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REVIEW ARTICLE ON PHARMACOLOGICAL POTENTIAL OF OPUNTIA FICUS INDICA

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ABSTRACT

Strong bioactive plant elements have attracted a lot of attention lately for their potential to prevent and treat a wide range of diseases in addition to enhancing general health. The cactus pear (Opuntia ficus Indica) is a perfect option for the creation of pharmaceuticals and foods that promote health because of its multifunctional action and possibly active ingredients. Even though cactus pears are valued for their pharmacological properties in several countries, they are still hardly utilized in contemporary medicine and nutrition. Recent research on cactus pear, however, has shown that various plant sections may be useful in the creation of medications and nutritious foods. Therefore, the purpose of this review is to provide an overview of current advancements in the use of cacti for various pharmacological purposes.

KEYWORDS: Pharmacological, Cactus, Opuntia ficus Indica, Bioactive constituents.

INTRODUCTION

Strong-containment plants have attracted a lot of attention lately for their potential to prevent and treat a wide range of illnesses in addition to enhancing general health. Most people agree that the active ingredients in plants, whether they be complete plants, plant parts (flowers, fruits, roots, or leaves), plant materials, or a combination of these, are what give herbal treatments their therapeutic effects (Ahn, 1998; De Smet, 2002).[1,2] The prickly pear, or Opuntia ficus indica, is a member of the Cactaceae family of cacti. The 130 genera and

around 1500 species that make up the family Cactaceae are thought to have originated in the New World. They are very helpful in dry and semi-arid conditions since they need so little water (Griffith, 2004; Pareek et al. 2003[3,4]).

The soft cladodes of cacti are eaten as fresh green vegetables and salad dressings; they also yield tasty, nutritious fruits (Griffith, 2004).[3] Among other things, cactus is utilized in nutrition, health, and cosmetics. Value-added items such jam, wine, body lotions, shampoos, and creams are made from the fruit and cactus stem (Pareek et al. 2003).[4] Due to its anti-inflammatory properties and ability to treat a variety of illnesses and ailments, it has also been traditionally utilized in folk medicine in a number of counties for a variety of medical purposes (Hunt et al. 2006; Salim et al. 2009).[5,6] According to recent scientific research, cacti or its many components contain potentially useful phytochemicals that could be very beneficial to human health and medicine (Almimi et al. 2010; Valente et al. 2010).[7,8] In herbal medicine, one of the most important steps in producing products rich in phytochemicals is generally the extraction of phytochemicals from plant materials using solvents. Scholars have directed their inquiry on cacti in order to ascertain the characteristics of the plant that may serve as a foundation for application in the avoidance and management of various illnesses (Harnandaz et al. 2011).[9]

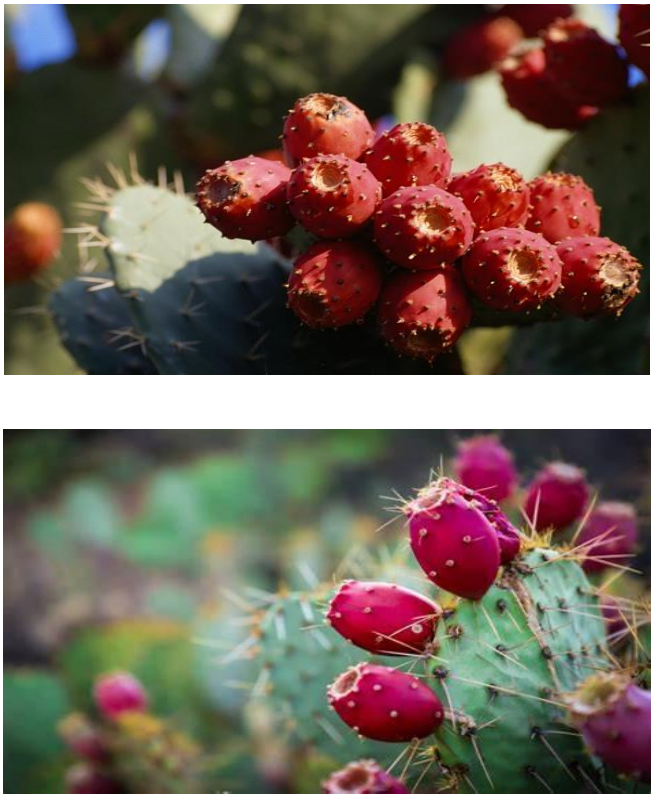

Fig. Opuntia ficus indica.

Furthermore, new research on cacti has shown that various plant parts may be suitable for use in the production of medications and nutritious foods. Consequently, the purpose of this review is to provide an overview of current research on the pharmacological significance of cacti.

Origin and Distribution of opuntia ficus indica

Opuntia spp. The plant, which has its origins in tropical and subtropical America, has been transported by humans to other continents. A good plant for areas lacking water is the cactus pear (Opuntia ficus indica). It is a multipurpose, succulent, xerophytic, spiny, or spineless plant. Griffith (2004).[3]

Botanic description kingdom

Plantae division: Magnoliophyta

Class: Magnoliopsida

Order: Caryophyllales

Family: Cactaceae

Traditional uses

In many counties, cactus pears (Opuntia ficus indica) are used as traditional medicine to heal burns, wounds, edema, and dyspepsia. According to reports from various investigations, its alcoholic extracts have antimicrobial, hypoglycemic, and anti-inflammatory properties. Furthermore, diabetics have long been treated with the prickly pear cactus stem (Saenz, 2000).[10]

Phytochemical composition of opuntia ficus indica

Ascorbic acids, vitamins, carotenoids, fibers, amino acids, and antioxidant substances (flavonoids, betaxanthin, betacyanin, and alkanoids) have all been linked to the cladodes and skin fruit of cacti (Ennouri et al. 2014; Yasmeen et al. 2012).[11,12] Additionally, several flavonoids, including quetctin and kaempferol, are found in cactus flowers (Kunti, 2004; Moussa et al. 2011).[13,14]

Pharmacological actions

Humans have been using Opuntia ficus indica for many years. The majority of Opuntia ficus indica has been used as medicine in addition to being eaten or drunk. In more recent times, it

has also been made into juice, jam, frozen fruit, and spray-dried powder (Salim et al. 2009).[15]

Table 1 presents an overview of the various pharmacological properties of Opuntia ficus indica, which have been reported in various investigations.

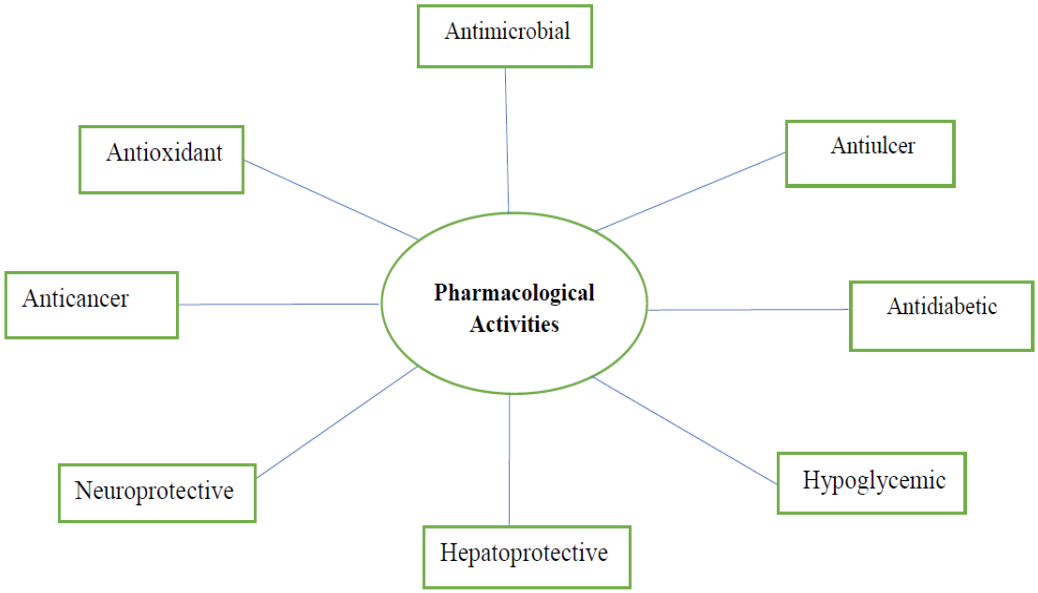

Table 1: Main biological effects of cactus preparations.

Biological activity	Source of cactus products
Antimicrobial	➢ Methanol extract of cladodes and skin fruit ➢ Ethanol extracts of cladodes and skin fruit ➢ Chloroform extracts of cladodes and skin fruit ➢ Hexane extracts of cladodes ➢ Aqueous alcoholic extracts of cladodes Cactus stem extract
Anti-inflammatory and antioxidant	Butanol and methanol extract of fruit
Hypolipidemic and Hypocholesterolemic	➢ Cladodes powder ➢ Cladodes (Glycoprotein) ➢ Seed powder and oils
Antidiabetic	➢ Capsule: cladodes and skin fruit extract ➢ Cactus powder in capsule ➢ Aqueous extract of skin fruit and cladodes and mixture cladodes and skin fruit extracts Capsule
Hypoglycemic	➢ Polysaccharide extracts from cladodes ➢ Extract powder racket after drying
Anti-inflammatory	➢ Indicaxanthin from fruit ➢ Lipohylized extracts of cladodes

	➢ Indicaxanthin from cactus pear fruit ➢ Methanol extracts of cactus stem and Methanol extracts of prickly pear fruit
Antioxidant	➢ Betalain a pigment purified from fresh pulp of cactus pear ➢ Betanin prickly pear fruit extracts ➢ Ethanol extract of stem ➢ Cactus pear fruit ➢ Flavonoids fraction from of juice of whole fruits ➢ Glycoprotein isolated from Opuntia ficus indica var. sabotenmakino
Anticancer	Cactus pear fruit extract
Hepatoprotective	Cladodes extract
Neuroprotective	Methanol extract of skin fruit
Antiulcer	Lyophilized cladodes Pectin polysaccharides cladodes

Anti-ulcer Activity

Opuntia ficus indica (L.) Mill. cladodes is used in Sicilian folk medicine to heal stomach ulcers (Galati et al., 2001). Pre-treatment test in rats indicated a preventive activity against ethanol-induced ulcer (Galati et al., 2003). It was clear that the stomach cytoarchitecture is typically preserved by the acute ingestion of lyophilized O. ficus indica cladodes. The mucilage could stop the necrotizing agent from penetrating the stomach mucosa. Moreover it produces a protective layer and protects the deep necrotic lesions generated by ethanol (Trachtenberg and Mayer, 1981). The primary components of O. ficus indica cladodes consist of a mixture of mucilage and pectin. O. ficus indica cladodes' pectin polysaccharides may have an impact on the regeneration of the gastrointestinal mucosa. O. ficus indica cladodes can stop the ulcerogenic agent to prevent damage, but this preventive treatment can lead to cytoprotection phenomena by breaking up the epithelial cells and stimulating an increase in mucus production in ethanol-induced ulcers, which tend to dissolve the components of the stomach's mucous membrane and lower the level of tissue protein (Galati et al., 2002).[16]

Anti-inflammatory activity

Numerous studies have evocated the analgesic and antiinflammatory actions of the genus Opuntia by using either fruit extract, the lyophilized cladodes, or the phytosterols from fruit and stem extracts (park et al., 1998). Opuntia ficus indica has been reported to have anti-inflammatory activity. β-Sitosterol identified as the active anti-inflammatory principle from the stem extract though its activity appears to be relatively weaker compared with that of hydrocortisone (park et al., 2001). This is the first direct evidence on the anti-inflammatory

activity of β-Sitosterol. Lyophilized aqueous extract (100–400 mg/kg, i.p.) of the fruits of Opuntia dillenii (Ker-Gawl) Haw was evaluated for analgesic activity using writhing and hot plate test in mice and rat, respectively and also anti-inflammatory activity using carrageenaninduced paw edema in rats, the results exhibited dose dependent action (Loro et al., 1999.[17]

Neuroprotective

Opuntia ficus-indica has been reported to have neuroprotective action in primary cultured rat cortical cells (Dok-. Go et al., 2003). Opuntia ficus indica contains three flavonoid, quercetin, (+)-dihydroquercetin, and quercetin 3-methyl ether, are reported as active antioxidative neuroprotectants that exhibiting protective actions. It has been reported that Opuntia ficus indica shows protective action against the oxidative injury induced by H202, Xanthine/Xanthine Oxidase (X/XO), or Buthionesulfoximine (BSO) in primary cultured rat cortical cells, inhibiting lipid peroxidation, and scavenging DPPH radicals (Dok-Go et al., 2003). Moreover recently reported that quercetin, a component of Opuntia ficus-indica, had a neuroprotective action against Nmethyl-d-aspartate (NMDA), kainate (KA), and oxygen–glucose deprivation (OGD)-induced neurotoxicity in cultured rat cortical cell and in vivo global ischemia induced cultured gerbils cortical cells, (Ha et al., 2003). Methanol extract of Opuntia ficus-indica (MEOF) has a neuroprotective action against (NMDA), (KA), and (OGD)-induced neuronal injury in cultured mouse cortical cells and also reported the neuroprotective effect of MEOF in the hippocampal against neuronal damage evoked by global ischemia in gerbils (Kim et al., 2006).[18]

Antiviral activity

In a fascinating study, Ahmad et al. showed that giving cactus stem extract (Opuntia streptacantha) to mice, horses, and people inhibits the intracellular replication of several DNA and RNA viruses, including HIV-1, Equine herpes virus, Pseudorabies virus, influenza virus, and Herpes simplex virus Type 2. The same scientists also reported an inactivation of extracellular viruses.

But the active inhibitory elements of the cactus extract utilized in this study were not examined, and no other research has addressed this particular subject to date (Ahmad et al., 1996).[19]

Anticancer activity

Recent studies suggests that the cactus pear fruit extract (i) inhibits the proliferation of cervical, ovarian and bladder cancer cell lines in vitro, and (ii) suppresses tumor growth in the nude mice ovarian cancer model in vivo. These experiments showed that inhibition was dose- (1, 5, 10 and 25% cactus pear extract) and time- (1, 3 or 5 day treatment) dependent on in vitro-cultured cancer cells. The intra-peritoneal administration of cactus extract solution into mice did not affect the animal body weight, which indicated that cactus did not have a significant toxic effect in animals. Growth inhibition of cultured-cancer cells was associated with an increase in apoptotic cells and the cell cycle arrest at the G1-phase. Moreover, the induced growth inhibition seems dependent on the P53 pathway, which is the major tumor suppressor. Annexin IV was increased and the VEGF decreased in the tumor tissue obtained from animals having received the cactus solution. The antiproliferative effect of betanin, isolated from the fruits of Opuntia ficus indica, was evaluated on human chronic myeloid leukemia cell line (K562). The results show dose and time dependent decrease in the proliferation of K562 cells treated with betanin with an IC50 of 40 μM. Further studies involving scanning and transmission electron microscopy revealed the apoptotic characteristics such as chromatin condensation, cell shrinkage and membrane blebbing. Agarose electrophoresis of genomic DNA of cells treated with betanin showed fragmentation pattern typical for apoptotic cells. Flow cytometric analysis of cells treated with 40 mM betanin showed 28.4% of cells in sub G0/G1 phase. Betanin treatment to the cells also induced the release of cytochrome c into the cytosol, PARP cleavage, down regulation Bcl-2, and reduction in the membrane potentials. These studies demonstrate that betanin induces apoptosis in K562 cells through the intrinsic pathway and is mediated by the release of cytochrome c from mitochondria into the cytosol, and PARP cleavage. The mechanisms responsible for executing the antiproliferative effects include: (i) induction of alterations in the cell differentiation pattern, which plays a vital role in the invasiveness and metastatic progression of the tumors, (ii) blockade of pre neoplastic cell expansion or induction of apoptosis, and (iii) intervention of metabolic activation of carcinogens by scavenging ROS (Loro et al., 1999; Sreekanth et al., 2007). Anti-viral activity An interesting study by Ahmad et al. demonstrated that administration of a cactus stem extract (Opuntia streptacantha) to mice, horses, and humans inhibits 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 syncitial disease virus and HIV-1. An inactivation of extra-cellular viruses was also reported by the same authors.[20]

Hangover from alcohol

Opuntia ficus indica has also been shown to help with hangover symptoms in people. The intensity of the hangover caused by alcohol consumption might be attributed to inflammation brought on by contaminants in the alcohol and alcohol metabolic byproducts. Human alcohol hangover symptoms as nausea, dry mouth, and anorexia are lessened by an extract of the Opuntia ficus indica (OFI) plant (Wiese et al., 2004).[21]

Antidiabetic characteristic

In this work, rats with diabetes caused by alloxan were used to examine the nutritional content, antioxidant activity, and impact of cactus pear (Opuntia ficus-indica) fruit juice on biochemical parameters, enzyme activities, and lipid peroxidation. To cause diabetes, a single dosage of alloxan (130 mg/kg BW) was administered. Rats with alloxan-induced diabetes received a single or repeated oral treatment (5 ml/rat once, twice, three, or four times) of cactus fruit juice every day for five weeks. In the serum of rats given alloxan-induced diabetes, there was a significant ($P < 0.05$) increase in the levels of glucose, cholesterol, urea, creatinine, aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), and malondialdehyde (MDA). Conversely, there was a significant ($P < 0.05$) decrease in the levels of superoxide dismutase (SOD), reduced glutathione (GSH), HDL cholesterol, protein, hemoglobin, and liver glycogen. Treatment of the diabetic rats with single or repeated dose of cactus fruit juice could restore the modifications of the aforesaid parameters to their normal levels (Hassan et al., 2011).[22]

Hepatoprotective agent

Additionally, the cladodes extract of Opuntia ficus indica protects mice's livers from damage caused by an Chlorpyrifos is an organophosphorous insecticide (CPF). The weight of the liver was measured, and spectrophotometric methods were used to quantify several biochemical parameters, including albumin, cholesterol, lactate dehydrogenase (LDH), phosphatase alkaline (PAL), aspartate amino transferase (ASAT), alanine amino transferase (ALAT), and phosphatase alkaline (PAL). Research has demonstrated that CPF has a significant impact on every metric examined. However, we observed a recovery of all of their levels when this herbicide was applied in relation to cacti. Consequently, the liver is shielded and the toxicity caused by this organophosphorous pesticide is reduced by Opuntia ficus indica stem extract (Ncibi et al., 2008).[23]

Antioxidant activity

To ascertain the mechanism or mechanisms underlying Opuntia ficus-indica var. Saboten (OFS) stem ethanol extract's antioxidant activity was evaluated. In a thiocyanate test method, the ethanol extract showed concentration-dependent suppression of linoleic acid oxidation. It was also discovered that the OFS ethanol extract effectively shielded plasmid DNA from strand breakage brought on by hydroxyl radicals in a Fenton's reaction mixture.

Additionally, the extract demonstrated a noteworthy ($p < 0.01$) dose-dependent shielding of mouse splenocytes from cytotoxicity induced by glucose oxidase. Lastly, it was noted that the OFS extract had a significant concentration of phenolics (180.3 mg/g), which may be the active ingredients in charge of the extract's antioxidant qualities (Lee et al., 2002).[24]

Anti-atherogenic properties

Atherosclerosis is a metabolic disease characterized by persistent inflammation linked to the thickening and solidification of large to medium-sized blood vessels due to plaque formation. Giglio et al.'s initial intervention study, published in 1985, suggested that pasta enhanced with an O. ficus-indica concentrate could be beneficial for improving certain metabolic indices, lowering atherogenic lipoproteins like small, dense low-density lipoprotein (sdLDL), and decreasing low-density lipoprotein particle sizes. O. ficus-indica fruit extract shows potential as a preventative, anti-inflammatory, and antioxidative agent by reducing stress brought on by oxidation from a high-fat diet and restoring normal parenchyma in endothelial inflammation.[25]

Anti-multiplicity action

After betanin was extracted from O. ficus-indica products, its anti-proliferative qualities were tested using a human constant, K562, a myeloid leukemia cell line. The findings reveal a percentage and time-subordinate decrease in the growth of 40 μM betanin-treated K562 cells. Further investigation with transmission and scanning electron microscopy revealed the characteristics of apoptosis, such as chromatin condensation, shrinking of the cell, and membrane blebbing.

Flow cytometric data revealed that in cells treated with 40 mM betanin, the genomic DNA displayed an apoptotic pattern of fragmentation on agarose electrophoresis; sub G0/G1 stage was present in 28.4% of cases. Benin treatment also resulted in Bcl-2 downregulation, cytochrome c release into the cytoplasm, breakdown of polyadenosine diphosphateribose

polymerase (PARP), and a decrease in membrane potential in the treated cells. The results of these studies demonstrate that betanin induces apoptosis in K562 cells internally through the mechanism of mitochondria releasing cytochrome c into the cytoplasm and PARP breaking. The antiproliferative qualities are mediated through the following mechanisms: (i) teaching of anomalies in the cell diversity pattern, which is critical for the invasiveness and spread of metastatic tumors. (ii) scavenging ROS87 to stop carcinogens from being metabolically activated; (iii) stopping precancerous cells from growing or leading them to undergo apoptosis.[26]

Spermatogenetic action

Studies on the O. ficus-indica cladode, which is prevalent in several compounds with antioxidant characteristics, have shown that it has a positive effect on the breakdown of sperm DNA after human semen is cryopreserved88. An additional investigation examined the effects of lipid peroxidation, DNA breakage, and characteristics of ram semen on liquid storage in trios of egg yolk extenders (TEY) and skim milk (SM) at 5°C for a maximum of 72 hours. The cladodes of O. ficus-indica acetone extract were evaluated in this investigation. TEY had higher levels of total sperm motility and viability, while SM had higher levels of abnormalities, spontaneous lipid peroxidation, progressive motility, and membrane integrity. ($p < 0.05$) In a similar vein, even 72 hours after capacity, 1% Actex can significantly reduce the negative effects of fluid accumulating on sperm DNA discontinuity ($p<0.05$). In summary, adding 1% ACTEX89 to SM and TEY can improve slam semen quality. In a planned investigation, the effect of an ethanolic extract of O. ficus-indica on rats' testicular damage resulting from methotrexate (MTX), a chemotherapy medication used to treat various malignancies and inflammatory diseases, was assessed. It is detrimental to cells that divide and expand quickly, among other things. The cladodes extract increased the sperm boundaries (count and motility) and serum testosterone levels while protecting the rats' gonad histopathology and oxidative stress.[27]

Cardioprotective activity

The impacts of O. ficus-indica nopalitos on oxidizing pressure, endothelial dysfunction, arterial hypertension, and dyslipidemia were investigated in rats that were prematurely introduced to a cafeteria diet (CD). For thirty days, two equal groups of sixteen young male wistar rats were created and given a CD that had 50% junk food mix and 50% hyperlipidic diet, with or without 50 g of fresh O. ficus-indica nopalitos as a supplement. Arterial pressure

did not respond well to augmentation with O. ficus-indica nopalitos. Conversely, O. ficus-indica nopalitos significantly lower serum levels of triacylglycerol and total cholesterol. They also lower levels of hydroperoxide and thiobarbituric acid reactive substances, which dampen lipid peroxidation; they lower carbonyl concentrations, which lessen protein oxidation; and they boost antioxidant enzyme activity, which enhances antioxidant capacity. Furthermore, O. ficusindica nopalitos treats endothelial dysfunction and lowers serum uric acid levels.[28]

Nephroprotective properties

One of the conditions that O. ficus-indica is used to treat is metal-induced toxicity. The toxicity of lithium carbonate is prevented in rats by O. ficus-indica, as shown by the study conducted by Saad et al., 35. For a duration of 30 days, male Wistar rats were administered a single dosage of 25 mg/kg b.w. of lithium carbonate twice a day to induce nephrotoxicity. A 100 mg/kg b.w. aqueous extract of O. ficus-indica was gavaged over a period of 60 days. O. ficus-indica extract treatment appeared to provide protection against the actions of both enzymatic and nonenzymatic antioxidants by reducing the degree of intensity of lipid peroxidation and elevating the kidneys from lithium carbonate-induced oxidative stress, as per the study's findings.

Immunomodulatory activity

Increased host resistance to unexpected pathogenic threats can result from stimulating the innate immune system using immunomodulators; several innate system immunmodulators, such as cytokines, have been found,[28] chemicals that are separated from fungus and microorganisms,[29] and compounds that have been extracted from plants.[30,31] An intriguing investigation by Ahn et al.,[32] shown that O. ficus-indica extract has a significant immunemodulatory impact, supporting its value as a treatment for immune-related disorders. It also improves immunity by managing both the inflammatory response and its proponents.[33]

Side Effects and Toxicology of O. ficus-indica

Kleiner et al.,[34] reported that, little knowledge is available on cactus side effects. O. ficus-indica seed ingestion has been linked to a low colonic blockage. Orally, generally, O. ficus-indica is highly received. However, case studies and books of traditional folk medicine have documented that it may produce low colonic blockage, headache, nausea, mild diarrhoea, increased frequency and volume of stools, and fullness in the abdomen[34,35,36] Because herbal treatments are "natural," the general public and some medical experts feel that they are

generally safe. However, the shocking dearth of data supporting this belief. But, heavy metals like lead, mercury, or arsenic as well as other unreported medications that are purposely and illegally added to the plants in order to achieve a specific result can also cause negative effects in herbal goods.[37] Furthermore, additional factors (Such as bacteria, microbial toxins, and hereditary factors) may potentially impact the amount of active ingredients in the product made of herbs. Because all plant treatments contain chemicals that are registered in the Hazardous Substances Data Bank (National Library of Medicine, Bethesda, Maryland) and considered potentially hazardous, more research is necessary to fully evaluate the benefits and drawbacks of using O. ficus-indica.

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CONCLUSION

Although modern medicine may be available in most countries for the treatment of many chronic degenerative diseases, folk medicine (Phytomedicine) has remained popular for historical and cultural reasons. Despite the fact that Opuntia ficus-indica is commonly used around the world, there is a lack of in-depth study on the mechanism of action of pharmacological effects of its active ingredients. Few plant species that provide medicinal herbs have been scientifically evaluated for their possible medical applications. Due to a great number of potentially active nutrients from Opuntia ficus-indica, fruits and cladodes are claimed to be health-promoting food. This review presented evidence of the potential antioxidant properties of cactus or their components (phytochemicals) and their role in regulating and maintaining normal processes in living organisms. Natural antioxidants obtained from plant-based extracts of cactus are currently a subject of intensive research, and are of interest to both food scientists and health professionals. Preclinical and clinical information indicates that Opuntia ficus-indica is efficacious for certain chronic diseases.

There is a dearth in the field of pharmacodynamics and pharmacokinetics or safety aspects of the genus Opuntia. There have been very few studies pertaining to the molecular aspects of genus Opuntia, which is clearly evident by the sequence of information available in the public domains. Even though genus Opuntia is rich in healing properties, due to the lacunae in many aspects, there is an urgent requirement for further investigations to delineate its

precise mechanisms and possible therapeutic values, particularly in the field of chronic diseases.

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