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REVIEW ARTICLE

A REVIEW: *OPUNTIA FICUS-INDICA* AS A SOURCE OF BIOACTIVE COMPOUND INGREDIENTS FOR FUNCTIONAL FOODS, NUTRITION, HUMAN DISEASE AND HEALTH

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Abstract

Originally from Mexico, today, prickly pears (*Opuntia ficus-indica* (L.) Mill.) can be found worldwide, but they are most common in Africa, Australia, and the countries of the Mediterranean. The *Cactaceae* family, which has more than 1500 species of cactus, includes prickly pears. Additionally, consumers are becoming more and more interested in it because it contains bioactive substances like carotenoids, sterols, polyunsaturated fatty acids, polyphenols, and vitamins that are linked to important biological and functional activities such as effects on antioxidants, inflammation, and hypoglycemia as it prospers in dry and semiarid areas, this plant is very effective in preventing desertification and can be exploited in fields and gardens as a fence. Although it is frequently used today to make culinary products like jams and juices, it is also eaten as a fruit. If one wishes to create novel products with health-promoting properties for food, cosmetics, or pharmaceutical fields, as a feasible wellspring of phytochemicals for practical food sources, natural additions, or nutritional supplements, prickly pears are affordable.
Keywords: Biological and functional activities, *Opuntia ficus-indica* (L.) Mill., pharmaceutical fields, phytochemicals, prickly pear.

INTRODUCTION

Opuntia ficus-indica is a plant that fills generally in bone-dry locales of the world and is developed in hotter environments for its eatable organic product. It is likewise ordinarily known by the names thorny pear, prickly plant pear, cactus organic product, Barbary fig, nopal cactus, and Indian fig. Because of its capacity to treat various infections, *O. ficus-indica* is much of the time utilized in customary medication[1]. Scientific names of *O. ficus-indica* (Synonyms) are *O. ficus-indica* var. *gymnocarpa* (F. A. C. Weber) Speg., *O. amyclaea* Ten., *Cactus ficus-indica* L., *O. paraguayensis*, *Cactus decumanus* Willd., *O. cordobensis* Speg., *O. megacantha* Salm-Dyck *Opuntia gymnocarpa* F.A.C. Weber, *O. decumana* (Willd.) Haw., *O. hispanica* Griffiths, *O. maxima* Mill[2]. In Latin America, cacti have long been regarded as a staple food and a source of sustenance for the underprivileged. Of these, *Opuntia* has become the most valuable commercial variety globally. Numerous nations, including Brazil, Mexico, Italy, Argentina, China, Tunisia, and Israel, cultivate it[3]. Because of its many characteristics *O. ficus-indica* (Figure 1) suitable for a wide range of things, like animal and human feed, the food, cosmetic, and pharmaceutical productions, building infrastructure and using alternative fuels, prevention of soil erosion, protection of wildlife, and bee nectar[4-6]. Studies have shown that *O. ficus-indica* products of the soil can be used as a wellspring of minerals and phytochemicals, which contributes to its therapeutic qualities. Because *O. ficus-indica*is a decent wellspring of wellbeing advancing supplements and contributes to a balanced diet, it is widely appreciated[5]. Antioxidants, anti-diabetic, anti-inflammatory, diuretic, analgesic, anti-hypercholestero-

lemia, and anti-carcinogenic are some of the therapeutic qualities of *O. ficus-indica*[7-10].

These characteristics make it possible to prevent hangovers, reduce lipid oxidation and associated health risks, prevent some cancers, reduce the danger of type 2 diabetes and coronary artery disease, two of the leading reasons for passing away globally[5,10]. Products made from cacti can be an efficient way to obtain phytochemicals including fiber, mucilage, pigments, and antioxidants[11]. This review describes what is currently known about *O. ficus-indica* food products, with an emphasis on how they are used as food and medicine.

Figure 1: The *O. ficus-indica* (L.) Mill. fruit and cladodes.

Cactus used in traditional

Ancient civilizations have utilized cacti for generations to treat illnesses and mend wounds. Various nations have long employed the fruits, flowers, and cladodes of cacti in folk medicine. In order to control type 2 diabetes, traditional medical professionals in Mexico advise consuming fresh cladodes juice as well as fresh, fried, or grilled cladodes[12]. Cladodes are still utilized as medicinal substances for treating stomach ulcers and for their ability to promote healing. Additionally, dried cactus flower remedies for preventing urological issues and prostate cancer are well-known[11]. *O. ficus-indica* has been employed in conventional medicine to treat burns, wounds, edema, hyperlipidemia, obesity, and catarrhal gastritis[13]. Dryer and pounded into a powder, cladodes are sources of nutritive fiber that able to be included naturally to a diversity of dishes to increase their healthful qualities[14].

Nutraceutical products

Foods with therapeutic benefits and health-promoting ingredients are called nutraceutical products. Studies have shown that cladodes and cactus fruit both contain significant amounts of vital nutrients, minerals, antioxidants, and vitamins, cacti appear to be an outstanding phytochemical source with important nutraceutical qualities[15]. Because its bioactive components may be collected from the cactus plant's various anatomical components, including its flowers, fruit, cladodes, roots, and seeds, it can be fully utilized[16]. To benefit from the many health advantages of cladodes, food supplements made from dried cladodes flour are now marketed. The nutraceutical market today offers a number of produced items, including toast, soups, tortillas, cereal bars with flaxseed, biscuits, and snacks. Because cactus fiber increases excretion and binds dietary fat, it aids in weight loss, which lowers the amount of dietary fat accessible for absorption, nopal tablets are readily available in markets. Cactus fruits are used as part of syrups, sweets, liquors, juices, and marmalades to create a wide variety of functional meals that are presented as healthy options. To benefit from the therapeutic characteristics of cactus plants, dessert dishes, cereal bars, ice cream and other processed cuisine made from cactus fruits available. However, when fruit is processed to make juice and preserves, a significant proportion of seeds are left over. Solid seeds that make up 10–15% of the weight in pulp are present in cactus pear fruit. As a profitable byproduct of the plant, the oil is extracted from the seeds by pressing or grinding them. Although there are many seeds in the fruits, there is not much oil (7-15% of the total seed weight). To extract one liter of oil, more than a ton of these small seeds are required. Up to 80% of the fats in Cactus seed oil are unsaturated fatty acids[17]. When creating food products that support health, fruits and nuts are great options[18]. *O. ficus-indica* was the first fruit crop specifically designed for semi-arid, non-irrigated regions, the most significant species of cacti used in modern agriculture. It is useful as food, fuel, fodder, color and a way to re-establish ecosystems[19]. Members of the genus *Opuntia* are known to produce mucilage. Since gels are complex carbohydrates with high water absorption capacity, they ought to be taken into account as a possible source of synthetic hydrocolloids. In some countries, small farmers use the gum extracted from Cactus to filter their drinking water. Recently, Cactus extract has been evaluated for increasing soil water infiltration[20]. A newly discovered crop for semi-arid parts of the planet is the cactus pear, has new opportunities for value addition thanks to the new functions of specific chemicals[14]. When permanent fencing cannot be built due to a lack of funds or natural resources, cacti are frequently employed as a substitute[21].

Cactus in health and disease

Human health care has always benefited from the utilization of natural resources like various plants and fruits. The majority of traditional medicine is based on plant components, and it is used by approx 80% of the people on the planet. Numerous scientific studies on beneficial fruits and plants have found that the elements that give rise to their positive special effects may be due to the existence of physiologically engaged compounds. These compounds, specifically phyto-chemicals, are typically unnecessary nutrients[16]. Most of the almost 1500 species in the genus *Opuntia* include elements that are beneficial to health.

Pharmacological and therapeutic effect of cactus

Antioxidants activity

Antioxidant phytochemicals help to maintain wellness by guarding in opposition to oxidative damage brought on through oxygen species that are reactive[22]. Studies and reports have demonstrated that *O. ficus-indica* fruit extract has a dose-dependent inhibitory impact on erythrocytes against ethanol-induced *in vitro* lipid oxidation[23,24]. Additionally, it was discovered that the

same extract effectively shielded plasmid DNA against hydroxyl radical-induced strand breakage.

Diverse phenolic components, including quercetin, (+)-dihydroquercetin, and quercetin-3-methyl ether, were discovered in significant concentrations in the ethanol extract of *O. ficus-indica*, according to phytochemical analyses. These chemicals may be in charge of the antioxidant activity of the extract[25,26]. In ethanol-fed rats given prickly pear, scavenging activity was demonstrated to return to levels almost normal in a dose-dependent manner[23,27]. Similar phytochemical studies on the extracts of red-skinned fruits of prickly pear found carotenoids, ascorbic acid, taurine, betalains, flavonoids (luteolin, kaempferol, isorhamnetin, and quercetin), as well as their capacity to scavenge free radicals[28,29]. Ascorbic acid has been linked to as much as 68% of the antioxidant activity observed in cactus juices[23,30]. Extracts of *Opuntia* betacyanins and polyphenols may function as an electron donor to scavenge newly generated free radicals and transform them into more stable compounds[29]. Likewise, the antioxidant properties of flavonol glycosides present in *Aloe vera* flower extract are added to food products as additives, cosmetics, and pharmaceuticals[29,31]. The antioxidant activity of *O. ficus-indica* fruit was assessed at various phases of its ageing process in related investigations. The outcomes showed that *O. ficus-indica* fruit functions to increase antioxidant activity in normal humans, senescence-accelerated mice (SAM), and *in vitro* cultures[32]. To evaluate the antioxidant activity of *O. ficus-indica*, human studies have been accomplished. After consuming 300 g of *O. ficus-indica* for three days, the blood samples of ten healthy individuals shown a notable rise in antioxidant activity, with 20% of the samples in plasma and 5% in blood showing this effect[23,33]. Moreover, Boutakiout *et al.*,[34] study suggested that the cladodes of prickly pears are a great supply of naturally occurring antioxidants.

Additionally, the experimental research carried out by, Saad *et al.*,[35] researchers have demonstrated that the cladode extract of *O. ficus-indica* (100 mg/kg body weight) could decrease the damage caused by oxidative lithium by raising the concentrations of the antioxidant enzymes (catalase, glutathione peroxidase and superoxide dismutase). This result is most likely brought about by the extract's ability to lower membrane cell lipoperoxidation and free radical scavenging. Morán-Ramos *et al.*,[36] demonstrated that, the hepatic substance of malondialdehyde (MDA), a biomarker of lipid peroxidation, decreased, according to the authors' observations, when they examined the impact of *O. ficus-indica* on various oxidative pressure related boundaries. The authors concluded that *O. ficus-indica* caused a decrease in oxidative pressure was most likely the result of an instantaneous cooperation between the cell reinforcement particles found in this plant and the responding species because there were no progressions in the statement of the qualities encoding the cell reinforcement chemicals catalase (CAT), glutathione peroxidase (GPx), and superoxide dismutase (SOD), nor in their activity.

Analgesic activity

The search for new analgesics and anti-inflammatory medications with less adverse effects derived from natural ingredients and plants for therapeutic purposes has gained momentum. In this particular situation, using *O. ficus-indica* fruit ethanol extracts and stems, the pharmacological effects of cacti were evaluated. The syndrome of writhing brought on by acetic acid was avoided by both extracts, *indica*ting their analgesic qualities[37]. Halmi *et al.*,[38] observed the analgesic effects of the *O. ficus-indica* cladodes extract at three different concentrations on the peripheral and central nervous systems, the writhing test with acetic acid, the tail flick, and the hotplate. The findings of this study demonstrated that, after being given to rats, the cladodes' aqueous extract exhibits cerebral and peripheral analgesic effects similar to aspirin. In another study, decoction was used to produce *O. ficus-indica* cladodes extracts, and the hot plate and the plant extracts were tested for their analgesic properties in mice using tail flick methods. These results suggest that the plant may be a centrally acting analgesic, supporting the herb historical use as an analgesic[39].

Anti-inflammatory activity

The fruits have analgesic and anti-inflammatory qualities and lyophilized cladodes of the genus *Opuntia* have been supported by numerous investigations. These extracts contain an active anti-inflammatory component known as beta-sitosterols[18,40]. Leucocyte migration was found to be decreased by ethanolic *O. ficus-indica*s stem extracts, which decreased acute inflammation similarly to further nonsteroidal anti-inflammatory medications (NSAIDs) without any adverse consequences[26]. Numerous animal researches have demonstrated the capacity of *O. ficus-indica* helps reduce inflammation. The methanol *O. ficus-indica* extracts proved protective properties in gerbils to prevent nerve cell harm resulting from worldwide ischemia in the hippocampus area[41,42]. When betalain, an *O. ficus-indica* pigment extracted from fresh cactus pear pulp, was present in non-cytotoxic micromolar amounts, less cell adhesive molecules, like intercellular adhesive molecule 1 (ICAM-1), were stated by human umbilical vein endothelial cells (HUVECs)[40,42]. It has also received notice that the extract betalain can protect degenerative conditions like low-limb ischemia, atherosclerosis, atherothrombosis, and stroke, which all have a direct impact on endothelial function. According to reports, a butanol fraction (derived from *O. ficus-indica* 50% ethanol extracts and hydrolysis products) can prevent the degradation of IκB-α, lower iNOS protein and mRNA expressions, and display peroxynitrite scavenging activity on the BV-2 mice microglial cell line[42,43]. Another research shown that *O. ficus-indica* is effective in treating human alcohol hangover symptoms. Alcohol impurities and alcohol metabolic byproducts may produce inflammation, which is the root of the severity of the hangover. In humans, an *O. ficus-indica* plant extract reduces the effects of an alcoholic hangover, including nausea, dry mouth, and anorexia[44].

Anti-ulcerogenic activity

Medicinal plants like the *Opuntia* species provide safe and effective treatment to peptic ulcers and other gastrointestinal conditions with fewer side effects[45]. As part of standard care, gastric ulcers have been treated with *O. ficus-indica* cladodes. *O. ficus-indica*'s anti-ulcer properties are linked to the process of making mucilage, which may lessen inflammation and lessen the damage that ethanol does to the stomach[46,47]. Oral therapy of *O. ficus-indica* significantly decreased the process of development of stomach lesions and stomach ulcers in ethanol or HCl-induced gastric injury caused by aspirin[48]. The cladodes hydrocolloid may have dispersed across the gastrointestinal mucosa, functioning as a buffer, and increasing mucus production due to secretory cell proliferation, which would have produced the protective effect[49]. Traditional medical practices in sicily, cladodes of *O. ficus-indica* are employed in alleviate the cicatrisant effect of stomach ulcers. The effects of cladodes lyophilized (1 g/kg) on ulcers caused by ethanol in rats were investigated. Most likely, the primary antiulcer agent was the mucilage of *O. ficus-indica*[50,51].

Wound healing activity

The skin's tensile strength separates the wound segments was used to determine the effectiveness of *O. ficus-indica* stems on wound healing. *O. ficus-indica* extracts have been established in numerous trials to aid in wound healing. When applied topically to rats, the methanolic concentrate of *O. ficus-indica* stems and their n-hexane and ethyl acetic acid derivation divisions were found to show extensive injury recuperating movement[52]. In studies carried out by Trombetta *et al*.,[53] they discussed the possibility applications of two freeze-dried polysaccharide removes from *O. ficus-indica* cladodes for the treatment of overall, completely thick rat injuries. In this experimental setting, polysaccharides from cladodes of *O. ficus-indica* increased skin healing when treated topically for six days. Furthermore, it has been shown that by increasing the production of the proteins loricrin and filaggrin, found in differentiated keratinocytes and keratinocytes, *O. ficus-indica* cladode extracts may improve keratinocyte function and protect the epidermal barrier. The extract has a barrier effect because it prevents inflammatory molecules from producing reactive oxygen species (ROS)[54]. Both components of polymers are substances with a high molecular weight, like highly branched xyloarabinan and linear galactan polymer, and low-molecular-weight substances, such as eucomic, piscidic, D-mannitol, lactic acid, and 2-hydroxy-4-(4′-ydroxyphenyl)- butanoic acids may donate to the scarring features of *O. ficus-indica* cladodes. These extracts have the ability to promote cell regeneration on the scratched keratinocyte monolayer, demonstrating the potent anti-inflammatory and wound -healing qualities of *O. ficus-indica* components[54,55]. Likewise, it turns out polysaccharides taken from the *O. ficus-indica* cactus pear promote the growth of fibroblasts and keratinocytes[54,56].

Anti-microbial activity

Numerous researches have been published that support *O. ficus-indica* has antimicrobial action. On five meals-borne bacteria (*Staphylococcus aureus, Escherichia coli, Salmonella typhimurium, Bacillus subtilis,* and *Pseudomonas fluorescens*), the ethyl acetate derivation concentrates of *O. ficus-indica* displayed antibacterial action[57,58]. Strong antibacterial activity has been shown by ethanol, methanol, and chloroform extracts of cladoid and skin fruit extracts of *O. ficus-indica* against Gram-positive and Gram-negative microorganisms. It has also been discovered to have mild antifungal action against *Aspergillus niger*[59,60]. Campylobacter is quite possibly of the most widely recognized bacterium that causes food-borne bacterial gastroenteritis in people. According to epi-demiological research, eating poultry products raises your risk of contracting this illness significantly. Notably, there are noticeable bactericidal effects of *O. ficus-indica* extracts on the development of *Campylobacter coli* and *Campylobacter jejuni*. Additionally, Campylobacter adhesion to Vero cells is significantly decreased[61,29]. Studies on *Vibrio cholerae* have also examined the antimicrobial properties of methanolic, ethanolic, and watery concentrates of *O. ficus-indica;* the outcomes demonstrated that the methanolic separate was the best[62]. Blando *et al*.,[63] examined the possibility of using polyphenolic extracts from *O. ficus-indica* cladodes at two different developmental phases to prevent the production of biofilms by *S. aureus* and the growth of certain enter bacteria. That's what the discoveries showed though juvenile cladode extricate was more successful at repressing at a measurement of 1500 µg/mL, mature cladode remove hindered gram-negative microscopic organisms (*E. coli, S. typhimurium,* and *E. aerogenes*) at a convergence of 2000 µg/mL. Additionally, the antibacterial efficacy of *O. ficus-indica* cladodes' alcoholic and water extracts against *Proteus mirabilis* and *Vibrio cholera* has been documented. These extracts damage membranes, increasing their permeability and resulting in significant drops in pH and ATP. All in all, these findings clearly demonstrate *O. ficus-indica* has pharmacological interest in avoiding food contamination by *Vibrio cholerae* and *Campylobacter*[15]. Moreover, Sánchez *et al*.,[64] emphasised the 4 mg/mL minimum bactericidal concentration (MBC), for *O. ficus-indica* cladodes against *E. coli* and 1 mg/mL for *S. aureus*, respectively. The higher polyphenol contented of *O. ficus-indica* cladodes extracts, particularly isorhamnetin, which has been shown to have antimicrobial action, may be responsible for its antibacterial activity[65]. The anti-pneumonia properties of fruit peel have been the focus of recent research. The researchers showed that the beneficial components in the wasted fruit from *O. ficus-indica* have the ability to prevent pneumonia-causing bacteria[66].

Anti-viral activity

The growth of localized wounds caused by the Cucumber mosaic virus (CMV) on Faba bean plants was significantly inhibited by *O. ficus-indica* cladodes extract[67]. The same scientists conducted a second investigation in which they isolated Opuntin B, an

antiviral protein, from thorny pear cladode. The isolated protein's enzymatic activity evaluation revealed that it causes electrophoretic mobility shifting of (CMV) RNAs and destroys plant genomic RNA in its whole[9]. Furthermore, based on the action of certain of its phytochemical ingredients, the antiCOVID19 utility of *O. ficus-indica* has been studied as a cause of possible anti-viral medicines. Astragalin, a chiral phytochemical, appears to be associated with the antiviral activity[68]. It was discovered the ethanol extract of *O. ficus-indica* had antiviral action against the enveloped virus known as the *Peste des Petits* ruminant virus of the genus *Morbillivirus* that contains RNA as its genetic material[69]. Recently, Alqurashi *et al*.,[70] have proved the anti-viral action of *O. ficus-indica* oil against herpes simplex sort 2 (HSV-2) infections at 300 µg/mL of oil.

Neuroprotective activity

Neuroprotective *O. ficus-indica* effects have been reported to documented in essential refined rodent cortical cells. Three flavonoids included in *O. ficus-indica*(+)-dihydroquercetin, quercetin, and quercetin-3-methyl ether have been shown to have protective properties against free radicals. It has been demonstrated in primary rat cortical cells in culture that *O. ficus-indica* exhibits protective effect against oxidative damage brought on by H_2O_2, Buthione-sulfoximine (BSO), or Xanthine-Xanthine Oxidase (X-XO), scavenging DPPH radicals and reducing lipid peroxidation[25]. Furthermore, research has shown that the *O. ficus-indica* component quercetin had neuroprotective effects against the neurotoxins caused by Oxygen-glucose deprivation (OGD), kainate (KA), and N-methyl-d-aspartate (NMDA) in rat cultures cortex cells and global ischemia *in vivo* in gerbil cortical cells that have been cultured[71]. In cortical cells from mice grown in culture, has been demonstrated that *O. ficus-indica* extract have a neuroprotective effect against damage to neurons generated by (KA), (OGD), and (NMDA). Additionally, it has been shown to have a neuroprotective effect in gerbils' hippocampus against neuronal harm brought about by worldwide ischemia[72].

Hepatoprotective activity

O. ficus-indica effect on hepatic steatosis and damage studied in scientific reports, Morán-Ramos *et al*.,[36] conducted research using Zucker (fa/fa) rats, a genetically obese model with fatty liver. The discoveries imply that *O. ficus-indica* enhanced the fatty acid oxidation ability, hence limiting the build-up of fatty acids as triglycerides. Furthermore, the primary flavonoids in *O. ficus-indica* include isorhamnetin-3-O-β-D-glucoside, (+)-taxifolin, and quercetin 3-O-methyl ether, and narcissin were effectively divided by Kim *et al*.,[73] and (+)-taxifolin, one of these isolated molecules, showed notable defence against alcoholic oxidative stress on hepatocytes. Studies on cellular glutathione and associated enzymes suggested that (+)-taxifolin's hepatoprotective effects might be attributed to keeping GSH levels stable. In conclusion, it was proposed that *O. ficus-indica* and its dynamic ingredient, (+)-taxifolin, could lessen the oxidative stress caused by alcohol on the liver. Additionally, *O. ficus-indica* cladodes extract protects mice's livers from harm caused by chlorpyrifos (CPF) and organo-phosphorous insecticides[74].

Antidiabetic, antiobesity, and antihypertensive activities

Providing diabetic rodents with a solitary or rehashed portion of cactus natural product juice could return their blood glucose, urea, creatinine, aspartate amino-transferase (AST), alkaline phosphatase (ALP), alanine aminotransferase (ALT), malondi-aldehyde (MDA), superoxide dismutase (SOD), diminished glutathione (GSH), cholesterol, HDL cholesterol, hemoglobin, protein, and liver glycogen to typical[75]. Another study showed that in diabetic rats by streptozotocin given a diet rich in fat, nopal water extract (NPWE) dramatically improves the dys-regulated metabolism of carbohydrates. According to the findings, NPWE formulations may be utilised as a nutraceutical to treat type 2 diabetes[76]. With *O. ficus-indica* nopalitos, diabetes mellitus and its consequences can be controlled. It has been established that they enhance transport of cholesterol in reverse in rats, streptozoine (STZ) and a high fat diet (HFD)made type 2 diabetes (T2D) by improving blood pressure and glucose homeostasis, raising activity of lecithin cholesterol acyltransferase (LCAT), and reducing tissue lipid peroxidation through enhanced antioxidant defense mediated by enzymes[77].

Terzo *et al*.,[78] designated a study wherein the fruit *O. ficus-indica* was used to isolate indicaxanthin, which was found to have positive effects on the glucose dysmetabolism of rats. In fact, the HFD-treated mice's fasting glycaemic readings were notably less than those of the mice given an HFD. Additionally, compared to untreated HFD mice, they demonstrated lower plasma insulin concentration, greater insulin sensitivity, and superior glycaemic management, as demonstrated by the drop in blood glucose levels during the intraperitoneal glucose resilience test. More lately, Sirotkin[79] provided a thorough and fascinating review on *O. ficus-indica*, explaining how its suppression of fat oxidation and synthesis has an impact on fat and obesity in both people and animals. However, additional clinical research is necessary to determine its suitability as an anti-obesity nutraceutical, as noted by Corona-Cervantes *et al*.,[80]. Rats were shown to be significantly diuretic when *O. ficus-indica* cladode was dissolved in gel or aqueous extract, and normotensive rabbits showed hypotensive and diuretic effects from the lyophilized extract without experiencing a decline in renal function tests[81].

Hypolipidemic and hypocholesterolemic

Dehydrated *O. ficus-indica* cladodes were given to rats with normal cholesterol and LDL plasma concentration; however this impacted nothing on the rats overall or LDL plasma levels. On the other hand, triglyceride levels, LDL, and plasma cholesterol were found to decrease in rats that were either normal or hyperlipidemic after receiving lyophilized cladodes orally on a daily basis; HDL levels remained unchanged. The decrease was particularly noticeable in rats with elevated cholesterol levels[82]. The soluble fibre found in the dry cladodes may be the cause of these

effects[83]. The hypocholesterolemia potential effect of an aqueous *O. ficus-indica* extract (AOE) was assessed by Padila-Camberos *et al*.,[84]. authors demonstrated that, the polyphenolic chemicals included in AOE play a factor in its ability to inhibit pancreatic lipase and prevent hypercholesterolemia.

Anti-atherogenic activity

Atherosclerosis is a metabolic sickness set apart by diligent irritation connected to the continuous solidifying and thickness of the huge to medium-sized courses because of plaque development. The initial intervention study that was published by Giglio *et al*., [85] indicating that pasta enhanced with an *O. ficus-indica* concentrate might be valuable for lowering atherogenic lipoproteins, such as small, dense low-density lipoprotein (sdLDL), and for improving certain metabolic indices and low-density lipoprotein particle sizes. *O. ficus-indica* fruit extract demonstrates promise as a preventive, anti-inflammatory and anti-oxidative agent by restoring normal parenchyma in endothelial inflammation as well as stress caused by oxidation caused by a high fat diet[86].

Anti-proliferative activity

A human constant K562, a myeloid leukaemia cell line, was used to test the anti-proliferative properties of betanin, which was removed from the products of *O. ficus-indica*. The findings demonstrate a portion and time-subordinate decrease in the expansion of 40 μM betanin-treated K562 cells. Additional research using transmission and scanning electron microscopy identified the apoptotic features, including membrane blebbing, cell shrinkage, and chromatin condensation. The cells' genomic DNA after being exposed to betanindis played an apoptotic pattern of fragmentation on agarose electrophoresis in cells treated with 40 mM betanin, sub G0/G1 stage was present in 28.4% of cases., according to flow cytometric measurements. Additionally, the cells treated with benin underwent downregulation of Bcl-2, cytochrome c release to the cytoplasm, degradation of polyadenosinediphosphate-ribose polymerase (PARP), and membrane potential decrease. These investigations show that betanin causes K562 cells to undergo apoptosis via the internal route, which is intermediated via PARP breakage and the process by which mitochondria release cytochrome c into the cytoplasm. The following mechanisms carry out the antiproliferative properties: (i) instruction of abnormalities in the pattern of cell diversity, which is essential for the tumours' invasiveness and metastatic progression. (ii) preventing the growth of precancerous cells or causing them to undergo apoptosis; and (iii) preventing carcinogens from becoming metabolically activated by scavenging ROS[87].

Spermatogenic activity

Research on *O. ficus-indica* cladode, that is abundant in several chemicals possessing anti-oxidant properties, has demonstrated its favourable impact on the disintegration of sperm DNA following the cryopreservation of human semen[88]. Another study looked at how lipid peroxidation, DNA breakage, and ram semen properties affected liquid storage in trios egg yolk extenders (TEY) and skim milk (SM) at 5°C for up to 72 hours. This study assessed the cladodes of *O. ficus-indica* acetone extract. While SM had higher levels of anomalies, spontaneous lipid peroxidation, progressive motility, and membrane integrity, TEY had better levels of total sperm motility and viability ($p<0.05$). The findings also showed that, in comparison to the control group, adding 1% the cladodes of *O. ficus-indica* acetone extract to the SM or TEY extender improved membrane integrity, viability, and motility of sperm while lowering abnormalities and lipid peroxidation up to 72 hours in storage. Similarly, 1% ACTEX can really decrease the hindering impacts of fluid stockpiling on sperm DNA discontinuity even following 72 hours of capacity ($p<0.05$). To summarize, slam semen quality can be raised by enhancing SM and TEY with 1% ACTEX[89]. In a study premeditated to estimate the impact of *O. ficus-indica* ethanolic extract on rats' testicular injury caused by methotrexate (MTX), a chemotherapeutic drug used to treat inflammatory illnesses and a number of cancers. It has a number of negative effects, particularly on rapidly dividing and growing cells. The gonad histology and oxidative stress of rats were protected against by cladodes extract, which also improved the sperm boundaries (count and motility) and serum testosterone levels. The discoveries revealed that *O. ficus-indica* cladodes extract significantly increased fertility in mice and ameliorated MTX-induced testicular damage[90].

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. ficus-indica* nopalitos treats endothelial dysfunction and lowers serum uric acid levels[91].

Nephroprotective activity

Metal-induced toxicity is among of the conditions that *O. ficus-indica* is used to treat. The study demonstrated by Saad *et al*.,[35] has demonstrated how *O. ficus-indica* shields rats against the toxicity caused by lithium carbonate. Male Wistar rats were given a single dosage for 30 days; take 25 mg/kg b.w. of lithium carbonate twice a day in order to cause nephrotoxicity. Over the course of 60 days, *O. ficus-indica* 100 mg/kg b.w. aqueous extract was gavaged. By lowering the degree of intensity of peroxidation of lipids and raising the kidneys from lithium carbonate-induced oxidative stress, *O. ficus-indica* extract treatment seemed to offer protection against the activities of both enzymatic and

nonenzymatic antioxidants, according to the study's findings. The increased concentration of antioxidant phytochemicals found in male rats and their characteristics were credited with providing this protection.

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[92], chemicals that are separated from fungus and microorganisms[93], and compounds that have been extracted from plants[94,95].

An intriguing investigation by Ahn *et al.*,[96] shown that *O. ficus-indica* extract has a significant immune-modulatory impact, supporting its value as a treatment for immune-related disorders. It also improves immunity by managing both the inflammatory response and its proponents.

Side effects and toxicology of *O. ficus-indica*

Kleiner *et al.*,[97] 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[97,98,99]. 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[99]. 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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AUTHOR'S CONTRIBUTION

Ahmed FA: leadership and oversight of the design and implementation of the research activity. **El-Azab MM:** data collection, writing: preparing the first draft. **Ibrahim MA:** visualization and research. **Fahmy WGE,** and **Fahmy DM:** reviewing and modifying. Every author gave their approval to the manuscript's final draft.

DATA AVAILABILITY

Data will be made available on request.

CONFLICT OF INTEREST

None to declare.

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