDICA* CONTAINS HIGH AMOUNTS OF PHENOLIC COMPOUNDS SUCH AS QUERCETIN (+) - DIHYDROQUERCETIN AND QUERCETIN-3-METHYL ETHER WHICH ARE RESPONSIBLE FOR PROVIDING POTENT ANTIOXIDANT DEFENSE SYSTEM

Similar phytochemical investigations on the red-skinned fruits extracts reported the presence of ascorbic acid, carotenoids, betalains, taurine, flavonoids (quercetin, isorhamnetin, kaempferol, luteolin) and free radical scavenging ability^{54, 55}. Ascorbic acid contributes up to 68% of the antioxidant activity of cactus juices^{51, 60}. Polyphenols and betacyanin extracts of *Opuntia*, may play role as an electron donor to convert free radicals to more stable products, thereby scavenging the generated free radicals^{55, 56}. Similarly, flavonol glycosides in cactus flowers extract are used as additives in food, cosmetic and pharmaceutical products for their antioxidant power^{55, 57}. These compounds are more effective antioxidants than vitamins, since flavonoids, and phenolic compounds in general, are able to delay the pro-oxidative effects on proteins, DNA and lipids through the production of stable radicals^{51, 61}. *Opuntia ficus-indica* glycoprotein did not have any cytotoxic effect and instead protected liver cells because of its scavenging activity against G/GO-induced radical production^{51, 62}. These results show that *Opuntia ficus-indica* glycoprotein shows antioxidant and cytoprotective effects *in-vitro*, either directly or indirectly⁵¹.

Similar studies on *Opuntia-humifusa* have demonstrated the chemo preventive potential on chemical carcinogenesis in mouse skin by reducing the oxidative stress *via* the modulation of cutaneous lipid peroxidation, thereby enhancing the total antioxidant capacity, especially in phase II detoxifying enzyme system and partial apoptotic influence^{51, 58}. In other related studies in senescence-accelerated mice (SAM), the anti-oxidant activity of *Opuntia ficus indica* fruit was evaluated throughout the aging process. The effects on the anti-oxidant system, including thiobarbituric acid reacting substance (TBARS), glutathione (GSH), superoxide dismutase, and catalase, were studied in 7-month-old SAM-P8 after oral administration of *Opuntia* (1.2g/kg/day) for 30 days^{66, 67}. The revealed that the TBARS was markedly decreased in *Opuntia* treated mice compared to the control group ($P < 0.05$), while GSH content was significantly increased in *Opuntia* treated mice compared to the control group ($P < 0.0001$). These findings suggested that *Opuntia spp.* have a functional role in increasing anti-oxidant activity in SAM, normal human beings and *in-vitro* cultures⁶⁷. Studies have also been conducted in humans to test the antioxidant activity of *Opuntia ficus-indica*

was tested. In one study 10 healthy participants consumed a diet poor in antioxidant components for 3 days followed by the addition of 300 g/day of *Opuntia ficus-indica* to their meals for the period of 3 days. The blood samples showed a significant increase in antioxidant activity due to the consumption of the 300 g of *Opuntia ficus-indica* for 3 days which was evident to the extent of 20% in plasma and 5% in blood. The most significant result was in plasma (20%) when compared with the activity shown in the sample obtained before the intake of *Opuntia ficus-indica*^{51, 59}. The body's global antioxidant status^{63, 64}, as well as individual antioxidant vitamins, and a number of markers of oxidative stress have also been measured in plasma and cells of healthy volunteers before (baseline) and after fifteen days during which they ingested fresh fruit pulp of Sicilian *Opuntia ficus-indica* (250 g twice daily), in addition to their usual diet^{63, 65}. With respect to the baseline, a remarkable increase of plasma vitamin E and vitamin C was observed, whereas vitamin A and TEAC did not vary significantly.

Analgesic Effect: Inflammation and pain are common nonspecific manifestations of many disorders which are conventionally treated through non-steroidal anti-inflammatory drugs (NSAIDs) and opiates. However, these drugs are associated with adverse reactions like gastrointestinal disturbances, renal damage, respiratory depression, and possible dependence^{2, 68}. In recent years, there has been an increasing interest in finding new anti-inflammatory and analgesic drugs with possibly fewer side effects from natural sources and medicinal plants. In this context, ethanolic extract of the cladodes (300 – 600 mg/kg body weight) from *O. ficus-indica* var. *saboten* have demonstrated almost the same analgesic effect as acetylsalicylic acid (200 mg/kg body weight)^{2, 68} without toxic effects in mice ($LD_{50} > 2$ g/kg body weight) even at high dosages. In another similar study the *Opuntia elatior* fruit juice was tested at varying doses for abdominal constriction caused by intra peritoneal injection of acetic acid (0.75%) and the results indicated similar analgesic effect as diclofenac sodium and tramadol even upto 6 h of intake. Study noted that the fruits of *O. elatior* Mill. are rich with central and peripheral analgesic properties might be due to presence of phenolic and betanin content^{69, 70}.

Anti-inflammatory Action: Inflammatory response involves macrophages and neutrophils *via* several mediators that are responsible for the initiation, progression, persistence, regulation, and eventual resolution of the acute state of inflammation. In cases where this resolution does not occur, it leads to its progression into a chronic phase. Chronic inflammation is implicated in pathogenesis of many diseases like diabetes, hypertension and even cancer². Multiple studies have advocated that, the analgesic and anti-inflammatory actions of the fruits and lyophilised cladodes of genus *Opuntia*. Beta-sitosterols have been^{37, 73} identified as the active anti-inflammatory principle from these extracts. Decrease of acute inflammation by ethanolic *O. ficus indica* stem extracts was attributed to a lower leucocyte migration and the results were similar to other NSAID with no side effects^{2, 68}.

Various animal experiments have validated the anti-inflammatory potential of genus *Opuntia*. In λ -carrageenan-induced rat pleurisy, the oral administration of indica xanthin has decreased the inflammatory response^{56, 78}. In addition, *Opuntia* flowers contain phenolic compounds like quercetin and isorhamnetin glycosylated derivatives, which have been reported to decrease NO production^{56, 57}. Gastric lesions in rat animal studies were found to be reduced both by stem and fruit powders^{37, 74, 75}. Betanin and indicaxanthin present in the extracts have shown an inhibitory effect on the chlorination activity of myeloperoxidase at neutral rather than at pH 5^{37, 76}. In another study on the rat model of acute inflammation (pleurisy), the oral administration of indica xanthin decreases the exudate size and leukocytes recruitment in the pleural cavity, as well as the protein and mRNA expressions of PGE-2, NO, IL-1 β , iNOS, and cyclooxygenase-2 (COX2) in the recruited leukocytes^{6, 180}. In gerbils, protective effects of methanol extracts of *Opuntia ficus indica* given was observed against neuronal damages caused by global ischemia in the hippocampal region^{6, 81}. Similar studies were also carried out with *O. elatior* extract gel on lamda carrageenan-induced rats (*Rattus norvegicus* L.). The first group of rats was given a gel without active ingredient (negative control), groups of 2nd, 3rd and 4th rats were given gel cactus fruit extract in concentration of 5%, 10% and 15% respectively, and 5th groups of rats were

given diclofenac sodium gel (positive control). The results showed that the concentration of cactus fruit extract in proportion of 5%, 10% and 15% in the gel preparation presented different conditions on organoleptic observations and homogeneity even though there was no difference in the pH and viscosity during 14 days of storage. The results on anti-inflammatory activity test using concentration of 5%, 10%, and 15% have a protective effect against inflammation. Gel containing 10% of extract has anti-inflammatory activity which equals to 1% of sodium diclofenac activity^{70, 82}.

In human chondrocytes cultures, *Opuntia* extracts have decreased the release of nitric oxide (NO), glycosaminoglycan, prostaglandin-E2 (PGE-2) and other oxygen reactive species^{56, 77}. Similarly on human umbilical vein endothelial cells (HUVECs), non-cytotoxic micromolar concentrations of betalain (a pigment of *Opuntia ficus-indica* purified from fresh pulp of cactus pear) decreased the expression of cell adhesion molecules such as ICAM-1^{6, 73}. Betalain present in the extracts has also been acclaimed for its role in preventing degenerative disorders that specifically affect endothelial function, such as atherosclerosis, atherothrombosis, low limb ischemia, and stroke. On the murine microglial cell line (BV-2), a butanol fraction (obtained from 50% ethanol extracts of *Opuntia ficus indica* and hydrolysis products) has been reported to inhibit the production of NO in LPS-activated BV-2 cells via suppression of iNOS protein and mRNA expressions, inhibits the degradation of I κ B- α , and displays peroxynitrite scavenging activity^{6, 79}. Combination of superoxide (O₂⁻) and nitric oxide (NO) radicals leads to formation of cytotoxic reactive species Peroxynitrite (ONOO⁻) *in-vivo* by endothelial cells, kupffer cells, neutrophils, and macrophages. Protonation of peroxynitrite leads to the formation of highly reactive peroxynitrous acid (ONOOH). ONOO⁻ is responsible for cellular damage, signal transduction, and tissue injury due to DNA strand breakage and ultimately leading to apoptotic cell death due to tyrosine nitration, lipid peroxidation, and oxidation of thiol groups *etc.* affecting cell metabolism. Accumulation of peroxynitrite can lead to diseases such as Alzheimer's disease, rheumatoid arthritis, cancer and inflammation of body organs. Naturally occurring ONOO⁻ scavengers such as ascorbic acid,

γ -tocopherol, flavonoids, and polyhydroxyphenols which constitute the *Opuntia* species are effective against ONOO⁻ scavenging and reducing the inflammatory response of the body^{78, 79}.

Wound Healing Effects: Skin is the largest human organ and acts as a protective barrier between the internal organs and external environment. Wound healing is an automatic, dynamic, and cascade step of healing. Wound healing involves hemostasis phase, inflammatory phase, proliferative phase, and maturation phase. These phases are regulated by a pathological situation, metabolic disorders, and infections, or aging. Oxidative stress suppressed immune response, and inflammation can lead to chronic non-healing wounds⁸³.

Nopal and other *Opuntia spp.* extracts have been in use as traditional medicine for the treatment and cure of burns, skin disorders, and wound healing and the recent studies validate their effectiveness at the molecular and cellular levels for their use in recent dermatologic preparations as ointments, creams and gels, *etc.*^{83, 84} Several recent studies highlight the wound repairing and healing properties of *O. ficus-indica* cladode extracts by using keratinocytes stimulated by benzopyrene or TNF- α , it was also observed that *O. ficus-indica* cladode extracts may enhance protection the epidermal barrier and the keratinocyte function by stimulating the expression of filaggrin and loricrin, proteins present in differentiated keratinocytes and corneocytes. The barrier effect of the extract is due to an inhibition of ROS production evoked by the inflammatory agents⁸³.

The cicatrizing properties of *O. ficus-indica* cladodes may entail both high molecular weight polysaccharide components such as a linear galactan polymer and a highly branched xylo-arabinan, as well as low molecular weight components such as lactic acid, D-mannitol, piscidic, eucomic, and 2-hydroxy-4-(4'-hydroxyphenyl)-butanoic acids. These extracts could increase cell regeneration on a scratched keratinocytes monolayer, indicating that *O. ficus-indica* components have high anti-inflammatory and high wound healing properties^{83, 85}. Similarly, polysaccharides extracted from cactus pear of *O. ficus-indica* have been reported to enhance the proliferation of fibroblasts and keratinocytes^{83, 86}.

Similarly, cladode extracts from *O. humifusa* (Raf.) have also demonstrated activities that modulate the production of hyaluronic acid (HA) by increasing the expression of HA synthase in keratinocytes exhibited to UV-B treatment. Additionally, treatment using cladode extracts from *O. humifusa* also decreased the UV-B increased expression of hyaluronidase. Interestingly, the same protective effect on HA was observed in SKH-1 hairless mice exposed to UV-B, indicating that cladode extracts from *O. humifusa* have strong skin care capacities^{83, 87}.

The efficacy of *Opuntia ficus indica* on wound healing was examined by measuring the tensile strength of the skin strips from the wound segments. It was found that methanolic extract of *O. ficus indica* stems and their n-hexane and ethyl acetate fractions showed significant wound healing activity when topically administered to rats^{67, 88}. Hence, for topical or local applications, *Opuntia* hydrocolloids could be applied in wound creams (cooling cream) like *Aloe vera* (L.) Burm^{2, 89-91}. Cosmetic products would profit from cladode preparations.

Summarizing the above studies, we can conclude that *Opuntia spp.* has the potential to enhance the wound healing process and can also be effectively used as co-treatment of skin complications due to diabetes and other pathologies characterized by a defective wound healing⁸³.

Anti-ulcerogenic Effects: Gastrointestinal disorders such as peptic ulcers develop due to bacterial infections such as *Helicobacter pylori*, acid pepsin hyper secretion, and idiopathic factors, etc. But regular use of non-steroidal anti-inflammatory drugs (NSAIDs) such as steroids, anti-coagulants, selective serotonin reuptake inhibitors (SSRIs), etc. and drugs such as proton pump inhibitors, H2 receptors, cytoprotectants, demulcents, anti cholinergics, antacids, and prostaglandin analogues are used for the treatment of ulceration, but these drugs produce several side effects such as diarrhea, abdominal pain, constipation, nausea, and headache etc. Thus, medicinal plants such as *Opuntia* species offer safe and effective treatment with fewer side effects due to their potent antiulcerogenic properties^{63, 66-68}. *Opuntia ficus indica* (L.) Mill. Cladodes have been used to treat gastric ulcers as a

part of traditional medicine regime. Anti-ulcer effects of *O. ficus indica* are linked with the production of mucilage, which may cover ethanol-induced gastric damage and prevent inflammation^{62, 67, 72, 92}. Oral administration of *O. ficus indica* significantly inhibited gastric lesions and gastric ulcer formation in HCl ethanol or HCl aspirin-induced gastric injury. These findings indicate that *O. ficus indica* protects the gastric mucosa through an increased section of gastric mucins or through anti-inflammatory action^{67, 75}. The protective effect could be attributed to the cladodes' hydrocolloid behaving as a buffer, spreading out on the gastric mucosa, and increasing mucus production by increasing the number of secretory cells.

In a similar study, the anti-ulcer activity of *O. elatior* stem was evaluated by an ethanol-induced gastric ulcer in albino rats. Alcoholic extract at 100, 200 and 400 mg/kg, per oral doses significantly (P < 0.01) decreased the ulcer score, ulcer number, ulcer index, free acidity, and total acidity in the ethanol-induced ulcer model in rats. The results of the study demonstrated the antiulcer activity of stem extract of *O. elatior* Mill. This may be due to the presence of flavonoid, which is the cytoprotective active material for which antiulcerogenic efficacy has been extensively confirmed⁷⁰.

Hypoglycemic and Antidiabetic Effect: The intake of nopal (*O. ficus-indica*) in a regular diet has been reported to enhance the postprandial stimulation of glucose, insulin, glucose-dependent insulinotropic peptide (GIP) index, and the glucagon-like peptide 1 (GLP-1) index on T2DM patients after intake of a high-carbohydrate or high-soyprotein breakfast^{83, 93}. The hypoglycemic efficacy could be increased after heating *Opuntia* extracts, as reported,^{83, 94} in patients consuming broiled *O. streptacantha* extracts. Similarly, glycemia and glycated hemoglobin were found to be decreased to normal values in streptozotocin (STZ) induced diabetes in rats through supplementation with an extract of *O. fuliginosa* prickly pear^{83, 95}. Likewise, *O. humifusa* stems boost blood glucose and cholesterol decrease in STZ-treated rats^{83, 96}. In a related study, it was^{83, 97} reported that *O. streptacantha* extracts do not decrease glycemia in STZ treated rats when compared to the control but do demonstrate an anti-hyperglycemic effect when used before an oral

glucose tolerance test (OGTT) while the same extracts administered before an OGTT produced an anti-hyperglycemic effect compared to the control group. The *O. streptacantha* extracts improve glycemic control by blocking the hepatic glucose output, especially in the fasting state^{83, 98}. The hypoglycemic mechanism summoned by *Opuntia spp.* ingestion could be because of dietary fibers such as pectin and mucilage,^{83, 94} which may decrease the absorption of glucose by enhancing the viscosity of food in the gut”^{83, 99, 100}. Many other studies have demonstrated similar results. A combination of insulin and purified extract of cactus (*Opuntia fuliginosagriffiths*) have been found to reduce blood glucose and glycated hemoglobin levels to normal^{37, 101}. In this study, the oral dose of the extract (1 mg/kg body weight per day) necessary to control diabetes contrast with the high quantities of insulin required for an equivalent hypoglycemic effect. In another recent study, supplementation of diets with cactus seed oil (25mg/kg) decreased the serum glucose concentration, which is associated with a glycogen formation in the liver and skeletal muscle”^{37, 102}.

Similar results have also been observed with *O. dillenii* on alloxan-induced diabetic rabbits^{103, 104}. The use of juice from ripe fruits (5 ml/kg body weight) did not affect the plasma glucose concentrations, whereas it remarkably decreased the glucose levels resulting from oral administration of glucose (1 g/kg b.w.). This effect was not present when normoglycemic rabbits were intravenously loaded with glucose. Fruit juice expressed no effect on glucose-induced plasma insulin levels. It was believed that some compounds of the reported part of *O. dillenii* deprived the intestinal absorption of glucose, and others could have an insulin-like character^{103, 104}.

Clinical studies have also reported the anti-diabetic effects of *Opuntia*. In one such study with 46 types 2 diabetes patients, tablets of *O. dillenii* crude drug (2.5 g) for four weeks consumed as four tablets each day 30 minutes before three meals remarkably improved the clinical symptoms and the glycometabolism of patients^{103, 105}.

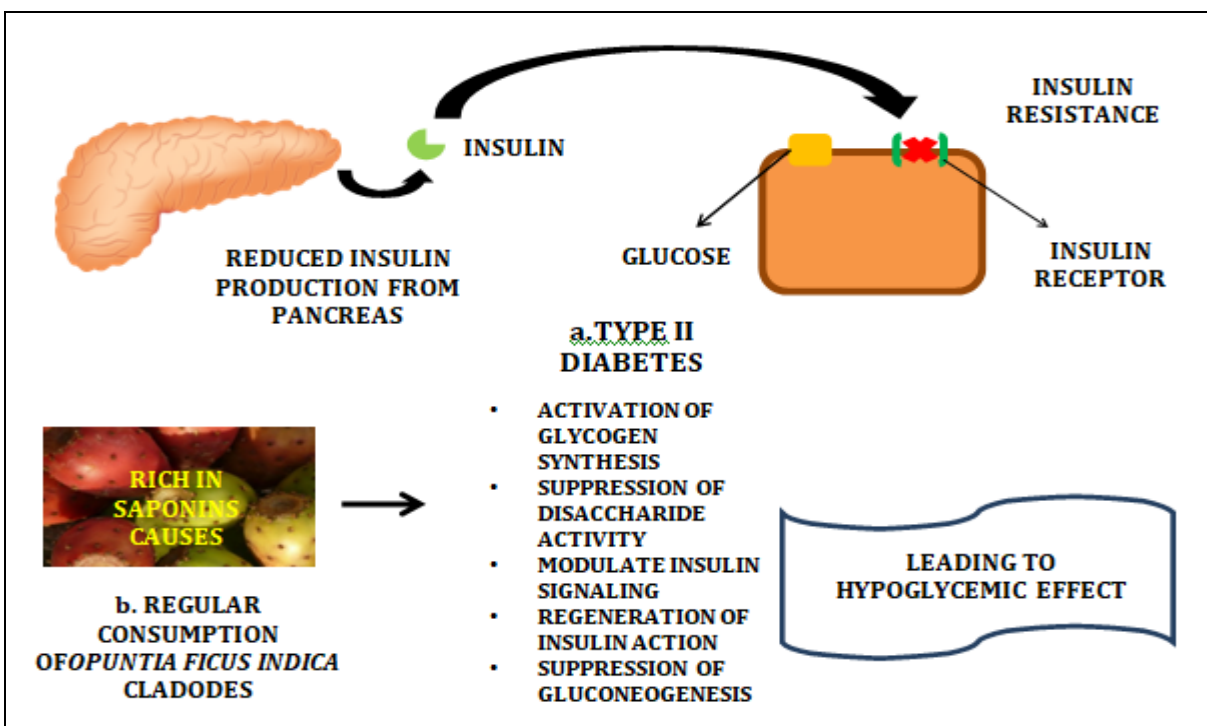


FIG. 8A: TYPE II DIABETES MELLITUS B. SAPONIN, THE NATURAL ANTI- DIABETIC FACTOR PRESENT IN OPUNTIA FICUS INDICA, LEADS TO HYPOGLYCEMIC EFFECT BY ACTIVATING THE GLYCOGEN SYNTHESIS, SUPPRESSION OF DISACCHARIDE ACTIVITY, REGULATING INSULIN SIGNALING, REGENERATION OF INSULIN ACTION, AND SUPPRESSION OF GLUCONEOGENESIS

Studies have also demonstrated that glucose and insulin levels in healthy fasting subjects were stable

when eating cladodes; thus contributing to a positive effect to overall health in diabetes mellitus

type II (non-insulin-dependent diabetes) patients. This was attributed to decreased postprandial sugar absorption. Followed by a glucose challenge test, the increase in insulin and glucose was found to be remarkably decreased. Also, the glucose and insulin plasma levels were found to be reduced. After 10 days of regular cladode consumption before meals, a remarkable decrease of the serum glucose level was observed^{2, 106, 107}. Since these effects were not dependant on glucagon, cortisone, and human growth hormone levels, which are closely interrelated with glucose metabolism, a gastric entero hormone was marked responsible for the hypoglycemic effect as shown in **Fig. 8**^{2, 106}.

Anti-hyperlipidemic Properties and Cholesterol-Lowering Properties: Various studies have indicated that regular consumption of prickly pears from *O. robusta*, by patients affected with familial heterozygous hypercholesterolemia, considerably decreased the plasma levels of LDL cholesterol and the plasma and urine content of 8-epi-prostaglandin F2 α , an F2 isoprostane reproduced through the peroxidation of arachidonic acid^{83, 108}.

These lipid decreasing properties were further established on mice fed with a hypercholesterolemic diet. When the animals were provided with a methanolic extract from *O. joconostle* (polyphenol enriched) seeds, they showed a significant reduction in circulating LDL cholesterol and triglyceride levels by comparison with animals fed with a placebo^{83, 109}.

In a series of studies with Guinea pigs, it was^{2, 111-113} shown that the reduction of blood lipids could be triggered by pectin from *Opuntia*. The proposed mechanism involved increased binding of bile acid, decreased lipid absorption, lower blood lipid levels, and finally weight reduction^{2, 111, 112}. In a follow-up study, the same authors presented evidence that the low-density lipoprotein (LDL)-catabolism was found to be more important than the modulation and de novo synthesis in the liver^{2, 113}.

Consumption of *Opuntia ficus-indica* dried leaves as a dietary supplement has been reported to improve some blood lipids parameters and risk factors associated with metabolic syndrome in humans too. A monocentric, randomized, placebo-controlled, double-blind study on 68 women suffering from metabolic syndrome and having a

body mass index between 25 and 40 *Opuntia ficus indica* capsules at a dosage of 1.6g per meal reported a significant increase in HDL-C levels and a tendency toward decreased triglyceride levels. Forty-two females consuming dried leaves of *Opuntia ficus-indica* with no additional hypo-lipemic treatment showed a significant reduction in LDL-C, especially after day 14. At the end of the research, 39% of the women in the group administered dried *Opuntia ficus-indica* leaves were no longer diagnosed with metabolic syndrome. This was the case for only 8% of the placebo group^{51, 110}.

Anti-Atherogenic Effect of *Opuntia Spp.*: Most antioxidants are anti-atherogenic as they neutralize the formation of ROS by vascular cells and show anti-inflammatory and anti-apoptotic properties in case of the effects of oxidized LDL on vascular cells^{83, 115}. Comparison of the anti-atherogenic properties of *Opuntia* powders achieved from the cladodes of 5 different wild spp. (*O. streptacantha* var. cardona, tuna loca, *O. hyptiacantha*, and *O. megacantha*), medium (*O. albicarpa*), and domesticated (*O. ficus-indica*)^{83, 116}. Specifically, the effect of cladodes was observed on oxidation of LDL evoked by murine endothelial cells (an *in-vitro* model mimicking the mechanism of LDL oxidation occurring *in-vivo* in the vascular wall). Cladode powdered and solubilized in the culture medium dose-dependently inhibited LDL oxidation and the subsequent formation of foam cells by macrophages, which suggests that *Opuntia spp.* could stop the early steps of atherogenesis^{83, 116}. This inhibitory effect of *Opuntia spp.* entails an inhibition of NADPH oxidase (NOX2), which results in a decreased production of intracellular and extracellular superoxide anion, the main ROS involved in the LDL oxidation process as shown in **Fig. 9**^{83, 116, 117}. In similar *in-vivo* studies on apoE-KO mice with developed atherosclerotic lesions the supplementation of the diet with *O. streptacantha* or *O. ficus-indica* powdered cladodes (10 mg/kg for 15 weeks) demonstrated marked reduction of the development of atherosclerotic lesions^{83, 117}. Along with the actions on lipids and lipoproteins, the consumption of the prickly pear (250g/day) has also been found to be significantly effective in reducing the platelets proteins, platelet factor 4 and beta-thromboglobulin, and ADP-induced platelet aggregation, and improves platelet sensitivity

against prostacyclin and prostaglandin E1 in healthy volunteers as well as in patients with mild familial heterozygous hypercholesterolemia. Thus, it appears that prickly pears can induce at least part

of its beneficial action on the cardio-vascular system by decreasing platelet activity and improving haemostatic balance^{67, 118, 119}.

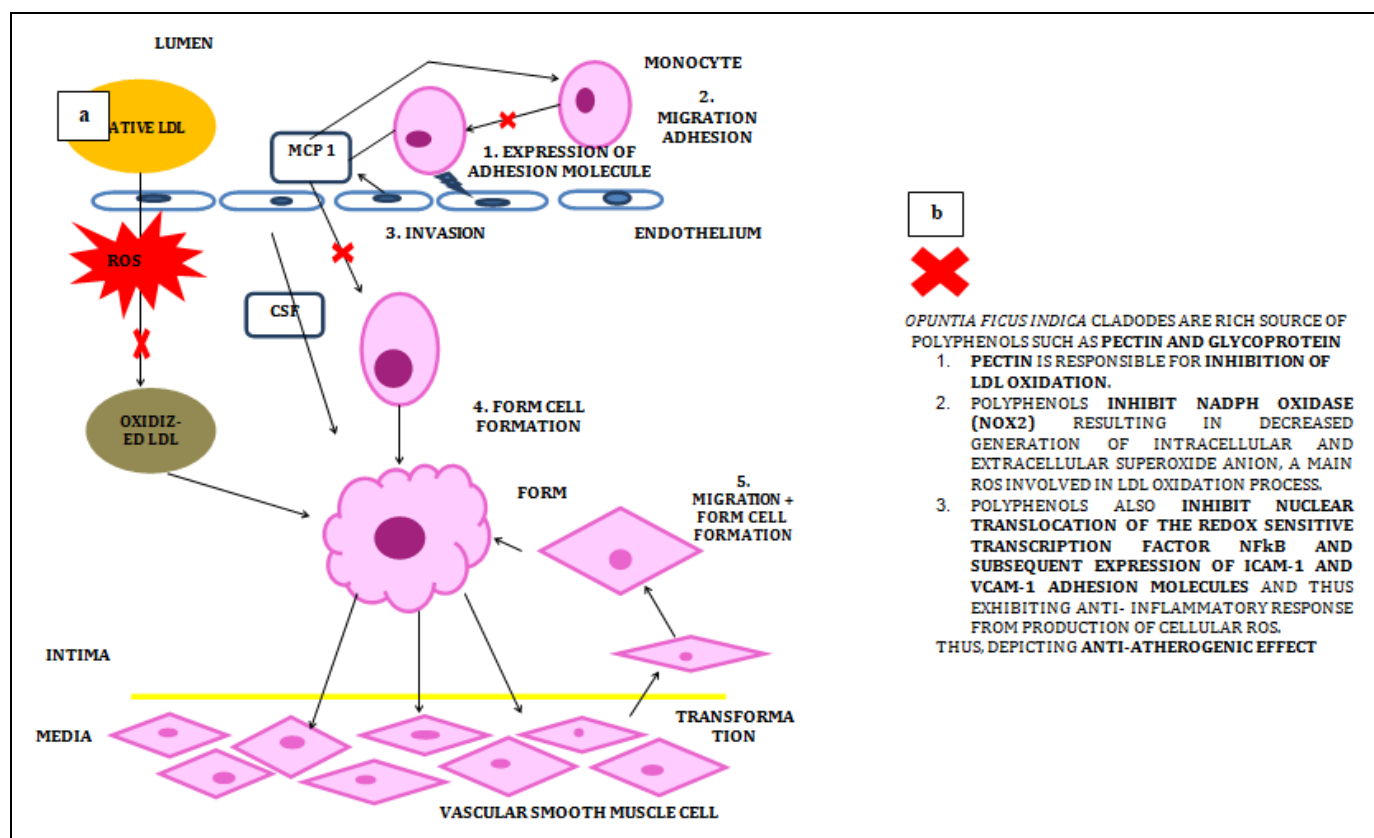


FIG. 9: A. PATHOPHYSIOLOGY OF ATHEROSCLEROSIS B. *OPUNTIA FICUS INDICA* ARE RICH SOURCE OF POLYPHENOLS SUCH AS PECTIN AND GLYCOPROTEIN. POLYPHENOLS INHIBIT THE MECHANISM OF ATHEROMA BY INHIBITION OF LDL AND NADPH OXIDATION. POLYPHENOLS ALSO GENERATE ANTI-INFLAMMATORY RESPONSE BY INHIBITING NUCLEAR TRANSLOCATION AND FURTHER EXPRESSION OF ICAM-1 AND VCAM-1 ADHESION MOLECULES

Anti-Microbial Activity: Secondary metabolites present in plant extracts have demonstrated well-established anti microbial activities. Several studies conducted have found that flavanoids may work by inhibiting the cytoplasmic membrane functioning and inhibition of DNA gyrase and β -hydroxyacyl carrier protein dehydratase activities. Terpenes and coumarins show anti microbial activity by promoting membrane disruptions and reduction in cell respiration, respectively. Tannins act on microorganisms' membranes as well as bind to polysaccharides or enzymes, promoting inactivation¹²⁰. *Opuntia* extracts, too have demonstrated bactericidal effects against many microbes, including *Campylobacter jejuni* and *Campylobacter coli*, both reason of foodborne gastro-enteritis⁵⁶ and *Vibrio cholera*^{56, 120}. Various studies have been reported to corroborate

the same. The antibacterial activity of methanol, ethanol, chloroform extracts of cladodes, and skin fruit extracts of *Opuntia ficus indica* have demonstrated great antibacterial activity against both Gram-positive and Gram-negative bacteria^{122, 123}. Antibacterial effects against *Staphylococcus aureus*, *Pseudomonas aeruginosa*, and *Escherichia coli*; along with mild antifungal activity against *Aspergillus niger* have also been reported^{122, 123}. The extracts of *Opuntia* fruits have been tested for their antibacterial and antifungal effects against *Enterococcus faecium* and *Candida albicans* with promising results^{56, 123}. Antimicrobial activity of the peel extracts of *O. elatior* also demonstrated remarkable antimicrobial actions in a dose dependent manner against both bacteria (Gram-positive and Gram-negative) and fungi based on

growth inhibition zone and compared with the standard drugs^{69,70}.

Anti-Viral Properties: Cladode extract from *O. streptacantha* Lem. have demonstrated antiviral properties towards DNA viruses, such as herpes, and RNA viruses, including influenza type A and human immunodeficiency virus (HIV)-1. The constituents of the extract interfered with intracellular replication of a number of DNA- and RNA-viruses such as Herpes simplex virus Type 2, Equine herpes virus, pseudorabies virus, influenza virus, respiratory syncytial disease virus. An inhibition of extra-cellular viruses was also reported. The main principle was found to be present in the outer non-cuticular tissue and attributed to a protein with unknown mechanisms of action^{2, 124}. Both the replication of DNA and RNA viruses was inhibited^{37, 124}.

Anti-spermatogenic Properties: Alarming rate, at which the world's population is increasing, is creating problems for all developed and undeveloped countries by creating a burden on social and economic growth. Development of ideal male contraceptive with no side effects and easy reversible options from medicinal plants such as *Opuntia* species, *Piper*, *Curcuma longafistula*, etc., which demonstrate remarkable anti-spermatogenic properties, can provide a solution for population control^{2, 125}.

The defatted methanolic extract of *O. dillenii* Haw. has demonstrated anti-spermatogenic effects in tests on rats. According to the study,^{2, 125} the flavone derivatives vitexin and myricetin present in the extract were found to be the active principles behind the activity. The addition of 250 mg extract per kg body weight in a diet for 60 days led to the reasonable reduction in the weight of testis, epididymis, seminal vesicle, and ventral prostate and significant reduction of Sertoli cells, Leydig cells, and gametes. The motility of the sperms was also found to be diminished^{2, 125}. Similar results were obtained in another study with *Opuntia elatior* fruits on male mice. In this study, supplementation with 250 and 500 mg/kg ethanolic fruit extract of *O. elatior* resulted in significant decreases in the weight of the testis and epididymis when compared to control. Additionally, 18.12% reduction was also observed in the sperm count along with 17.82% increase in the total percentage

of abnormal spermatozoa. The fertility indices with 36.08% decrease in the litter size showed the contraceptive effect of the fruit extract on mice. The weight of the testis and epididymis, total sperm count, and the percentage of the abnormal spermatozoa were returned to the normal levels after the cessation of the treatment for 30 days. The study concluded that extract from *O. elatior* fruit may be an effective contraceptive agent to regulate male fertility^{70, 126}.

Opuntia species are rich in different bioactive compounds such as phytochemicals (phenolic acids, flavonoids, carotenoids, tannins, lignans etc.), vitamins (provitamin A, C, E and K), amino acids, minerals (potassium, calcium and magnesium) and dietary fibers etc. These bioactive compounds are produced as secondary metabolites that promote toxicological and pharmaceutical effects in humans as well as animals^{2, 20-25}. Due to high phytochemical content, cactus pear is a valuable source of medicinal properties such as antioxidant potential, radical scavenging activity, anti-ulcerogenic benefits, anti-inflammatory, hypoglycemic effect, anti-spermatogenic effect etc. thus, being a potent source of medicinal plant and a potential nutraceutical.

Betalains: Betalains are pigments specifically from red to violet (betacyanins) and yellow to orange (betaxanthins) present in different plant parts of members of the Caryophyllales, including the cactus family^{21, 127}. They are natural, water-soluble nitrogen pigments, synthesized from the amino acid tyrosine, stable at 4–7 pH range and, depending on this particular, utilized as dyes for low-acidity foods^{1, 128}. These pigments are responsible for the gamut of the fruit color of the prickly pear fruit and add valuable constituents to its nutritional nature. The concentration of these pigments is responsible for the differences and intensity in color types of the fruit, from deep red/violet and variations of pale green to yellow-orange. The characterization of betalains in prickly pear fruits has revealed that these pigments have antioxidant properties^{21, 129-131}. Thus, it can be stated that the prickly pear fruit is an antioxidant-rich fruit with characteristics that can potentially stop or delay cell damage in the human body. Moreover, the remarkable presence of nutrients and antioxidants in the prickly pear fruit is evidence that the consumption of the whole fruit is

more beneficial from a health perspective because more potentially nutraceutical and active pharmaceutical ingredients are absorbed and utilized by our bodies.

The most remarkable feature of cactus pear fruits and flowers are the yellow (betaxanthins) and red (betacyanins) betalains, which gives the fruits and flowers its aesthetic look and more chances of pollination¹⁰⁶. It has been reported that “fruits of cactus pear contain various betalains whose

concentration depends on different species of *Opuntia*, cultivation, environmental conditions and geographic region, etc. The various betacyanins found in *Opuntia* fruits include betanidin, betanin, isobetanin, isobetanidin, neobetanin, phyllocactin, and gomphrenin I”¹⁰⁶. It has also been brought to attention that “*O. streptacantha* (Cardona cultivar), (Rojalisa cultivar), and *O. megacantha* (Naranjona cultivar) contain traces of betanidin 5-O-β-sophoroside”¹⁰⁶.

TABLE 1: DISTRIBUTION AND CONTENTS OF BETALAINS IN THE VARIOUS PARTS OF *OPUNTIA FICUS INDICA*

S. no.	Species	Part/Extraction /Fraction	Activity Tested	Compound	Values	Ref
1	<i>Opuntia ficus-indica</i> (L.)	Pulp of red <i>Opuntia ficus indica</i>	Betalainic profile	Betaxanthins Histidine-Bx (Muscaaurin VII) Glutamine-Bx (Vulgaxanthin I) γ-aminobutyric acid-Bx Proline-Bx (Indicaxanthin) Methionine-Bx Betacyanins Betanidin-5-O-β-glucoside (Betanin) Isobetanidin-5-O-β-glucoside (Isobetanin) Betanidin-6-O-β-glucoside (Gompherenin I) Betanidin	Betaxanthins Red pulp: 4.69 ± 0.359 gBE*/100 g DE Betacyanins Red pulp: 11.05 ± 0.753 gBE*/100 g DE	132
2	<i>Opuntia ficus-indica</i> (L.)	Pulp of orange <i>Opuntia ficus indica</i>	Betalainic profile	Betaxanthins Histidine-Bx (Muscaaurin VII) Glutamine-Bx (Vulgaxanthin I) γ-aminobutyric acid-Bx Proline-Bx (Indicaxanthin) Methionine-Bx Betacyanins Betanidin-5-O-β-glucoside (Betanin) Isobetanidin-5-O-β-glucoside (Isobetanin)	Betaxanthins Orange pulp: 11.89 ± 1.050 gBE*/100 g DE Betacyanins Orange pulp: 0.66 ± 0.039 gBE*/100 g DE	132
3	<i>Opuntia ficus-indica</i> (L.)	Pulp of yellow <i>Opuntia ficus indica</i>	Betalainic profile	Betaxanthins Histidine-Bx (Muscaaurin VII) Glutamine-Bx (Vulgaxanthin I) γ-aminobutyric acid-Bx Proline-Bx (Indicaxanthin) Methionine-Bx Betacyanins Betanidin-5-O-β-glucoside (Betanin) Isobetanidin-5-O-β-glucoside (Isobetanin)	Betaxanthins Yellow pulp: 9.47 ± 0.276 gBE*/100 g DE Betacyanins Yellow pulp: 0.67 ± 0.041 gBE*/100 g DE	132
4	<i>Opuntia ficus-indica</i> (L.)	Peel of red <i>Opuntia ficus indica</i>	Betalainic profile	Betaxanthins Histidine-Bx (Muscaaurin VII) Glutamine-Bx (Vulgaxanthin I) γ-aminobutyric acid-Bx Proline-Bx (Indicaxanthin) Methionine-Bx Betacyanins Betanidin-5-O-β-glucoside (Betanin) Isobetanidin-5-O-β-glucoside	Betaxanthins Red peel: 2.93 ± 0.134 gBE*/100 g DE Betacyanins Red peel: 22.54 ± 2.162 gBE*/100 g DE	132

				(Isobetainin) Betanidin-6-O-β-glucoside (Gompherenin I) Betanidin		
5	<i>Opuntia ficus-indica</i> (L.)	Peel of orange <i>Opuntia ficus indica</i>	Betalainic profile	Betaxanthins Histidine-Bx (Muscaaurin VII) Glutamine-Bx (Vulgaxanthin I) γ-aminobutyric acid-Bx Proline-Bx (Indicaxanthin) Methionine-Bx Betacyanins Betanidin-5-O-β-glucoside (Betainin) Isobetainidin-5-O-β-glucoside (Isobetainin) Betanidin-6-O-β-glucoside (Gompherenin I) Betanidin	Betaxanthins Orange peel: 8.37 ± 0.182 gBE*/100 g DE Betacyanins Orange peel: 1.67 ± 0.070 gBE*/100 g DE	132
6	<i>Opuntia ficus-indica</i> (L.)	Peel of yellow <i>Opuntia ficus indica</i>	Betalainic profile	Betaxanthins Histidine-Bx (Muscaaurin VII) Glutamine-Bx (Vulgaxanthin I) γ-aminobutyric acid-Bx Proline-Bx (Indicaxanthin) Methionine-Bx Betacyanins Betanidin-5-O-β-glucoside (Betainin) Isobetainidin-5-O-β-glucoside (Isobetainin) Betanidin-6-O-β-glucoside (Gompherenin I) Betanidin	Betaxanthins Yellow peel: 5.67 ± 0.423 gBE*/100 g DE Betacyanins Yellow peel: 0.948 ± 0.023 gBE*/100 g DE	132
7	<i>Opuntia ficus-indica</i> (L.) Mill.	Purple fruit of <i>Opuntia ficus-indica</i> (L.) Mill.	Photometric quantification of betalain	Betacyanin	39.3 ± 5.2 mg/100 g FW	133
8	<i>Opuntia ficus-indica</i> (L.) Mill.	Orange fruit of <i>Opuntia ficus-indica</i> (L.) Mill.	Photometric quantification of betalain	Betacyanin	3.6 ± 0.9 mg/100 g FW	133
9	<i>Opuntia stricta</i> (Haw.)	Extract of fruits of <i>Opuntia stricta</i> (Haw.)	Betalains Concentration	Betainin	4.73 ± 0.07 g/L	3
10	<i>Opuntia stricta</i> (Haw.)	Fermented fruits of <i>Opuntia stricta</i> (Haw.)	Betalains Concentration	Betainin	9.65 ± 0.05 g/L	3
11	<i>Opuntia ficus-indica</i> (reddish purple)	Extraction fruit flesh in methanol	Spectrophotometric quantification of betalains	Betaxanthin and betacyanin	30 mg/100 g and 19 mg/100 g respectively	4
12	<i>Opuntia ficus-indica</i> (yellow)	Extraction fruit flesh in methanol	Spectrophotometric quantification of betalains	Betacyanin	25 mg/100 g	4
13	<i>Opuntia ficus-indica</i> (L.) Mill.	Extraction fruit flesh in methanol	Spectrophotometric quantification of betalains	Betacyanin	14.5 mg/100 g	4
14	<i>Opuntia stricta</i> Haw.	Extraction fruit flesh in methanol	Spectrophotometric quantification of betalains	Betacyanin	70 mg/100 g	4
15	<i>Opuntia undulata</i> Griff	Extraction fruit flesh in methanol	Spectrophotometric quantification of betalains	Betacyanin	18.5 mg/100 g	4
16	<i>Opuntia ficus-indica</i>	Extraction fruit flesh in methanol	Spectrophotometric quantification of	Betaxanthin and betacyanin	4.8–49.6 mg/l and 66.5–80.4	4

	(L.) Mill. cv. 'Rossa' (red)		betalains		mg/l respectively	
17	<i>Opuntia ficus-indica</i>	Extraction fruit flesh in methanol	Spectrophotometric quantification of betalains	Betaxanthin and betacyanin	10.5–53.7 mg/l and 5.4–19.6 mg/l respectively	4
18	(L.) Mill. cv. 'Giulla' (orange-yellow)					
18	<i>Opuntia ficus-indica</i>	Methanolic extract of yellow whole fruit	HPLC coupled with electrospray mass spectrometry	Betanin	155.9 ± 24.7	5
19	<i>Opuntia ficus-indica</i>	Methanolic extract of yellow whole fruit	HPLC coupled with electrospray mass spectrometry	Isobetainin	46.1 ± 15.2	5
20	<i>Opuntia ficus-indica</i>	Methanolic extract of yellow whole fruit	HPLC coupled with electrospray mass spectrometry	Gomphrenin I	6.5 ± 1.1	5
21	<i>Opuntia ficus-indica</i>	Methanolic extract of yellow whole fruit	HPLC coupled with electrospray mass spectrometry	Histidine-betaxanthin (muscaarin)	152.0 ± 44.8	5
22	<i>Opuntia ficus-indica</i>	Methanolic extract of yellow whole fruit	HPLC coupled with electrospray mass spectrometry	Glutamine-betaxanthin (vulgaxanthin)	76.6 ± 5.1	5
23	<i>Opuntia ficus-indica</i>	Methanolic extract of yellow whole fruit	HPLC coupled with electrospray mass spectrometry	Aminobutyric acid-betaxanthin	86.2 ± 4.8	5
24	<i>Opuntia ficus-indica</i>	Methanolic extract of yellow whole fruit	HPLC coupled with electrospray mass spectrometry	Proline-betaxanthin (indicaxanthin)	6550.6 ± 336.4	5
25	<i>Opuntia ficus-indica</i>	Methanolic extract of yellow whole fruit	HPLC coupled with electrospray mass spectrometry	Valine-betaxanthin	34.1 ± 3.7	5
26	<i>Opuntia ficus-indica</i>	Methanolic extract of yellow whole fruit	HPLC coupled with electrospray mass spectrometry	Valine-betaxanthin isomer	30.7 ± 0.5	5
27	<i>Opuntia ficus-indica</i>	Methanolic extract of yellow whole fruit	HPLC coupled with electrospray mass spectrometry	Isoleucine-betaxanthin	58.5 ± 3.8	5
28	<i>Opuntia ficus-indica</i>	Methanolic extract of yellow whole fruit	HPLC coupled with electrospray mass spectrometry	Leucine-betaxanthin (vulgaxanthin)	64.8 ± 4.4	5
29	<i>Opuntia ficus-indica</i>	Methanolic extract of yellow whole fruit	HPLC coupled with electrospray mass spectrometry	Phenylalanine-betaxanthin	32.6 ± 3.0	5
30	<i>Opuntia ficus-indica</i>	Methanolic extract of yellow pulp fruit	HPLC coupled with electrospray mass spectrometry	Betanin	25.3 ± 1.1	5
31	<i>Opuntia ficus-indica</i>	Methanolic extract of yellow pulp fruit	HPLC coupled with electrospray mass spectrometry	Isobetainin	10.8 ± 2.4	5
32	<i>Opuntia ficus-indica</i>	Methanolic extract of yellow pulp fruit	HPLC coupled with electrospray mass spectrometry	Gomphrenin I	5.4 ± 1.2	5
33	<i>Opuntia ficus-indica</i>	Methanolic extract of yellow pulp fruit	HPLC coupled with electrospray mass spectrometry	Histidine-betaxanthin (muscaarin)	55.0 ± 1.4	5
34	<i>Opuntia ficus-indica</i>	Methanolic extract of yellow pulp fruit	HPLC coupled with electrospray mass spectrometry	Glutamine-betaxanthin (vulgaxanthin)	38.3 ± 9.8	5
35	<i>Opuntia</i>	Methanolic	HPLC coupled with	Aminobutyric acid-betaxanthin	61.3 ± 10.1	5

36	<i>Opuntia ficus-indica</i>	extract of yellow pulp fruit	electrospray mass spectrometry	Proline-betaxanthin (indicaxanthin)	6180.3 ± 279.0	5
37	<i>Opuntia ficus-indica</i>	Methanolic extract of yellow pulp fruit	HPLC coupled with electro-spray mass spectrometry	Valine-betaxanthin	16.5 ± 0.5	5
38	<i>Opuntia ficus-indica</i>	Methanolic extract of yellow pulp fruit	HPLC coupled with electro-spray mass spectrometry	Valine-betaxanthin isomer	14.4 ± 4.0	5
39	<i>Opuntia ficus-indica</i>	Methanolic extract of yellow pulp fruit	HPLC coupled with electro-spray mass spectrometry	Isoleucine-betaxanthin	53.3 ± 6.0	5
40	<i>Opuntia ficus-indica</i>	Methanolic extract of yellow pulp fruit	HPLC coupled with electro-spray mass spectrometry	Leucine-betaxanthin (vulgaxanthin)	44.9 ± 9.2	5
41	<i>Opuntia ficus-indica</i>	Methanolic extract of yellow pulp fruit	HPLC coupled with electro-spray mass spectrometry	Phenylalanine-betaxanthin	13.5 ± 1.3	5
42	<i>Opuntia ficus-indica</i>	Methanolic extract of red whole fruit	HPLC coupled with electro-spray mass spectrometry	Betanin	182.4 ± 13.2	5
43	<i>Opuntia ficus-indica</i>	Methanolic extract of red whole fruit	HPLC coupled with electro-spray mass spectrometry	Isobetainin	38.4 ± 5.7	5
44	<i>Opuntia ficus-indica</i>	Methanolic extract of red whole fruit	HPLC coupled with electro-spray mass spectrometry	Gomphrenin I	8.8 ± 0.6	5
45	<i>Opuntia ficus-indica</i>	Methanolic extract of red whole fruit	HPLC coupled with electro-spray mass spectrometry	Histidine-betaxanthin (muscaarin)	90.0 ± 15.8	5
46	<i>Opuntia ficus-indica</i>	Methanolic extract of red whole fruit	HPLC coupled with electro-spray mass spectrometry	Glutamine-betaxanthin (vulgaxanthin)	30.5 ± 2.7	5
47	<i>Opuntia ficus-indica</i>	Methanolic extract of red whole fruit	HPLC coupled with electro-spray mass spectrometry	Aminobutyric acid-betaxanthin	51.3 ± 1.2	5
48	<i>Opuntia ficus-indica</i>	Methanolic extract of red whole fruit	HPLC coupled with electro-spray mass spectrometry	Proline-betaxanthin (indicaxanthin)	7224.0 ± 617.1	5
49	<i>Opuntia ficus-indica</i>	Methanolic extract of red whole fruit	HPLC coupled with electro-spray mass spectrometry	Valine-betaxanthin	15.4 ± 0.2	5
50	<i>Opuntia ficus-indica</i>	Methanolic extract of red whole fruit	HPLC coupled with electro-spray mass spectrometry	Valine-betaxanthin isomer	12.4 ± 1.0	5
51	<i>Opuntia ficus-indica</i>	Methanolic extract of red whole fruit	HPLC coupled with electro-spray mass spectrometry	Isoleucine-betaxanthin	36.5 ± 2.1	5
52	<i>Opuntia ficus-indica</i>	Methanolic extract of red whole fruit	HPLC coupled with electro-spray mass spectrometry	Leucine-betaxanthin (vulgaxanthin)	44.2 ± 2.4	5
53	<i>Opuntia ficus-indica</i>	Methanolic extract of red whole fruit	HPLC coupled with electro-spray mass spectrometry	Phenylalanine-betaxanthin	26.3 ± 0.2	5
54	<i>Opuntia ficus-indica</i>	Methanolic extract of red pulp fruit	HPLC coupled with electro-spray mass spectrometry	Betanin	169.1 ± 6.3	5
55	<i>Opuntia</i>	Methanolic	HPLC coupled with	Isobetainin	82.5 ± 12.6	5

56	<i>Opuntia ficus-indica</i>	extract of red pulp fruit	electrospray mass spectrometry	Gomphrenin I	8.8 ± 0.7	5
57	<i>Opuntia ficus-indica</i>	Methanolic extract of red pulp fruit	HPLC coupled with electrospray mass spectrometry	Histidine-betaxanthin (muscaarin)	50.6 ± 7.1	5
58	<i>Opuntia ficus-indica</i>	Methanolic extract of red pulp fruit	HPLC coupled with electrospray mass spectrometry	Glutamine-betaxanthin (vulgaxanthin)	25.4 ± 10.6	5
59	<i>Opuntia ficus-indica</i>	Methanolic extract of red pulp fruit	HPLC coupled with electrospray mass spectrometry	Aminobutyric acid-betaxanthin	84.9 ± 12.4	5
60	<i>Opuntia ficus-indica</i>	Methanolic extract of red pulp fruit	HPLC coupled with electrospray mass spectrometry	Proline-betaxanthin (indicaxanthin)	8525.3 ± 297.9	5
61	<i>Opuntia ficus-indica</i>	Methanolic extract of red pulp fruit	HPLC coupled with electrospray mass spectrometry	Valine-betaxanthin	25.9 ± 2.7	5
62	<i>Opuntia ficus-indica</i>	Methanolic extract of red pulp fruit	HPLC coupled with electrospray mass spectrometry	Valine-betaxanthin isomer	21.3 ± 3.4	5
63	<i>Opuntia ficus-indica</i>	Methanolic extract of red pulp fruit	HPLC coupled with electrospray mass spectrometry	Isoleucine-betaxanthin	54.5 ± 5.0	5
64	<i>Opuntia ficus-indica</i>	Methanolic extract of red pulp fruit	HPLC coupled with electrospray mass spectrometry	Leucine-betaxanthin (vulgaxanthin)	46.6 ± 5.6	5
65	<i>Opuntia ficus-indica</i>	Methanolic extract of red pulp fruit	HPLC coupled with electrospray mass spectrometry	Phenylalanine-betaxanthin	26.9 ± 4.0	5
66	<i>Opuntia ficus-indica</i>	Methanolic extract of red yellow whole fruit	HPLC coupled with electrospray mass spectrometry	Betanin	226.3 ± 11.5	5
67	<i>Opuntia ficus-indica</i>	Methanolic extract of red yellow whole fruit	HPLC coupled with electrospray mass spectrometry	Isobetanin	55.4 ± 10.6	5
68	<i>Opuntia ficus-indica</i>	Methanolic extract of red yellow whole fruit	HPLC coupled with electrospray mass spectrometry	Gomphrenin I	11.0 ± 0.7	5
69	<i>Opuntia ficus-indica</i>	Methanolic extract of red yellow whole fruit	HPLC coupled with electrospray mass spectrometry	Histidine-betaxanthin (muscaarin)	155.6 ± 42.4	5
70	<i>Opuntia ficus-indica</i>	Methanolic extract of red yellow whole fruit	HPLC coupled with electrospray mass spectrometry	Glutamine-betaxanthin (vulgaxanthin)	48.7 ± 3.1	5
71	<i>Opuntia ficus-indica</i>	Methanolic extract of red yellow whole fruit	HPLC coupled with electrospray mass spectrometry	Aminobutyric acid-betaxanthin	100.2 ± 3.8	5
72	<i>Opuntia ficus-indica</i>	Methanolic extract of red yellow whole fruit	HPLC coupled with electrospray mass spectrometry	Proline-betaxanthin (indicaxanthin)	7656.1 ± 277.3	5
73	<i>Opuntia ficus-indica</i>	Methanolic extract of red yellow whole fruit	HPLC coupled with electrospray mass spectrometry	Valine-betaxanthin	43.9 ± 3.3	5
74	<i>Opuntia ficus-indica</i>	Methanolic extract of red yellow whole fruit	HPLC coupled with electrospray mass spectrometry	Valine-betaxanthin isomer	33.0 ± 9.6	5
75	<i>Opuntia</i>	Methanolic	HPLC coupled with	Isoleucine-betaxanthin	72.9 ± 1.0	5

76	<i>Opuntia ficus-indica</i>	extract of red yellow whole fruit	electrospray mass spectrometry	Leucine-betaxanthin (vulgaxanthin)	69.7 ± 2.1	5
77	<i>Opuntia ficus-indica</i>	Methanolic extract of red yellow whole fruit	HPLC coupled with electrospray mass spectrometry	Phenylalanine-betaxanthin	51.1 ± 9.5	5
78	<i>Opuntia ficus-indica</i>	Methanolic extract of red yellow whole fruit	HPLC coupled with electrospray mass spectrometry	Betanin	216.2 ± 39.8	5
79	<i>Opuntia ficus-indica</i>	Methanolic extract of red yellow pulp fruit	HPLC coupled with electrospray mass spectrometry	Isobetainin	45.3 ± 3.1	5
80	<i>Opuntia ficus-indica</i>	Methanolic extract of red yellow pulp fruit	HPLC coupled with electrospray mass spectrometry	Gomphrenin I	11.8 ± 1.3	5
81	<i>Opuntia ficus-indica</i>	Methanolic extract of red yellow pulp fruit	HPLC coupled with electrospray mass spectrometry	Histidine-betaxanthin (muscaarin)	21.3 ± 1.5	5
82	<i>Opuntia ficus-indica</i>	Methanolic extract of red yellow pulp fruit	HPLC coupled with electrospray mass spectrometry	Glutamine-betaxanthin (vulgaxanthin)	11.5 ± 0.8	5
83	<i>Opuntia ficus-indica</i>	Methanolic extract of red yellow pulp fruit	HPLC coupled with electrospray mass spectrometry	Aminobutyric acid-betaxanthin	68.6 ± 12.8	5
84	<i>Opuntia ficus-indica</i>	Methanolic extract of red yellow pulp fruit	HPLC coupled with electrospray mass spectrometry	Proline-betaxanthin (indicaxanthin)	8987.1 ± 502.5	5
85	<i>Opuntia ficus-indica</i>	Methanolic extract of red yellow pulp fruit	HPLC coupled with electrospray mass spectrometry	Valine-betaxanthin	22.0 ± 3.8	5
86	<i>Opuntia ficus-indica</i>	Methanolic extract of red yellow pulp fruit	HPLC coupled with electrospray mass spectrometry	Valine-betaxanthin isomer	24.8 ± 1.0	5
87	<i>Opuntia ficus-indica</i>	Methanolic extract of red yellow pulp fruit	HPLC coupled with electrospray mass spectrometry	Isoleucine-betaxanthin	65.7 ± 8.1	5
88	<i>Opuntia ficus-indica</i>	Methanolic extract of red yellow pulp fruit	HPLC coupled with electrospray mass spectrometry	Leucine-betaxanthin (vulgaxanthin)	56.5 ± 8.7	5
89	<i>Opuntia ficus-indica</i>	Methanolic extract of red yellow pulp fruit	HPLC coupled with electrospray mass spectrometry	Phenylalanine-betaxanthin	38.4 ± 7.6	5

Phenolic Compounds: Polyphenols are the class of organic molecules widely distributed in the plant kingdom. Their chemical structures are differentiated by the presence of several phenolic groups. These compounds are classified as the byproducts of plant metabolism. The keen interest in polyphenols is due to their notable antioxidant potential, which is responsible for health benefits such as the prevention of inflammation, cardiovascular dysregulation, anticancer properties, and neurodegenerative diseases, *etc.*^{34, 134} Flavonoids is a major constituent of *Opuntia spp.* as they have anti-oxidative effects and have more

efficacy and stability than the vitamins in producing stable radicals. All plant parts of *Opuntia* cacti have a high number of various flavonoids and phenolic compounds present. The *Opuntia* flower has been found to contain gallic acid and 6-isohamnetin 3-O-robinobioside as major compounds. Whereas in the case of fruit pulp, high content of isorhamnetin glycosides (50.6 mg/100g) contribute to the total phenolic content, which is 218.8 mg/100 g. fruit seeds contain high phenolic compounds such as feruloyl derivatives, sinapoyldiglucoside, and tannins. The fruit peel also has a high content of flavonoid derivatives

such as kaempferol and quercetin. Overall, it was found that flowers of *Opuntia* were the most important source of the polyphenols and flavonoids^{34, 135}. The total phenolic compound content in *Opuntia* species is dynamic and dependant on the following factors such as stages of plant, maturity, harvest, season, environment conditions, post-harvest treatments, and different species. The study has been reported in which it was found that “*O. ficus-indica* fruits contain 218 mg GAE/100 g FW, but the wild species *O. stricta* also exhibited high concentrations of these metabolites (204 mg GAE/100 g FW), followed by *O. undulata*, *O. megacantha*, *O. streptacantha*, and *O. dinellii* (164.6, 130, 120, and 117 mg/100 g FW pear, respectively)”. When compared on the basis of colour of fruits it was found reported that, “purple fruits of *O. ficus indica* cultivated in Italy, Spain, USA, Tunisia, and Saudi Arabia contain higher levels of phenolics (89–218.8 mg GAE/ 100 g FW) than the orange fruits (69.8 mg GAE/100 g FW). However, the Mexican cultivars, *O. megacantha* (orange fruits), *O. streptacantha*, and *O. robusta* (purple fruits), exhibited a similar phenolic compound concentration (120–140 mg GAE/100 g FW).” Pads of *Opuntia* have also been reported as source of polyphenols such as *O. violacea*, *O.*

megacantha, *O. atropes*, and *O. albicarpa* contain high concentration of phenolic acids (17.8–20 mg GAE/g DW), while *O. rastrera* and *O. undulata* present the lowest values (0.39–0.95 mg GAE/g DW).

The phenolic profile in *Opuntia* is vast and complex, with more than 30 compounds identified in cladodes of different species, more than 20 in seeds, and 44 compounds in juices. The most common compounds present in *Opuntia* tissues from wild and cultivated species include kaempferol, quercetin, isorhamnetin, and isorhamnetin glucoside. Kaempferol 3-O-arabinofuranoside was detected only in *O. streptacantha*, quercetin 3-O-rhamnosyl-(1-2)-[rhamnosyl-(1-6)]-glucoside was detected only in *O. ficus-indica* cladodes, and isorhamnetin-3-O-rutinoside was present in the juice and peel from *O. dillenii*. The rare piscidic acid and derivatives, restricted to plants exhibiting crassulacean acid metabolism and succulence, were detected in juices from *O. ficus-indica*. In seeds, sinapoyl-glucose, sinapoyl-diglucoside, three isomers of feruloyl-sucrose, catechin, rutin, and quercetin derivatives were detected. Taurine, an unusual sulfonic acid, was identified in Sicilian and African cultivars⁸³.

TABLE 2: DISTRIBUTION AND CONTENTS OF PHENOLIC COMPOUNDS IN THE VARIOUS PARTS OF *OPUNTIA FICUS INDICA*

S. no.	Species	Part/Extraction/ Fraction	Activity Tested	Compounds	Values	Ref
1	<i>Opuntia ficus-indica</i> (L.) Mill (Nopal cactus)	Flower	HPLC–PDA-ESI-MS/MS	Gallic acid	1630–4900 mg/100g	34, 35, 134, 136, 137
2	<i>Opuntia ficus-indica</i> (L.) Mill (Nopal cactus)	Flower	HPLC–PDA-ESI-MS/MS	Quercetin 3-O-Rutinoside	709 mg/100g	34, 35, 134, 136, 137
3	<i>Opuntia ficus-indica</i> (L.) Mill (Nopal cactus)	Flower	HPLC–PDA-ESI-MS/MS	4 Kaempferol 3-O-Rutinoside	400 mg/100g	34, 35, 134, 136, 137
4	<i>Opuntia ficus-indica</i> (L.) Mill (Nopal cactus)	Flower	HPLC–PDA-ESI-MS/MS	5 Quercetin 3-O-Glucoside	447 mg/100g	34, 35, 134, 136, 137
5	<i>Opuntia ficus-indica</i> (L.) Mill (Nopal cactus)	Flower	HPLC–PDA-ESI-MS/MS	6 Isorhamnetin 3-O-Robinoside	4269 mg/100g	34, 35, 134, 136, 137
6	<i>Opuntia ficus-indica</i> (L.) Mill (Nopal cactus)	Flower	HPLC–PDA-ESI-MS/MS	7 Isorhamnetin 3-O-Galactoside	979 mg/100g	34, 35, 134, 136, 137
7	<i>Opuntia ficus-indica</i> (L.) Mill (Nopal cactus)	Flower	HPLC–PDA-ESI-MS/MS	8 Isorhamnetin 3-O-Glucoside	724 mg/100g	34, 35, 134, 136, 137
8	<i>Opuntia ficus-indica</i> (L.) Mill (Nopal cactus)	Flower	HPLC–PDA-ESI-MS/MS	9 Kaempferol 3-O-Arabinoside	324 mg/100g	34, 35, 134, 136, 137

						137
9	<i>Opuntia ficus-indica</i> (L.) Mill (Nopal cactus)	Pulp	High-performance liquid chromatography-diode array detection	Total phenolic acid	218.8 mg/100g	19, 27, 34, 138-141
10	<i>Opuntia ficus-indica</i> (L.) Mill (Nopal cactus)	Pulp	High-performance liquid chromatography-diode array detection	Quercetin	9 mg/100g	19, 27, 34, 138-141
11	<i>Opuntia ficus-indica</i> (L.) Mill (Nopal cactus)	Pulp	High-performance liquid chromatography-diode array detection	Isorhamnetin	4.94 mg/100g	19, 27, 34, 138-141
12	<i>Opuntia ficus-indica</i> (L.) Mill (Nopal cactus)	Pulp	High-performance liquid chromatography-diode array detection	Kaempferol	0.78 mg/100g	19, 27, 34, 138-141
13	<i>Opuntia ficus-indica</i> (L.) Mill (Nopal cactus)	Pulp	High-performance liquid chromatography-diode array detection	Luteolin	0.84 mg/100g	19, 27, 34, 138-141
14	<i>Opuntia ficus-indica</i> (L.) Mill (Nopal cactus)	Pulp	High-performance liquid chromatography-diode array detection	Isorhamnetin glycosides	50.6 mg/100g	19, 27, 34, 138-141
15	<i>Opuntia ficus-indica</i> (L.) Mill (Nopal cactus)	Pulp	High-performance liquid chromatography-diode array detection	Kaempferol	2.7 mg/100g	19, 27, 34, 138-141
16	<i>Opuntia ficus-indica</i> (L.) Mill (Nopal cactus)	Seed	Liquid chromatography coupled to mass spectrometry (LC-MSn) and to nuclear magnetic resonance (LC-NMR)	Total phenolic acid	48-89 mg/100g	20, 34
17	<i>Opuntia ficus-indica</i> (L.) Mill (Nopal cactus)	Seed	Liquid chromatography coupled to mass spectrometry (LC-MSn) and to nuclear magnetic resonance (LC-NMR)	Feruloyl-sucrose isomer 1	7.36-17.62 mg/100g	20, 34
18	<i>Opuntia ficus-indica</i> (L.) Mill (Nopal cactus)	Seed	Liquid chromatography coupled to mass spectrometry (LC-MSn) and to nuclear magnetic resonance (LC-NMR)	Feruloyl-sucrose isomer 2	2.9-17.1 mg/100g	20, 34
19	<i>Opuntia ficus-indica</i> (L.) Mill (Nopal cactus)	Seed	Liquid chromatography coupled to mass spectrometry (LC-MSn) and to nuclear magnetic resonance (LC-NMR)	Sinapoyl-diglucoside	12.6-23.4 mg/100g	20, 34
20	<i>Opuntia ficus-indica</i> (L.) Mill (Nopal cactus)	Seed	Liquid chromatography coupled to mass spectrometry (LC-MSn) and to nuclear magnetic resonance (LC-NMR)	Total Flavonoids	1.5-2.6 mg/100g	20, 34
21	<i>Opuntia ficus-indica</i> (L.) Mill (Nopal cactus)	Seed	Liquid chromatography coupled to mass spectrometry (LC-MSn) and to nuclear magnetic resonance (LC-NMR)	Total Tannins	4.1-6.6 mg/100g	20, 34
22	<i>Opuntia ficus-indica</i> (L.) Mill (Nopal cactus)	Peel	Microplate assay, ABTS assay, DPPH in microplate assay and lipid oxidation inhibition assay	Total phenolic acid	45,700 mg/100g	34, 142-144
23	<i>Opuntia ficus-indica</i> (L.) Mill (Nopal cactus)	Peel	Microplate assay, ABTS assay, DPPH in microplate assay and lipid oxidation inhibition assay	Total Flavonoid	6.95 mg/100g	34, 142-144

24	<i>Opuntia ficus-indica</i> (L.) Mill (Nopal cactus)	Peel	Microplate assay, ABTS assay, DPPH in microplate assay and lipid oxidation inhibition assay	Kaempferol	0.22 mg/100g	34, 142-144
25	<i>Opuntia ficus-indica</i> (L.) Mill (Nopal cactus)	Peel	Microplate assay, ABTS assay, DPPH in microplate assay and lipid oxidation inhibition assay	Quercetin	4.32 mg/100g	34, 142-144
26	<i>Opuntia ficus-indica</i> (L.) Mill (Nopal cactus)	Peel	Microplate assay, ABTS assay, DPPH in microplate assay and lipid oxidation inhibition assay	Isorhamnetin	2.41–91 mg/100g	34, 142-144
27	<i>Opuntia ficus-indica</i> (L.) Mill (Nopal cactus)	Cladode	TLC, HPLC-DAD and NMR techniques	Gallic acid	0.64–2.37 mg/100g	28, 34, 138, 145-147
28	<i>Opuntia ficus-indica</i> (L.) Mill (Nopal cactus)	Cladode	TLC, HPLC-DAD and NMR techniques	Coumaric	14.08–16.18 mg/100g	28, 34, 138, 145-147
29	<i>Opuntia ficus-indica</i> (L.) Mill (Nopal cactus)	Cladode	TLC, HPLC-DAD and NMR techniques	3,4-dihydroxybenzoic	0.06–5.02 mg/100g	28, 34, 138, 145-147
30	<i>Opuntia ficus-indica</i> (L.) Mill (Nopal cactus)	Cladode	TLC, HPLC-DAD and NMR techniques	4-hydroxybenzoic	0.5–4.72 mg/100g	28, 34, 138, 145-147
31	<i>Opuntia ficus-indica</i> (L.) Mill (Nopal cactus)	Cladode	TLC, HPLC-DAD and NMR techniques	Ferulic acid	0.56–34.77 mg/100g	28, 34, 138, 145-147
32	<i>Opuntia ficus-indica</i> (L.) Mill (Nopal cactus)	Cladode	TLC, HPLC-DAD and NMR techniques	Salicylic acid	0.58–3.54 mg/100g	28, 34, 138, 145-147
33	<i>Opuntia ficus-indica</i> (L.) Mill (Nopal cactus)	Cladode	TLC, HPLC-DAD and NMR techniques	Isoquercetin	2.29–39.67 mg/100g	28, 34, 138, 145-147
34	<i>Opuntia ficus-indica</i> (L.) Mill (Nopal cactus)	Cladode	TLC, HPLC-DAD and NMR techniques	Isorhamnetin-3-O-glucoside	4.59–32.21 mg/100g	28, 34, 138, 145-147
35	<i>Opuntia ficus-indica</i> (L.) Mill (Nopal cactus)	Cladode	TLC, HPLC-DAD and NMR techniques	Nicotiflorin	2.89–146.5 mg/100g	28, 34, 138, 145-147
36	<i>Opuntia ficus-indica</i> (L.) Mill (Nopal cactus)	Cladode	TLC, HPLC-DAD and NMR techniques	Rutin	2.36–26.17 mg/100g	28, 34, 138, 145-147
37	<i>Opuntia ficus-indica</i> (L.) Mill (Nopal cactus)	Cladode	TLC, HPLC-DAD and NMR techniques	Narcissin	14.69–137.1 mg/100g	28, 34, 138, 145-147

Amino Acids: *Opuntia ficus indica* has a large number of amino acids present which have been found in various phytochemical investigations. High levels of amino acids such as proline, taurine and serine have been reported in the cladodes of *Opuntia*. Up to 8 essential amino acids have been reported in cactus plants such as alanine, arginine, glutamin acid, lysine, tyrosine, etc. In the cladodes of *Opuntia* cactus, the most abundant amino acid reported is glutamine followed by leucine, lysine, valine, arginine, phenylalanine, and isoleucine. In the seeds of cactus, glutamic acid has been reported

as the highest content with the percentage varying from 15.73% to 20.27%, after which comes the arginine with 4.81% to 14.61%. In contrast, the cacti fruit has two major amino acids namely proline and taurine. Thus, seeds of cacti fruit and pulp is considered a valuable source of amino acids. In the extensive study of fresh *Opuntia* cacti the amino acids in an alcoholic extract from fresh phyllo-clades comprised leucine, phenylalanine, valine, methionine, proline, alanine, glutamic acid, threonine, glycine, serine, lysine, cysteine, and c-aminobutyric acid, respectively. Some studies have

reported the presence of amino acid patterns of *Opuntia* pads containing eighteen compounds. Another research study on the composition of Tunisian *O. ficus-indica* var. *inermis* protein reported content of amino acids as follows, “13.0% glutamic acid, 10.6% asparaginic acid, 8.3% leucine, 7.7% alanine, 7.0% valine, 6.5% proline, 5.9% lysine, 5.5% arginine, 5.2% isoleucine, 5.1% phenylalanine, 4.8% glycine, 4.3% threonine, 4.3% serine, 4.1% tyrosine, 2.3% histidine, 2.1% methionine, and 0.8% cysteine”^{2, 148}.

TABLE 3: DISTRIBUTION AND CONTENTS OF PHENOLS AND FLAVONOIDS IN THE VARIOUS PARTS OF *OPUNTIA FICUS INDICA*

S. no.	Species	Part/Extraction/ Fraction	Activity Tested	Compound	Values	Ref
1	<i>Opuntia ficus-indica</i> (L.) Mill (Nopal cactus)	Cladode	Ion exchange chromatography of alkaline hydrolysates.	Alanine	1.25 g/100g	24, 34, 149
2	<i>Opuntia ficus-indica</i> (L.) Mill (Nopal cactus)	Cladode	Ion exchange chromatography of alkaline hydrolysates.	Arginine	5.01 g/100g	24, 34, 149
3	<i>Opuntia ficus-indica</i> (L.) Mill (Nopal cactus)	Cladode	Ion exchange chromatography of alkaline hydrolysates.	Asparagine	3.13 g/100g	24, 34, 149
4	<i>Opuntia ficus-indica</i> (L.) Mill (Nopal cactus)	Cladode	Ion exchange chromatography of alkaline hydrolysates.	Asparaginic acid	4.38 g/100g	24, 34, 149
5	<i>Opuntia ficus-indica</i> (L.) Mill (Nopal cactus)	Cladode	Ion exchange chromatography of alkaline hydrolysates.	Glutamic acid	5.43 g/100g	24, 34, 149
6	<i>Opuntia ficus-indica</i> (L.) Mill (Nopal cactus)	Cladode	Ion exchange chromatography of alkaline hydrolysates.	Glutamine	36.12 g/100g	24, 34, 149
7	<i>Opuntia ficus-indica</i> (L.) Mill (Nopal cactus)	Cladode	Ion exchange chromatography of alkaline hydrolysates.	Cystine	1.04 g/100g	24, 34, 149
8	<i>Opuntia ficus-indica</i> (L.) Mill (Nopal cactus)	Cladode	Ion exchange chromatography of alkaline hydrolysates.	Histidine	4.18 g/100g	24, 34, 149
9	<i>Opuntia ficusindica</i> (L.) Mill (Nopal cactus)	Cladode	Ion exchange chromatography of alkaline hydrolysates.	Isoleucine	3.97 g/100g	24, 34, 149
10	<i>Opuntia ficusindica</i> (L.) Mill (Nopal cactus)	Cladode	Ion exchange chromatography of alkaline hydrolysates.	Leucine	2.71 g/100g	24, 34, 149
11	<i>Opuntia ficus-indica</i> (L.) Mill (Nopal cactus)	Cladode	Ion exchange chromatography of alkaline hydrolysates.	Lysine	5.22 g/100g	24, 34, 149
12	<i>Opuntia ficus-indica</i> (L.) Mill (Nopal cactus)	Cladode	Ion exchange chromatography of alkaline hydrolysates.	Methionine	2.92 g/100g	24, 34, 149
13	<i>Opuntia ficus-indica</i> (L.) Mill (Nopal cactus)	Cladode	Ion exchange chromatography of alkaline hydrolysates.	Phenylalanine	3.55 g/100g	24, 34, 149
14	<i>Opuntia ficus-indica</i> (L.) Mill (Nopal cactus)	Cladode	Ion exchange chromatography of alkaline hydrolysates.	Serine	6.68 g/100g	24, 34, 149
15	<i>Opuntia ficus-indica</i> (L.) Mill (Nopal cactus)	Cladode	Ion exchange chromatography of alkaline hydrolysates.	Threonine	4.18 g/100g	24, 34, 149
16	<i>Opuntia ficus-indica</i> (L.) Mill (Nopal cactus)	Cladode	Ion exchange chromatography of alkaline hydrolysates.	Tyrosine	1.46 g/100g	24, 34, 149
17	<i>Opuntia ficus-indica</i> (L.) Mill (Nopal cactus)	Cladode	Ion exchange chromatography of alkaline hydrolysates.	Tryptophane	1.04 g/100g	24, 34, 149
18	<i>Opuntia ficus-indica</i> (L.) Mill (Nopal cactus)	Cladode	Ion exchange chromatography of alkaline hydrolysates.	Valine	7.72 g/100g	24, 34, 149
19	<i>Opuntia ficus-indica</i> (L.) Mill (Nopal cactus)	Cladode	Ion exchange chromatography of alkaline hydrolysates.	α -Aminobutyric acid	Trace	24, 34, 149
20	<i>Opuntia ficusindica</i> (L.) Mill (Nopal cactus)	Cladode	Ion exchange chromatography of alkaline hydrolysates.	Carnosine	Trace	24, 34, 149
21	<i>Opuntia ficus-indica</i> (L.) Mill (Nopal cactus)	Cladode	Ion exchange chromatography of alkaline hydrolysates.	Citrulline	Trace	24, 34, 149
22	<i>Opuntia ficus-indica</i> (L.) Mill (Nopal cactus)	Cladode	Ion exchange chromatography of alkaline hydrolysates.	Ornithine	Trace	24, 34, 149
23	<i>Opuntia ficus-indica</i> (L.) Mill (Nopal cactus)	Cladode	Ion exchange chromatography of alkaline hydrolysates.	Proline	Trace	24, 34, 149
24	<i>Opuntia ficus-indica</i> (L.) Mill (Nopal cactus)	Cladode	Ion exchange chromatography of alkaline hydrolysates.	Taurine	Trace	24, 34, 149

25	<i>Opuntia ficus-indica</i> (L.) Mill (Nopal cactus)	Cladode	Ion exchange chromatography of alkaline hydrolysates.	Glycine	Trace	24, 34, 149
26	<i>Opuntia ficus-indica</i> (L.) Mill (Nopal cactus)	Fruit	Ion exchange chromatography of alkaline hydrolysates.	Alanine	3.17 g/100g	24, 34, 149
27	<i>Opuntia ficus-indica</i> (L.) Mill (Nopal cactus)	Fruit	Ion exchange chromatography of alkaline hydrolysates.	Arginine	1.11 g/100g	24, 34, 149
28	<i>Opuntia ficus-indica</i> (L.) Mill (Nopal cactus)	Fruit	Ion exchange chromatography of alkaline hydrolysates.	Asparagine	1.51 g/100g	24, 34, 149
29	<i>Opuntia ficus-indica</i> (L.) Mill (Nopal cactus)	Fruit	Ion exchange chromatography of alkaline hydrolysates.	Asparaginic acid	Trace	24, 34, 149
30	<i>Opuntia ficus-indica</i> (L.) Mill (Nopal cactus)	Fruit	Ion exchange chromatography of alkaline hydrolysates.	Glutamic acid	2.40 g/100g	24, 34, 149
31	<i>Opuntia ficus-indica</i> (L.) Mill (Nopal cactus)	Fruit	Ion exchange chromatography of alkaline hydrolysates.	Glutamine	12.59 g/100g	24, 34, 149
32	<i>Opuntia ficus-indica</i> (L.) Mill (Nopal cactus)	Fruit	Ion exchange chromatography of alkaline hydrolysates.	Cystine	0.41 g/100g	24, 34, 149
33	<i>Opuntia ficus-indica</i> (L.) Mill (Nopal cactus)	Fruit	Ion exchange chromatography of alkaline hydrolysates.	Histidine	1.64 g/100g	24, 34, 149
34	<i>Opuntia ficus-indica</i> (L.) Mill (Nopal cactus)	Fruit	Ion exchange chromatography of alkaline hydrolysates.	Isoleucine	1.13 g/100g	24, 34, 149
35	<i>Opuntia ficus-indica</i> (L.) Mill (Nopal cactus)	Fruit	Ion exchange chromatography of alkaline hydrolysates.	Leucine	0.75 g/100g	24, 34, 149
36	<i>Opuntia ficus-indica</i> (L.) Mill (Nopal cactus)	Fruit	Ion exchange chromatography of alkaline hydrolysates.	Lysine	0.63 g/100g	24, 34, 149
37	<i>Opuntia ficus-indica</i> (L.) Mill (Nopal cactus)	Fruit	Ion exchange chromatography of alkaline hydrolysates.	Methionine	2.01 g/100g	24, 34, 149
38	<i>Opuntia ficus-indica</i> (L.) Mill (Nopal cactus)	Fruit	Ion exchange chromatography of alkaline hydrolysates.	Phenylalanine	0.85 g/100g	24, 34, 149
39	<i>Opuntia ficus-indica</i> (L.) Mill (Nopal cactus)	Fruit	Ion exchange chromatography of alkaline hydrolysates.	Serine	6.34 g/100g	24, 34, 149
40	<i>Opuntia ficus-indica</i> (L.) Mill (Nopal cactus)	Fruit	Ion exchange chromatography of alkaline hydrolysates.	Threonine	0.48 g/100g	24, 34, 149
41	<i>Opuntia ficus-indica</i> (L.) Mill (Nopal cactus)	Fruit	Ion exchange chromatography of alkaline hydrolysates.	Tyrosine	0.45 g/100g	24, 34, 149
42	<i>Opuntia ficus-indica</i> (L.) Mill (Nopal cactus)	Fruit	Ion exchange chromatography of alkaline hydrolysates.	Tryptophane	0.46 g/100g	24, 34, 149
43	<i>Opuntia ficus-indica</i> (L.) Mill (Nopal cactus)	Fruit	Ion exchange chromatography of alkaline hydrolysates.	Valine	1.43 g/100g	24, 34, 149
44	<i>Opuntia ficus-indica</i> (L.) Mill (Nopal cactus)	Fruit	Ion exchange chromatography of alkaline hydrolysates.	α -Aminobutyric acid	0.04 g/100g	24, 34, 149
45	<i>Opuntia ficus-indica</i> (L.) Mill (Nopal cactus)	Fruit	Ion exchange chromatography of alkaline hydrolysates.	Carnosine	0.21 g/100g	24, 34, 149
46	<i>Opuntia ficus-indica</i> (L.) Mill (Nopal cactus)	Fruit	Ion exchange chromatography of alkaline hydrolysates.	Citrulline	0.59 g/100g	24, 34, 149
47	<i>Opuntia ficus-indica</i> (L.) Mill (Nopal cactus)	Fruit	Ion exchange chromatography of alkaline hydrolysates.	Ornithine	Trace	24, 34, 149
48	<i>Opuntia ficus-indica</i> (L.) Mill (Nopal cactus)	Fruit	Ion exchange chromatography of alkaline hydrolysates.	Proline	46.00 g/100g	24, 34, 149
49	<i>Opuntia ficus-indica</i> (L.) Mill (Nopal cactus)	Fruit	Ion exchange chromatography of alkaline hydrolysates.	Taurine	15.79 g/100g	24, 34, 149
50	<i>Opuntia ficus-indica</i> (L.) Mill (Nopal cactus)	Fruit	Ion exchange chromatography of alkaline hydrolysates.	Glycine	Trace	24, 34, 149
51	<i>Opuntia ficus-indica</i> (L.) Mill (Nopal cactus)	Seeds	Ion exchange chromatography of alkaline hydrolysates.	Alanine	4.75	24, 34, 149
52	<i>Opuntia ficus-indica</i> (L.) Mill (Nopal cactus)	Seeds	Ion exchange chromatography of alkaline hydrolysates.	Arginine	6.63	24, 34, 149
53	<i>Opuntia ficus-indica</i> (L.) Mill (Nopal cactus)	Seeds	Ion exchange chromatography of alkaline hydrolysates.	Asparagine	Trace	24, 34, 149
54	<i>Opuntia ficus-indica</i> (L.) Mill (Nopal cactus)	Seeds	Ion exchange chromatography of alkaline hydrolysates.	Asparaginic acid	10.42	24, 34, 149

55	<i>Opuntia ficus-indica</i> (L.) Mill (Nopal cactus)	Seeds	Ion exchange chromatography of alkaline hydrolysates.	Glutamic acid	21.68	24, 34, 149
56	<i>Opuntia ficus-indica</i> (L.) Mill (Nopal cactus)	Seeds	Ion exchange chromatography of alkaline hydrolysates.	Glutamine	Trace	24, 34, 149
57	<i>Opuntia ficus-indica</i> (L.) Mill (Nopal cactus)	Seeds	Ion exchange chromatography of alkaline hydrolysates.	Cystine	0.37	24, 34, 149
58	<i>Opuntia ficus-indica</i> (L.) Mill (Nopal cactus)	Seeds	Ion exchange chromatography of alkaline hydrolysates.	Histidine	3.11	24, 34, 149
59	<i>Opuntia ficus-indica</i> (L.) Mill (Nopal cactus)	Seeds	Ion exchange chromatography of alkaline hydrolysates.	Isoleucine	6.20	24, 34, 149
60	<i>Opuntia ficus-indica</i> (L.) Mill (Nopal cactus)	Seeds	Ion exchange chromatography of alkaline hydrolysates.	Leucine	9.94	24, 34, 149
61	<i>Opuntia ficus-indica</i> (L.) Mill (Nopal cactus)	Seeds	Ion exchange chromatography of alkaline hydrolysates.	Lysine	6.79	24, 34, 149
62	<i>Opuntia ficus-indica</i> (L.) Mill (Nopal cactus)	Seeds	Ion exchange chromatography of alkaline hydrolysates.	Methionine	0.70	24, 34, 149
63	<i>Opuntia ficus-indica</i> (L.) Mill (Nopal cactus)	Seeds	Ion exchange chromatography of alkaline hydrolysates.	Phenylalanine	5.25	24, 34, 149
64	<i>Opuntia ficus-indica</i> (L.) Mill (Nopal cactus)	Seeds	Ion exchange chromatography of alkaline hydrolysates.	Serine	8.46	24, 34, 149
65	<i>Opuntia ficus-indica</i> (L.) Mill (Nopal cactus)	Seeds	Ion exchange chromatography of alkaline hydrolysates.	Threonine	1.53	24, 34, 149
66	<i>Opuntia ficus-indica</i> (L.) Mill (Nopal cactus)	Seeds	Ion exchange chromatography of alkaline hydrolysates.	Tyrosine	3.09	24, 34, 149
67	<i>Opuntia ficus-indica</i> (L.) Mill (Nopal cactus)	Seeds	Ion exchange chromatography of alkaline hydrolysates.	Tryptophane	Trace	24, 34, 149
68	<i>Opuntia ficus-indica</i> (L.) Mill (Nopal cactus)	Seeds	Ion exchange chromatography of alkaline hydrolysates.	Valine	6.02.	24, 34, 149
69	<i>Opuntia ficus-indica</i> (L.) Mill (Nopal cactus)	Seeds	Ion exchange chromatography of alkaline hydrolysates.	α -Aminobutyric acid	Trace	24, 34, 149
70	<i>Opuntia ficus-indica</i> (L.) Mill (Nopal cactus)	Seeds	Ion exchange chromatography of alkaline hydrolysates.	Carnosine	Trace	24, 34, 149
71	<i>Opuntia ficus-indica</i> (L.) Mill (Nopal cactus)	Seeds	Ion exchange chromatography of alkaline hydrolysates.	Citrulline	Trace	24, 34, 149
72	<i>Opuntia ficus-indica</i> (L.) Mill (Nopal cactus)	Seeds	Ion exchange chromatography of alkaline hydrolysates.	Ornithine	Trace	24, 34, 149
73	<i>Opuntia ficus-indica</i> (L.) Mill (Nopal cactus)	Seeds	Ion exchange chromatography of alkaline hydrolysates.	Proline	Trace	24, 34, 149
74	<i>Opuntia ficus-indica</i> (L.) Mill (Nopal cactus)	Seeds	Ion exchange chromatography of alkaline hydrolysates.	Taurine	Trace	24, 34, 149
75	<i>Opuntia ficus-indica</i> (L.) Mill (Nopal cactus)	Seeds	Ion exchange chromatography of alkaline hydrolysates.	Glycine	5.06	24, 34, 149

CONCLUSION AND FUTURE PERSPECTIVES:

The *Opuntia ficus indica* is a reservoir of flavonoids such as kaempferol, quercetin, narcissin, dihydrokaempferol, dihydroquercetin, and eriodictyol. Other antioxidants in prickly pear fruits include betalains, pectin, carotenes, betalains, ascorbic acid, quercetin, and quercetin derivatives. This review presented the high potential for antioxidant activity, anti-inflammatory actions, analgesic effects such as wound healing properties, and anti-ulcer genic effects. *Opuntia spp.* even has the potential for treating chronic diseases such as cardiovascular effects such as anti-hyperlipidemic properties, cholesterol-lowering properties, etc. Prickly pear has also shown hypoglycemic and

anti-diabetic effects in treating diabetes mellitus. *Opuntia spp.* also exhibits anti-microbial properties, anti-viral properties, etc. *Opuntia* also has been effective in exhibiting anti-spermatogenic properties.

Opuntia ficus-indica (L.) Mill. is has the potential of being the most agro-economically important cactus crop species. There is evidence for the use of *Opuntia* in the human diet at least 9000 years ago or even as early as 12,000 years ago. Due to multiple uses of cactus, a cactus crop may be proven beneficial for the rehabilitation of degraded sites, including wastelands. The low cost of establishing and producing the crop, as well as its tolerance to extreme conditions, make cactus

potentially suited to becoming a viable future industry in India. The Thar desert in Rajasthan, Rann of Kutch in Gujarat, southwestern parts of Haryana, Bundelkhand, and other similar rainfed areas that are prone to severe drought would be very productive in the cultivation of *Opuntia* species.

Opuntia spp. can be contemplated as a nutraceutical, due to their ability to prevent or delay chronic disease development and promote a better health and quality of life. More extensive research can be done to examine the bioactive compounds of *Opuntia spp.* and explore its pharmacological properties as a high potential nutraceutical fruit.

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