

Review

Exploring the Potential Hepatoprotective Properties of Cactus (Cactaceae) in Liver Health and Disease Management: A Brief Review

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Abstract: Cacti are renowned for their resilience in arid environments and have been utilized as a valuable food source in various cultures for centuries. The potential effects of cactus (Cactaceae) consumption on liver health have garnered significant scientific interest in recent years. This review aimed to consolidate and analyze existing research findings regarding the relationship between cactus-derived compounds and their influence on liver function and health. Various cactus species, particularly *Opuntia* spp., are rich reservoirs of antioxidants, polyphenols, flavonoids, and betalains. In vitro and in vivo studies with animal models have shown that bioactive constituents of cactus exhibit anti-inflammatory, antioxidative, and antifibrotic properties, which potentially mitigate liver damage induced by oxidative stress, inflammation, and hepatotoxic agents. Understanding their mechanisms of action and conducting rigorous clinical studies with administration of cactus will ascertain their role in preventing and treating liver ailments, offering novel avenues in nutrition, hepatology, and natural medicine.

Keywords: antioxidants; anti-inflammatory; bioactive compounds; hepatoprotective; hepatotoxic



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1. Introduction

The prevalence and incidence of liver diseases span a spectrum from metabolic dysfunction-associated steatotic liver disease (MASLD) to cirrhosis and hepatocellular carcinoma, and continues to increase, posing substantial public health challenges worldwide [1]. The search for prevention strategies and alternative therapeutics has led researchers to explore the inclusion of foods and medicines derived from plant sources due to their perceived efficacy and safety profiles [2].

Among these natural sources, the Cactaceae family, particularly various cactus species, has gained attention for its diverse array of bioactive compounds and potential therapeutic implications in liver health and disease management [3].

Cacti belong to the Cactaceae family and encompass a diverse group of succulent plants adapted to arid and semi-arid regions worldwide. Beyond their ornamental value,

several cacti species have served as a staple food source for indigenous communities in regions such as Mexico, southwestern United States, and parts of Africa and South America. The nutritional richness and adaptability of cacti make them an important subject to explore in the context of sustainable food production and in traditional medicine [4].

The focus on cacti and their derivatives in liver health research stems from their observed bioactive compounds, including polyphenols, flavonoids, betalains, and polysaccharides, which have shown promise in various physiological systems [5].

Studies investigating the hepatoprotective properties of cactus extracts have unveiled their potential in mitigating liver injury induced by diverse etiological factors, including oxidative stress, inflammation, and hepatotoxic agents [6]. Nopal (*Opuntia* spp.) is one of the most studied cacti due to its wide distribution in several countries and to its importance as a rich source of bioactive constituents. Both the fruits and the stem (pads or cladodes) are edible, being part of several culinary preparations and as ingredients in processed foods [7]. However, studies evaluating the effects of other cacti on health and liver diseases are still scarce.

Previous investigations have demonstrated the ability of cactus-derived compounds to modulate hepatic enzymes, bolster antioxidant defenses, and attenuate lipid peroxidation, thereby alleviating liver damage and fostering hepatocellular regeneration [8]. Moreover, the mechanisms underlying these hepatoprotective effects involve regulating key signaling pathways implicated in inflammation, apoptosis, and fibrosis within the liver microenvironment [9]. Nonetheless, while these preliminary findings in animal and cell culture models present promising avenues, the translation of cactus-based therapies into clinical practice necessitates rigorous evaluation through well-designed human trials [10]. Challenges pertaining to standardizing cactus extracts, determining the optimal dosing regimens, and long-term safety profiles warrant meticulous investigation to validate their efficacy and safety in human populations [11].

This review aimed to consolidate and critically analyze the current body of evidence elucidating the potential of cactus-derived bioactive compounds in promoting liver health and mitigating liver diseases. By synthesizing the findings from studies, this exploration intended to provide insights into the therapeutic prospects of cacti in hepatology, fostering a comprehensive understanding of their role in the maintenance of liver health and disease management.

2. Search Strategy

A bibliographic search was performed to identify studies included in Embase, Pubmed, ScienceDirect, Scopus, and Web of Science, using different combinations of the following keywords: Cactus OR *cactaceae* OR *Acanthocalycium* OR *Acanthocereus* OR *Ariocarpus* OR *Arrojadoa* OR *Arthrocerus* OR *Astrophytum* OR *Austrocylindropuntia* OR *Aztekium* OR *Backebergia* OR *Blossfeldia* OR *Brasiliopuntia* OR *Cephalocereus* OR *Cereus* OR *Cipocereus* OR *Cleistocactus* OR *Coleocephalocereus* OR *Copiapoa* OR *Coryphantha* OR *Discocactus* OR *Echinocactus* OR *Echinopsis* OR *Efossus* OR *Epiphyllum* OR *Epithelantha* OR *Eriosyce* OR *Espostoa* OR *Espostoopsis* OR *Facheiroa* OR *Ferocactus* OR *Frailea* OR *Geohintonia* OR *Gymnocalycium* OR *Haageocereus* OR *Harrisia* OR *Hattoria* OR *Isolatocereus* OR *Lepismium* OR *Leuchtenbergia* OR *Leuenbergeria* OR *Lobivia* OR *Mammillaria* OR *Mammilloidya* OR *Matucana* OR *Melocactus* OR *Micranthocereus* OR *Myrtillocactus* OR *Neobuxbaumia* OR *Neomammillaria* OR *Neoporteria* OR *Neoraimondia* OR *Nopalea* OR *Obregonia* OR *Opuntia* OR *Oreocereus* OR *Oroya* OR *Pachycereus* OR *Parodia* OR *Pereskia* OR *Pereskiaopsis* OR *Pfeiffera* OR *Pilosocereus* OR *Polaskia* OR *Praecereus* OR *Pseudorhipsalis* OR *Quiabentia* OR *Rebutia* OR *Rhipsalis* OR *Schlumbergera* OR *Selenicereus* OR *Stenocactus* OR *Stenocereus* OR *Stephanocereus* OR *Stetsonia* OR *Strophocactus* OR *Tacinga* OR *Thelocactus* OR *Turbiniacarpus* OR *Uebelmannia* OR *Weingartia* OR *Xiquexique* AND steatosis OR liver damage OR hepatotoxic OR liver disease OR hepatoprotective OR liver function.

Original articles written in English which were published between 2003 and 2024 were included. In total, 83 studies which met the objectives of this review were selected after

screening the titles, abstracts, and full texts. The flowchart used for selection of the articles can be seen in Figure 1.

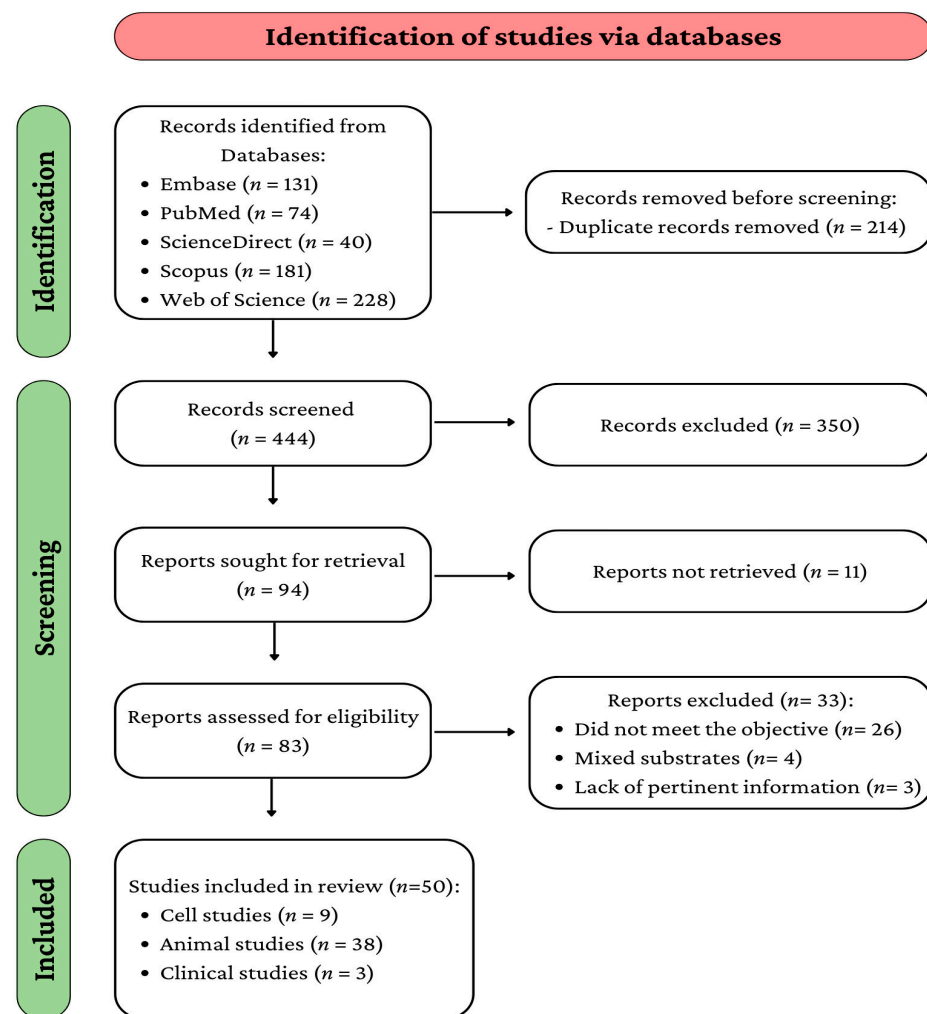


Figure 1. The PRISIMA 2020 flow diagram used to select the articles.

3. Nutritional Characteristics of the Cactus Family

The *Cactus* family has been studied as a promising sustainable food component, as they are very adaptable in adverse environmental situations, even resisting conditions with scarce water resources [4]. Cacti are also sources of bioactive compounds and provide potential beneficial health effects, including the maintenance of healthy liver function, since they have antioxidant and hepatoprotective properties [12]. Cacti generally contain a significant amount of dietary fiber, vitamins (including vitamin C, vitamin A, and vitamin B complex), minerals (such as calcium, magnesium, and potassium), natural pigments, terpenes, alkaloids, phenolic compounds, and antioxidants. Moreover, their low-calorie content and high water content contribute to their appeal as a healthy addition to diets [13].

The leaves, stems, flowers, fruit, exudate, and latex from different cacti species are used as herbal medicines for treating different disease conditions, and although *Opuntia* spp. is one of the most studied botanical genera of the Cactaceae family, there is limited information in the scientific literature about the nutritional composition and functionality of other cacti [13]. The *Opuntia* spp. cactus is widespread throughout the world and has good nutritional value. Both its cladodes and fruit (commonly known as prickly pear cactus) are considered edible and are generally eaten fresh. However, other food products have been developed due to their limited seasonality and short shelf-life, such as dried fruit, jams, beverages, teas, and nutraceuticals [4].

Furthermore, *Opuntia ficus-indica* has potential for application in various foods due to its chemical composition, mainly owing to its gelling and stabilizing properties, being nutritionally considered as an important source of dietary fiber, as well as containing ascorbic acid, vitamin E, carotenoids, amino acids, glucose, and fructose. In addition, prickly pear cacti have a high content of phenols (ferulic acid, feruloyl sucrose, and sinapoyl-diglucoside), betaxanthin, betacyanin, and flavonoids (isorhamnetin, kaempferol, quercetin, nicotiflorin, dihydroquercetin, penduletin, and lutein), which promote antioxidant action and hypolipidemic actions, and can prevent inflammatory diseases [14,15].

4. Effects of Cactus Consumption on Liver Function

The liver is an organ that plays a fundamental role in homeostasis and in maintaining various vital functions, such as fat and carbohydrate metabolism, bile excretion, regulation of the energy supply, and the ability to detoxify the body from endogenous and/or exogenous substances. However, these functions result in greater exposure and susceptibility to liver damage, considering that oxidative stress plays a crucial role in the etiopathogenesis of liver diseases [16,17]. In this context, including foods in the diet which can help maintain a healthy liver function is essential.

Opuntia spp. presents several mechanisms and benefits for liver function, with one of these benefits being its antioxidant action [18]. Cacti contain antioxidant compounds such as betanin, which play a crucial role in neutralizing free radicals, thereby reducing oxidative stress in the liver. Betanin, a betacyanin, has a chemical structure which gives it the ability to neutralize free radicals, which are the main compounds responsible for lipid peroxidation. This antioxidant capacity of betanin is notable, as it acts as an efficient reducer of peroxy radicals derived from unsaturated lipids present in biological membranes [19–21]. Furthermore, betanin acts as a scavenger of nitrogen dioxide, the radical initiator of the oxidative process of low-density lipoproteins (LDL) [12].

Another hepatoprotective effect found in this cactus is the ability to improve lipid metabolism [14]. *Opuntia* spp. influences the absorption of fats in the gastrointestinal tract due to its concentrations of soluble fiber and polyphenol. These components form complex fat molecules, which make their absorption by the small intestine difficult. As a result, a smaller amount of fat is absorbed by the body, which contributes to a reduction in blood lipid levels [22]. In addition to interfering with fat absorption, *Opuntia* spp. can also increase the excretion of lipids through the feces. This effect can be attributed to the properties of the fibers present in the cactus, which can bind to lipids and other compounds in the intestine, facilitating their elimination from the body [23].

Another point to consider is the protection against drug-induced damage [17]. These cacti have effects against damage induced by certain medications, such as paracetamol and carbon tetrachloride, in addition to the consumption of ethanol, which can be attributed to its antioxidant and anti-inflammatory properties [24–26]. Overall, *Opuntia* spp. is the most studied genus among the cacti when it comes to preserving liver health. Figure 2 summarizes the main effects of cacti on liver function.

4.1. In Vitro Studies

Some in vitro studies evaluated the effects of extracts obtained from *Opuntia* spp. in liver cells. In vitro studies with other cacti aiming to evaluate liver function have not yet been published. Flavonoids isolated from the ethanolic extract of *Opuntia ficus-indica* fruits were tested in the primary hepatocytes of rats exposed to ethanol at a concentration of 200 mM for 48 h. The results demonstrated that these flavonoids provided significant protection of the primary hepatocytes of rats exposed to ethanol, preserving the antioxidant properties of glutathione reductase [27].

EFFECTS OF CACTUS CONSUMPTION ON THE LIVER FUNCTION

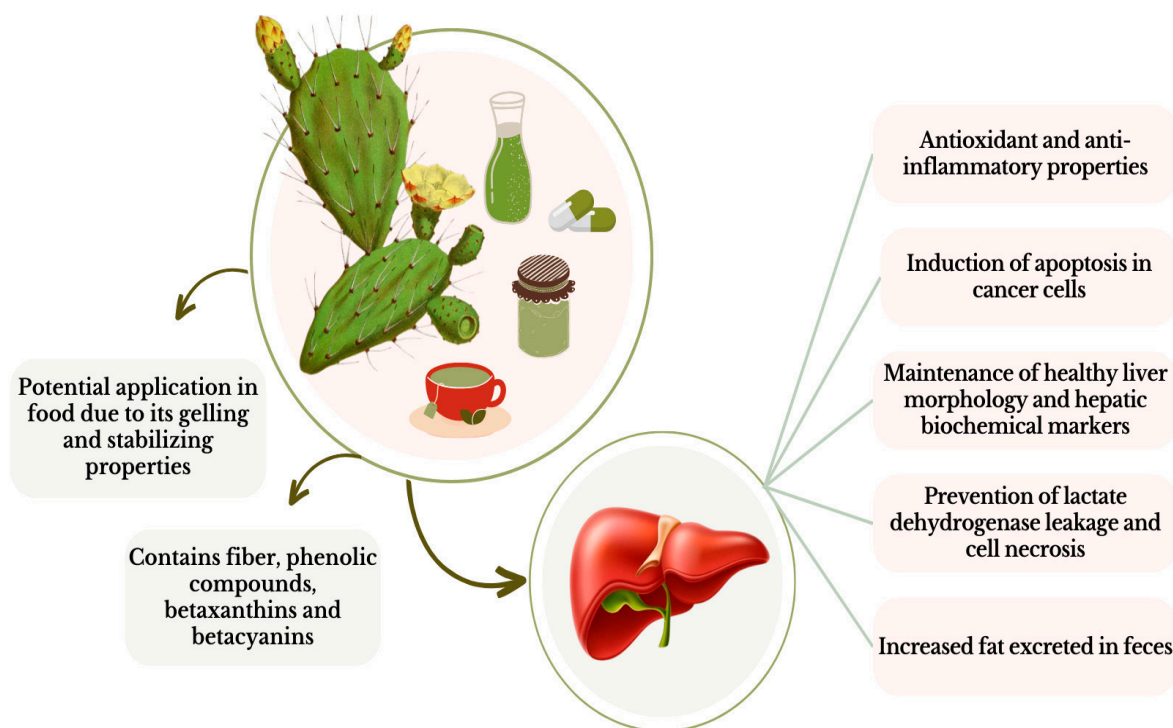


Figure 2. Summary of the effects of cactus consumption on liver function.

Another *in vitro* study evaluated the hepatoprotective activities of an aqueous extract of different parts of *Opuntia oligacantha* C.F. Först fruits, known as xoconostle, through establishing simulated gastrointestinal conditions. The aqueous extract had a high content of bioactive compounds (phenols, flavonoids, tannins, and betalains), and an anti-inflammatory effect was found due to its inhibitory effect on the enzyme elastase. This effect was considered to be hepatoprotective due to its ability to inhibit the enzymatic activity of B-glucuronidase. Xanthones are the main inhibitors of B-glucuronidase, which is used as an indicator of tumor-related and pathogenic activity in the liver. Therefore, the extract can be a preventive alternative against inflammation caused by liver diseases [28].

A previous study tested the hypothesis that an aqueous extract from *Opuntia ficus-indica* (L.) Mill cladodes can modulate the level of cholesterol transporters in liver cells. The extract decreased cholesterol uptake and levels of the efflux transporter proteins NPC1L1 and ABCG5/G8, and this result was also seen with the use of lipid-lowering drugs such as pravastatin. In addition, the extract decreased the level of ABCA1, the membrane cholesterol-transporter protein mediating the efflux of cholesterol to lipid-poor apolipoprotein (apoA1). Similar results were found for the drugs atorvastatin and simvastatin, which limit the availability of oxysterol ligands for liver X receptors (LXRs). These modifications may be related to a decrease in RNA transcription (protein expression), which may lead to a decrease in blood cholesterol levels following consumption of the aqueous extract from *Opuntia ficus-indica* (L.) Mill cladodes [29].

4.2. Animal Model Studies

Studies using rodents and fish as animal models were conducted to evaluate the effects of extracts from cladodes and fruits, floral decoctions, and compounds isolated from cacti on liver function. Most studies have evaluated the effects of cacti on liver function in terms of toxicity or antioxidant effects, especially for different species of *Opuntia* spp., *Pilosocereus gounellei* and *Pereskia grandifolia* (Table 1).

A previous study demonstrated that the oral administration of 3 mL of *Opuntia ficus-indica* (L.) fruit juice to adult rats, carried out 2 h after administration of carbon tetrachloride (CCl₄), for 9 consecutive days, resulted in protective and therapeutic effects against the damage induced by CCl₄. These effects included stabilization of hepatic transaminases, reduced apoptosis in epithelial cells, and preservation of the normal morphology of liver cells, as well as integrity of the central vein and portal triad, as evidenced by histopathological examinations [30].

Villa-Jaimes et al. [31] evaluated immunohistochemical analyses of the livers of adult rats pretreated with an aqueous extract of *Opuntia robusta* fruit (800 mg/kg) and the *Opuntia*-derived phytochemicals betanin (25 mg/kg) and N-acetylcysteine (50 mg/kg) for 5 days before inducing acute toxicity with diclofenac on the sixth day. The results of the immunohistochemical analysis revealed a significant increase in the number of active caspase-3-positive cells in the diclofenac-treated group compared with the control group. However, a similar number of cells that were positive for active caspase-3 was observed in the groups that received the prophylactic treatment with *Opuntia* fruit extract, betanin, and N-acetylcysteine compared with the control group. This increase in the number of caspase-3 positive cells suggested an increase in apoptotic cell death in the diclofenac toxicity model [31].

A study with healthy adult Wistar rats that received a floral decoction of *Opuntia microdasys* at a dose of 100 mg/kg/day or 200 mg/kg/day showed decreased body and liver weight, and ameliorated serum biochemical parameters such as glucose, aspartate aminotransferase (AST), alanine aminotransferase (ALT), gamma-glutamyl transferase (γ -GT) and the lipid profile, as well as oxidative stress biomarkers and oxidizing enzymes, with no differences among the groups. Furthermore, all livers showed a normal histoarchitecture, with the hepatic lobes showing a classic structure, regardless of the dose administered. The results also showed no signs of toxicity or mortality, demonstrating the safety of using these extracts [32].

The administration of *Opuntia robusta* and *Opuntia streptacantha* extracts (800 mg/kg/day) to healthy adult male Wistar rats did not show changes in hepatic plasma markers such as ALT, AST, and glutathione (GSH) or morphological changes, glycogen depletion, or necrosis. However, it prophylactically reduced leakage of lactate dehydrogenase and cell necrosis, suggesting that the extract could prevent acute liver failure [24]. Rats pretreated with furofuran lignans (50 μ M), a bioactive compound isolated from the seeds of *Opuntia ficus-indica*, for 2 h before exposure to ethanol (350 mM), demonstrated remarkable protection of the hepatocytes against alcohol-induced oxidative stress. This protection was manifested by a significant reduction in the levels of intracellular reactive oxygen species, preservation of antioxidant enzymes' activities, and maintenance of the glutathione content [25].

A study with fish conducted using dehydrated prickly pear fruit peels (*Opuntia ficus indica*) administered to tilapia (*Oreochromis niloticus*) weighing 21–25 g, at concentrations of 10% or 20% together with a commercial diet for 45 days, demonstrated a significant decline in AST and alkaline phosphatase (ALP) levels in fish fed diets with the addition of 20% of the peel. In addition to greater catalase enzyme activity, the level of superoxide dismutase (SOD) showed a significant improvement in both experimental groups and an improvement in the GSH level, with a decreased concentration of malondialdehyde (MDA). This was due to the prickly pear fruit peel being rich in phenolics, flavonoids, and polysaccharides, which are known for their ability to promote the formation and excretion of detoxifying metabolites, which gives them liver-protective activity and antioxidant activity. This action is highly correlated with the number of phenolic constituents, as they are good electron donors and can eliminate the chain reaction of free radicals, making them stable. Furthermore, prickly pear fruit peel (*Opuntia ficus indica*) also promoted improvements in the innate immune response through an increase in the activities of lysozyme, myeloperoxidase, and nitric oxide, which led to the induction of lysis of bacterial cell walls, thereby indicating immunostimulant potential [33].

Ora-pro-nobis (*Pereskia grandifolia*) extract was evaluated for toxicity via oral administration in adult male Wistar rats. These rats received extracts at doses of 30, 100, and 300 mg/kg for 3 weeks. It was reported that there were no significant changes in behavior, body weight, eating patterns, injuries, or abnormalities in organs including the liver and biochemical parameters in the blood, indicating that the plant did not cause immediate adverse effects in the rats [34]. Another study evaluated the acute toxicity of a dry ethanolic extract of Ora-pro-nobis (*Pereskia aculeata*), which was administered to female Wistar rats at doses of 1250 mg, 2500 mg, and 5000 mg/kg. This acute toxicity study showed no difference among groups in either the clinical evaluation or the histopathological analysis [35].

Regarding possible toxic effects from the consumption of cactus, a toxicity study of a saline extract of xique-xique (*Pilosocereus gounellei*) was carried out on healthy male and female mice. The mice were divided into groups with daily doses of 250, 500, or 1000 mg/kg or distilled water orally for 28 consecutive days. The groups that received the extract at doses of 250 and 500 mg/kg did not show behavioral changes; however, the group treated with 1000 mg/kg showed irritability and increased motility only 15 to 30 min after administration; after this period, they no longer demonstrated symptoms. Lymphocytic infiltrates were also observed around the bile duct and close to the centrilobular vein in the liver, showing parenchymal infiltration with thickening of the interalveolar septa in the lungs and activation of the lymph nodes in the spleen in the group that consumed 1000 mg/kg. However, total cholesterol and triglyceride levels significantly decreased in male and female mice receiving doses of 500 and 1000 mg/kg [36]. Even with the changes described in this study, the authors concluded by explaining that the extract was not associated with significant toxic effects and highlighted that the extract presented antipyretic activity, and hypoglycemic and hypolipidemic effects. Nevertheless, it is clear that the dose of 500 mg/kg was sufficient to produce positive effects without any behavioral, biochemical, or histological changes. However, further studies are still needed to verify the physiological mechanisms behind these changes at the highest dose.

Table 1. Studies of the effects of cacti on liver functions evaluated in animal models.

Study Design	Product	Dose/Administration Period	Mechanism/Repercussion	Reference
Adult Wistar rats	<i>Opuntia robusta</i> and <i>Opuntia streptacantha</i> extracts	800 mg/kg/day	Reduction in the AST and ALT enzymes	[24]
	Furofuran lignans isolated from the seeds of <i>Opuntia ficus-indica</i>	50 µM for a single dose	Reduction in the levels of intracellular reactive oxygen species, preservation of the activities of antioxidant enzymes, and the maintenance of GSH content	[25]
	<i>Opuntia ficus indica</i> (L.) fruit juice	3 mL/rat for 9 days	Stabilization of hepatic transaminases, reduced apoptosis in epithelial cells, and preservation of the normal morphology of liver cells	[30]
	<i>Opuntia microdasys</i> , floral decoction	100 mg/kg/day or 200 mg/kg/day	Reduction in the enzymes AST and ALT	[32]
	<i>Pereskia aculeata</i> , ethanolic extract	1250, 2500 or 5000 mg/kg in a single dose	It showed no toxicity	[35]

Table 1. Cont.

Study Design	Product	Dose/Administration Period	Mechanism/Repercussion	Reference
Tilapia fish (<i>Oreochromis niloticus</i>)	Prickly pear fruit (<i>Opuntia ficus indica</i>) Peel	100 g or 200 g of prickly pear fruit peel for 45 days	Decline in AST and ALP with 220 g; greater activity of the enzyme CAT, and higher SOD and GSH levels; a decrease in MDA	[33]
Adult Wistar rats	<i>Pereskia grandifolia</i> extract	30, 100, and 300 mg/kg for 3 weeks	It showed no toxicity; normal patterns of biochemical and histological parameters	[34]
	<i>Opuntia robusta</i> phytochemicals: betanin and N-acetylcysteine	800 mg/kg, 25 mg/kg, and 50 mg/kg	The number of cells positive for active caspase-3 was similar to the control group	[31]
Adult Swiss mice	<i>Pilosocereus gounellei</i> , saline extract	250, 500, or 1000 mg/kg for 4 weeks	There was a reversible behavioral change only at the highest dose; presence of proteins in the urine and lymphocytic infiltrates in the liver, lungs, and spleen; decreases in total cholesterol and triglycerides at doses of 500 and 1000 mg/kg.	[36]

Abbreviations: ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; CAT, catalase; GSH, glutathione; SOD, superoxide dismutase; MDA, malondialdehyde.

4.3. Clinical Studies

No clinical trials have been conducted with cacti that have focused on preserving liver function in healthy humans to date. On the other hand, some clinical studies have addressed the effects of *Pereskia aculeata* flour (400 g/6 months) on improving intestinal health [37]; the beneficial effects of ingesting cladodes and fruit-skin extract capsules from *Opuntia ficus-indica* (1 g/1 h) at rest and after resistance exercise in healthy men [38]; and the effects of fresh fruit pulp from *Opuntia ficus-indica* (250 g/6 weeks) and cooked nopal (300g/3 days) on the body's redox balance and antioxidant activity in healthy humans [39,40].

A randomized, double-blind study with healthy volunteers who had a diet standardized to 35% fat and consumed *Opuntia ficus-indica* fiber tablets (500 mg) for 45 days over a short period demonstrated a significant increase in the amount of fat excreted in the feces, indicating a notable lipid-lowering effect, which led to lower energy intake and can gradually promote weight loss [15].

A randomized cross-over study with two periods (2 weeks/period) of controlled feeding was carried out on 28 healthy volunteers (men and women) with an average age of 39 years and a BMI of 23 kg/m², and showed that *Opuntia ficus-indica* fruit (200 g/twice a day) intake modulated plasma inflammatory biomarkers such as tumor necrosis factor- α (TNF- α), interleukin (IL)-1 β , interferon- γ (INF- γ), IL-8, C-reactive protein (CRP), and the erythrocyte sedimentation rate (ESR), while increasing the anti-inflammatory marker IL-10 and increased dermal carotenoids, which are a biomarker of the body's antioxidant status [41].

5. Effects of Cactus Consumption on Liver Diseases

Some diseases can affect the liver, with alcoholic liver disease (ALD) and metabolic dysfunction-associated steatotic liver disease (MASLD) particularly standing out [42]. The development of ALD is complex and is closely linked to the amount and duration of the individual's alcohol consumption [43]. This disease progresses from alcoholic steatosis, passing through alcoholic hepatitis to alcoholic cirrhosis, an irreversible injury [44].

On the other hand, diseases such as metabolic syndrome, obesity, and diabetes can also promote the accumulation of excessive fat in the liver due to insulin resistance that decreases the efficacy of this hormone to control blood glucose, which results in hyperglycemia and the subsequent accumulation of fat in the liver [45,46]. Furthermore, both obesity and diabetes can induce a state of chronic inflammation and changes in liver enzyme levels, contributing to the development of MASLD [47]. In turn, dyslipidemia is characterized by abnormal levels of lipids in the blood, such as high cholesterol and triglycerides, and has a significant relationship with liver diseases due to the central role of the liver in lipid metabolism [48]. Dyslipidemia can also accelerate the progression of hepatic steatosis to more advanced stages, such as MASLD. This more severe phase involves inflammation and damage to liver cells that can progress to fibrosis and, in severe cases, to cirrhosis [49]. In this context, the search for low-cost non-drug adjuvant treatments which have effects on preventing or limiting the progress of liver diseases has been a concern, with the aim of minimizing hospital expenses and offering a better quality of life for patients.

Studies have shown the hepatoprotective effect of several types of cacti such as *Opuntia* spp., *Pilosocereus gounellei*, and *Pereskia grandifolia* [12,17,24,50]. This hepatoprotective effect has been attributed to the fiber, vitamins, minerals and bioactive compounds, such as betalains, carotenoids, ascorbic acid, flavonoids, and other phenolic compounds, that cacti have in their composition [17]. These functional components have potential anti-inflammatory, antihyperlipidemic, antihyperglycemic, and antiviral activity, which protect and preserve the structure and functionality of the liver [13,51]. In the following subsections, we discuss *in vitro* and *in vivo* studies that have evaluated the potential effects of cacti on liver diseases.

5.1. *In Vitro* Studies

In vitro studies have been conducted with extracts obtained from cladodes, leaves, or fruits from *Pereskia grandifolia*, *Hylocereus undatus*, and several species of *Opuntia* spp. using cell carcinoma models or the administration of chemical substances to induce damage to liver cells. Most studies have investigated the effects of these cacti on cell apoptosis and markers of oxidative stress and inflammation.

One study evaluated the antigenotoxic effects of a hydroalcoholic extract of young cladodes of *Opuntia ficus-indica*. A DNA fragmentation analysis of extracts from the liver of mice with oxidative damage induced by the mycotoxin zearalenone was carried out. The doses administered to the animals were 25, 50, and 100 mg/kg. The results of this study demonstrated that the dose of 100 mg/kg was able to prevent fragmentation of DNA in the liver of mice, demonstrating a protective effect against genotoxicity caused by mycotoxin zearalenone [52].

The potential hepatoprotective effect of a fruit extract from the species *Opuntia robusta* and *Opuntia streptacantha* against acute damage to the hepatocytes induced by diclofenac was evaluated. The results demonstrated a protective effect in liver cells by preventing an increase in the activity of caspase-3, reducing the mitochondrial production of reactive oxygen species (ROS), reducing the expression of the P53 gene and preventing necrosis of the hepatocytes [53].

A previous study demonstrated that doses of 40 and 80 µg/mL of a hydroalcoholic extract of *Opuntia dillenii* fruits attenuated hepatotoxicity in a hepatoblastoma (HepG2) cell line, evidenced by increased cell viability, reduced MDA levels, increased GSH levels, and decreased TNF-α concentrations [54]. An *in vitro* study using an ethanolic extract of *Opuntia monacantha* evaluated its anticancer potential against the human hepatoblastoma

(HepG2) cell line, first using the trypan blue method, which served to detect dead cells, and showed an increased tendency of dead cells in the *Opuntia* extract compared with untreated cells. These results suggest disruption of the cell membrane of liver cancer cells. In addition, the treated cells released a high level of lactate dehydrogenase compared with the untreated cells, demonstrating apoptosis as an effective preventative strategy against hepatocellular carcinoma. Furthermore, antioxidative potential via GSH, SOD, and CAT was demonstrated in cancer induced groups [55].

Peels of white-fleshed pitaya fruits (*Hylocereus undatus*) and the peels of prickly pear (*Opuntia ficus-indica*) were used to extract betacyanins with pressurizing hot water to evaluate the inhibition of steatohepatitis induced by oleic acid under simulated conditions. Next, the triglyceride level in HepG2 cells was analyzed to compare the preventive effect of each extract. At concentrations of 60 and 100 µg/mL, prickly pear (*Opuntia ficus-indica*) peel was able to significantly alleviate an overaccumulation of triglycerides in HepG2 cells. However, pitaya peels did not exhibit an inhibitory effect on the accumulation of triglycerides. Prickly pear peels suppressed the release of ALT and AST at medium and high concentrations, as well as significantly increasing the expression of carnitine palmitoyltransferase 1 (CPT1A1), which explained its antisteatotic activities through increased mitochondrial β-oxidation of fatty acids [56].

Evidence also demonstrated the hepatoprotective effects produced by ora-pro-nobis (*Pereskia grandifolia*) leaf extract. The extract showed anti-inflammatory activity, promoted by the inhibition of the phagocytosis process and dissemination of cellular macrophages. The extract also showed anticarcinogenic activity, demonstrated by the significant cytotoxic effect of *P. grandifolia* on HUH7 hepatocellular carcinoma cells, demonstrating the absence of toxicity and selective inhibition of hepatic cancer cells, inhibiting their growth and viability [34]. Table 2 summarizes the characteristics of in vitro studies and the main mechanisms and effects promoted by cacti on liver diseases.

Table 2. In vitro studies of the effects of cactus on liver diseases.

Study design	Species/product	Dose	Mechanism	Reference
Macrophage cells; Hepatocellular carcinoma HUH7 cells	<i>Pereskia grandifolia</i> leaf, aqueous extract	100, 200, 400, 800, and 1600 µg/mL concentrations	Reduction in inflammatory processes; inhibition of hepatocellular carcinoma cells' growth or viability	[34]
Diclofenac-induced damage in hepatocytes	Fruit juice extracts from <i>Opuntia robusta</i> and <i>Opuntia streptacantha</i>	125 µL/mL	Reduction of oxidative stress; prevention of cell necrosis	[53]
Acetate-induced hepatotoxicity in HepG2 cell line	<i>Opuntia dillenii</i> fruit, hydroalcoholic extract	20–80 µg/mL concentrations	Reduction in oxidative stress and inflammatory processes	[54]
Human hepatoblastoma (HepG2)	<i>Opuntia monacantha</i> , ethanolic extract	0.25, 0.5, 1, 2, or 3 mg/mL	Reduction in oxidative stress; apoptosis of cancer cells	[55]
Inhibition of oleic acid-induced steatohepatitis	Peels of white-fleshed pitaya fruits (<i>Hylocereus undatus</i>) and freeze-dried prickly pear peels (<i>Opuntia ficus-indica</i>)	60 and 100 µg/mL	Prickly pear peels suppressed the release of ALT and AST and increased carnitine palmitoyltransferase 1, increasing mitochondrial β-oxidation of fatty acids	[56]
DNA from liver extracts of mice with oxidative damage induced by the mycotoxin zearalenone	Hydroalcoholic extract of cladodes of <i>Opuntia ficus-indica</i>	25, 50, and 100 mg/kg	Prevention of DNA fragmentation in the liver	

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase.

The main in vitro activities of cacti on the liver diseases are antioxidant, anti-inflammatory, anticarcinogenic, and antisteatotic effects, and prevent the apoptosis of hepatocytes. In vivo studies carried out with model animals have reinforced these potential activities of cacti in liver tissue.

5.2. Animal Model Studies

Cactus compounds such as betalains and phenolic acids generally demonstrate potent antioxidant activity, scavenging free radicals and mitigating oxidative stress in liver tissues. These antioxidants have been linked to reduced hepatocyte damage and improved markers of liver function in experimental models [7]. Studies have indicated that certain cactus-derived compounds possess anti-inflammatory properties that attenuate liver inflammation and injury. These compounds modulate proinflammatory cytokines and pathways, potentially mitigating the hepatic inflammation associated with various liver diseases [6]. In turn, preclinical investigations have suggested that cactus extracts or isolated compounds exhibit hepatoprotective effects against toxic insults, including chemical-induced hepatotoxicity. These compounds may enhance regeneration of the liver, inhibit fibrosis, and promote detoxification mechanisms [57].

Obese male Zucker rats (7 weeks old) were subjected to an experimental diet formulated to provide 4% dehydrated nopal (*Opuntia ficus-indica*) for a period of 7 weeks. In the group treated with the addition of dehydrated nopal to the diet, there was a reduction in the content of lipid droplets in the liver, a lower concentration of hepatic triglycerides, and a reduction in the serum ALT, AST, and hepatic MDA concentrations compared with the obese group. One of the mechanisms underlying these results was an elevation in the serum concentration of adiponectin, an anti-inflammatory adipocytokine that limits the accumulation of hepatic fat through activation of the peroxisome proliferator (PPAR α). Furthermore, an improvement in hepatic insulin signaling was observed, accompanied by better signaling mediated via insulin receptor substrate 1 (IRS-1) and kinase-mediated insulin (AKT) signaling, which could explain the reduction in hepatic steatosis [58].

Another preclinical study showed that an aqueous extract of *Opuntia ficus-indica* cladodes protected against liver damage caused by the pesticide chlorpyrifos. This study used 36 male Swiss mice (5–6 weeks old) and lasted 48 h. The groups that used only chlorpyrifos (10 mg/kg and 150 mg/kg) showed significant changes in all the liver parameters studied and death in some animals at a dose of 150 mg/kg. The groups that used chlorpyrifos combined with the cactus extract (10 mg/kg chlorpyrifos + 100 mg/kg cactus and 150 mg/kg chlorpyrifos + 1.5 g/kg cactus) had a reduction in the parameters studied (AST, ALT, ALP, lactate dehydrogenase, cholesterol, and serum albumin). On the other hand, nopal alone (1.5 g/kg of cactus) did not affect the parameters studied compared with the control. Although this study did not present other data or the exact mechanism of action, the extract of *Opuntia ficus-indica* stems protected the liver and reduced toxicity induced by the pesticide chlorpyrifos [59].

An additional study evaluated the impact of different doses of *Opuntia ficus-indica* fruit juice (20 and 40 mL/kg) in rodents with ethanol-induced steatosis. The results showed that ethanol caused changes in the levels of AST, ALT, ALP, LDH, and gamma-glutamyl transferase (GGT); increased the oxidation of lipids and proteins, reduced glutathione (GSH), and altered the enzymes superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx). The administration of *Opuntia ficus-indica* fruit juice was able to attenuate the hepatotoxic effects caused by ethanol. Doses of 20 mL and 40 mL regulated hepatic biochemical markers, significantly reduced the oxidation of lipids and proteins in the liver, and repaired liver tissue injuries, including the minimization of fatty vacuoles produced by ethanol. These results may have been due to the ability of *Opuntia ficus-indica* fruit to reduce free radical chain reactions or increase endogenous antioxidant activities [60]; however, the exact mechanisms of how this effect occurs have not yet been explored.

Another study evaluated the effect of orally administering 250, 500, and 1000 mg/kg of *Opuntia ficus-indica* fruit seeds in the last 4 weeks of 10 weeks of feeding a high-fat diet in rats. The study showed that the treatment promoted a significant reduction in hepatic lipid content and reduced the cell damage which had been induced and increased by the high fat diet. It was also able to reduce the expression of the inflammatory markers Toll-like receptor 4, nuclear factor κ B (NF- κ B), TNF- α , interleukin 6 (IL-6), and interferon β . Furthermore, it prevented the accumulation of intrahepatic lipids, caused polarization of M2 macrophages, and promoted the suppression of the inflammatory pathway mediated by Toll-like receptors 4 [61].

The effect of administering dehydrated cladodes of *Opuntia ficus-indica* on biochemical and metabolic parameters of rats with obesity induced by a high-fat/sucrose diet was investigated. The rats were fed a high-fat diet with the addition of 5% sucrose to their drinking water for 7 months, after which they were fed the same diet with the addition of 5% nopal for 1 month. The results demonstrated that treatment with cladodes of nopal was able to reduce inflammation and the expression of genes for sterol regulatory element binding protein 1 (Srebp-1), fatty acid synthase (Fas), and acetyl CoA carboxylase (ACC), which are involved in the process of hepatic lipogenesis. Furthermore, consumption of nopal promoted a significant increase in the mRNA of the peroxisome proliferator-activated factor receptor (PPAR)- α , which is involved in the oxidation of fatty acids. The treatment reduced hepatic steatosis and the inflammatory process mediated by TNF- α [62].

A previous study evaluated the effects of an aqueous extract of *Opuntia ficus-indica* cladodes on rats with carbon tetrachloride-induced toxicity. Doses of 2 mL/kg or 5 mL/kg were administered for 15 days. The extract was able to promote a hepatoprotective effect, promoted by reduced hepatic enzyme activity of AST [63]. Hydroalcoholic extracts of young *Opuntia ficus-indica* cladodes were administered to Balb/C mice with oxidative damage induced by the mycotoxin zearalenone. Doses of 25, 50, and 100 mg/kg were administered within 24 h after administration of mycotoxin zearalenone. The results showed a reduction in MDA levels and a reduction in the enzyme activity of catalase in mice treated with the extracts. It was verified that the hydroalcoholic extracts from the lowest dose showed a total reduction in the oxidative damage induced by mycotoxin zearalenone for all markers tested, exerting a hepatoprotective effect [64]. These data corroborated a study carried out with vinegar made from *Opuntia ficus-indica* fruits. The vinegar was administered at a dose of 7 mg/kg for 11 months to rats fed a high-fat diet. The treated animals showed a reduction in levels of hepatic triglyceride and LDL-c, a reduction in AST and ALT enzymes, and increased SOD and hepatic GPx [65].

The effects of indicaxanthin, a plant pigment with biological properties obtained from *Opuntia ficus-indica* fruits, was evaluated in obese male rats. The rats received 0.4 mg/kg indicaxanthin for 4 weeks after 10 weeks on a high-fat diet. The observed effects were related to the attenuation of oxidative stress and hepatic inflammation through reductions in the concentrations of reactive oxygen and nitrogen species (RONS), malondialdehyde and nitric oxide (NO), in addition to lower expression of TNF- α , in the p-JNK, cyclooxygenase-2 (COX-2) and i-NOS protein in foci of inflamed livers [66].

Some preclinical studies that demonstrated the benefits against liver diseases of consuming these cactuses were conducted with the species *Opuntia dillenii*, more specifically with oil and polysaccharides extracted from this species. The oil was administered at a dose of 2 mL/kg for 14 days, 7 days before the first injection of CCl₄ and 7 days before the second. Treatment with *Opuntia dillenii* oil promoted considerable attenuation of elevated levels of AST, ALT, and ALP enzymes and reduced triglyceride concentrations and malondialdehyde levels in the liver [67].

Administration with an aqueous extract of polysaccharides (rhamnose, arabinose, galactose, glucose, and arabinuronic acid) from *Opuntia dillenii* in 10-week-old obese rats was carried out for 28 days. In this study, an increase in the activity of hepatic 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) reductase was observed in rats with hyperlipidemia; however, administration of the *Opuntia* compound by gavage at dosages of 200 mg/kg and 400 mg/kg resulted in significant inhibition of this enzyme's activity in rats with hyperlipidemia. On the basis of these results, the authors suggested that *Opuntia* may directly influence the endogenous biosynthesis of cholesterol, inhibiting the activity of hepatic HMG-CoA reductase, and consequently preventing fatty liver disease [68].

Another study with *Opuntia dillenii* polysaccharides (rhamnose, xylose, mannose, and glucose) revealed that treatment (200 mg/kg/day) for 4 weeks resulted in a significant decrease in MDA levels while also increasing the activity of SOD, CAT, and GPx in the livers of adult STZ-induced diabetic rats [69]. Similar results were observed by Zhao et al. [70], who also administered polysaccharides extracted from *Opuntia dillenii* to rats with diabetes induced by streptozotocin. Diabetic rats received this polysaccharide at doses of 50, 100, 200, and 400 mg/kg for 3 weeks, which also increased the activity of the hepatic SOD and GSH-Px enzymes and reduced the concentration of MDA, restoring these parameters to similar levels to those seen in the control group. These findings suggested that polysaccharides from *Opuntia dillenii* fruit have antioxidant properties, demonstrated by its ability to eliminate free radicals and reactivate the antioxidant defense system [69,70].

A polysaccharide obtained from *Opuntia dillenii* (Ker-Gaw) also exerted a hepatoprotective effect in mice with cadmium chloride-induced liver injury. Mice exposed to cadmium received a dose of 200 mg/kg of the polysaccharide for varying periods of time (7, 14, 21, 28, and 35 days), with evaluations of the liver index, biochemical and blood indicators, and pathological changes. Exposure to cadmium caused an increase in the levels of AST, ALT, and ALP and a reduction in hemoglobin, in addition to causing swelling and apoptosis of liver cells and infiltration of inflammatory cells. Administration of the polysaccharide demonstrated effective results against liver damage after 28 days, assessed by the reversal of changes caused in pathological indicators [71].

A study also showed the hepatoprotective effects of *Opuntia robusta* in rats with liver fibrosis induced by thioacetamide. Wistar rats received 800 mg/kg of aqueous extracts of *Opuntia robusta* fruit for 5 weeks. The results demonstrated a reduction in AST and ALT enzymes; a potential antioxidant effect, evidenced by an increase in GSH concentrations and a reduction in MDA levels; a decrease in damage to liver tissue; a reduction in fibrosis; and a cytoprotective effect at all stages of the process of fibrosis [12].

Fruit extract from *Opuntia robusta* and *Opuntia streptacantha* species also demonstrated a hepatoprotective effect against diclofenac-induced acute liver injury. The rats received pretreatment with daily doses of fruit extracts (800 mg/kg body weight) administered orally for 5 days before intoxication with diclofenac. The results demonstrated a protective effect against damage caused by diclofenac through reducing ALT and AST enzymes and preservation of the normal organizational patterns of the liver's parenchyma [53].

The benefits of cacti have also been observed in anticarcinogenic liver studies. *Opuntia ficus-indica* cladode juice, at a dose of 50 mg/kg body weight, was administered to adult male BalbC mice (20–25 g) subjected to liver damage by the genotoxin benzo(a)pyrene for 4 weeks. Treatment with the juice showed a reduction in the oxidative damage (MDA) induced by benzo(a)pyrene. This effect may have occurred through changes in the cell death pathway, a reduction in the modulation of p53 expression, and a reduction in the Bax/Bcl2 ratio [72]. Similar results were observed in a study of adult male BalbC mice (20–25 g) subjected to aflatoxin B1 (AFB1)-induced liver genotoxicity. Treatment with juice from *Opuntia ficus-indica* cladodes at a dose of 50 mg/kg body weight for 4 weeks achieved a reduction in MDA, an antigenotoxic effect shown by reducing the appearance of chromosomal aberrations and DNA fragmentation, and restriction of aflatoxin B1 damage by reducing the modulation of the expression of p53 and associated genes such as Bax and Bcl2 [73].

Antihepatotoxic and anticytotoxic effects have also been observed with the fruit of *Opuntia ficus-indica*. A study using male albino mice (25–30 g) with cyclophosphamide-induced hepatotoxicity used 2 mL/kg body weight of *Opuntia ficus indica* fruit juice for 10 days. The results showed that the nopal fruit restored serum levels of liver markers (AST, ALT, LDH), total protein and albumin, nucleic acids (DNA, RNA) of liver cells, and antioxidant markers (CAT, SOD, and MDA) [74].

The hepatoprotective effect of nopal cladodes on male mice (weighing 38–40 g) subjected to diarrhea caused by *Salmonella typhi* ATCC 19,430 was evaluated. The mice received cefixime (4 mg/kg body weight) and different concentrations of an aqueous extract of cladodes (250 mg/kg body weight, 500 mg/kg body weight, and 1000 mg/kg body weight). The extract at a dose of 1000 mg/kg body weight reduced the fecal load of *Salmonella typhi* ATCC 19,430 earlier and had a better result in attenuating liver damage. Hepatocellular damage was completely treated in all groups, and no histological changes were observed, except in the case of the negative control group. The levels of ALP, ALT, and AST were altered only in the untreated group. The exact mechanism of the hepatoprotective effect has not yet been clarified and is not exactly known [75].

Opuntia ficus-indica fruit seed oil showed hepatoprotective effects on lipopolysaccharide (LPS)-induced inflammation in the liver. Male C57BL/6 J mice (12–16 weeks old) infected with 100 µg LPS from *Escherichia coli* O111:B4 via tail injection were fed a standard diet with the addition of 6% nopal fruit oil for 28 days. The addition of oil mainly attenuated the hepatic expression of Il-1b and Il-6. Regarding peroxisomal antioxidant functions, the treatment prevented LPS-induced catalase activity. Pretreatment with the oil prevented the Acox1 gene associated with LPS and decreased its activity in the liver, showing efficient hepatoprotective effects against LPS, restoring hepatic peroxisomal β-oxidative and antioxidant capabilities. [76].

A study using chloroform or methanol extracts from *Opuntia monacantha* observed their hepatoprotective effect against paracetamol-induced liver damage in rabbits weighing 1.2–1.5 kg. The results showed that both extracts at 200, 400, and 600 mg/kg of body weight in the 1-week protocol showed significant hepatoprotective activity, as they reduced ALT, AST, ALP, and total bilirubin levels; in addition, no histopathological changes were observed in the liver tissue. The authors associated these results with the presence of polyphenols, flavonoids, alkaloids, tannins, saponins, and polysaccharides, without detailing the possible mechanisms of action of these constituents [77].

A study carried out with rat models fed a high-fat diet demonstrated that the addition of 39.8%, 41.2%, and 42.8% of diet with the addition of *Opuntia atropes* cladodes and *Opuntia joconostle* fruit flour was able to promote a decrease of 8.0% in the Lee index, as well as a total lipid and triacylglycerol content in the liver of 36.5–41.4% and 54.9–73.1%, respectively [78]. Héliès-Toussaint et al. [79] observed that administration of 0.5% *Opuntia Streptacantha* flour to obese rats over a period of 60 days had an effect against fatty liver in these animals.

In addition to studies investigating the potential of the *Opuntia* genus, research has also described the effects of xique-xique (*Pilosocereus gounellei*) on parameters of liver function in obese rats. The study investigated orally administration of 125, 250, or 500 mg/kg of a saline extract from xique-xique stems for 21 days after inducing obesity in rats by feeding them a high-fat diet for 10 weeks. The results indicated that treatment with the saline extract of *P. gounellei* promoted improvements in the concentrations of AST and ALT enzymes, mitigating the negative impact of obesity on the liver. Obese rats which received the treatment with the highest dose (500 mg/kg) showed similar lipid profile results, glucose levels, and insulin intolerance to rats in the control group. The rats treated with the extract also showed reduced ratios of the liver tissue index compared with untreated obese animals. Furthermore, there was a reduction in steatosis, inflammation, the deposition of and collagen in the liver tissue and an increase in superoxide dismutase concentrations in the liver [80].

Adult rats subjected to a diet rich in carbohydrates and fats were supplemented with 5% pitaya juice (*Hylocereus ocamponis*) in to their diet for 8 weeks. The high-carbohydrate and high-fat diet resulted in elevated levels of ALT, AST, and ALP in the plasma, indicative of liver dysfunction. Pitaya juice reduced the activities of ALP and ALT, while significantly increasing the activity of AST. These findings suggested that red pitaya juice attenuated liver damage caused by a diet high in carbohydrates and fats. The decrease in liver enzymes after the intervention probably reflects the reduction in fat deposition and the degree of necrosis in the liver cells. However, the increased level of AST may be attributed to myocardial damage, given that cardiac muscle is rich in aminotransferase enzymes, especially AST [81].

Furthermore, a study evaluated the effects of administering a hydroalcoholic extract from the fruit of pitaya (*Hylocereus polyrhizus*) on the oxidative and inflammatory parameters in mice with hepatic liver disease. Doses of 500 and 1000 mg/kg were administered for 11 weeks. The results indicated that animals treated with the extract showed considerable improvements in liver injury, accumulation of hepatic fat, and hepatic lipid metabolism, verified by the increased expression of AMPK and PPAR- α proteins and the reduced expression of SREBP. The extract was also able to inhibit the expression of CYP2E1 and Nrf2 proteins and reduce the concentrations of the inflammatory cytokine TNF- α and levels of IL-1 β in the liver [82].

The outcomes of administering betanin extracted from pitaya fruit (*Hylocereus ocamponis*) in non-alcoholic fatty liver disease were evaluated in 6-week-old male BALB/c mice fed a high-fat diet for 24 weeks. The treated group received 9.6 mg/day per animal of betanin diluted in purified water for 40 days. Betanin inhibited inflammatory infiltration of the liver and the necrosis of hepatocytes. All the mice developed hepatic steatosis; however, betanin produced a predominance of microvesicular steatosis in all the treated mice, and a decrease in the weight of epididymal fat. It was suggested that a reduction in the secretion of inflammatory cytokines by M1 Kupffer cells may be involved in the mechanism of the anti-inflammatory effect. In addition, the absence of necrotic hepatocytes found in mice treated with betanin was consistent with the lack of significant changes observed in the concentrations of liver and kidney markers, while the predominant presence of microvesicular steatosis suggested a joint reduction in the progression of hepatic steatosis, which may be associated with a possible decrease in the expression of TNF- α and a reduction in the generation of reactive oxygen species by inflammatory cells [83].

A previous study evaluated the effects of an ethanolic extract of ora-pro-nobis (*Pereskia grandifolia*) leaves on the liver parameters of rats. The MALFD model was implemented, in which diabetes was induced in rats that were subsequently fed a high-fat diet and exposed to cigarette smoke for a period of 4 weeks. The rats then received oral doses of the *P. grandifolia* extract (30, 100 and 300 mg/kg) or insulin in the final 2 weeks, in addition to simvastatin. The results demonstrated that the extracts reversed the increase in AST and ALT enzymes, as well as the changes in the lipid profile, oxidative stress, and liver damage caused by MAFLD [34].

The effect of white fruit juice from the *Hylocereus undatus* cactus against hepatic steatosis was evaluated in young male C57BL/6J mice with obesity induced by a high-fat diet. In this study, the treated mice were given water and the juice of the cactus fruit on demand for 14 weeks. The results showed that consumption of *Hylocereus undatus* fruit juice reduced hepatic steatosis and adipose hypertrophy. Analysis of hepatic gene expression indicated that the juice altered the expression profile of genes involved in lipid and cholesterol metabolism (Srebp1, HMGCoR, Cpt1b, HL, Insig1, and Insig2) and significantly increased the expression levels of FGF21-related genes (Klb, FGFR2, Egr1, and cFos) [84]. A similar study analyzed the effect of betacyanins from the red fruit of the *Hylocereus undatus* cactus. Four-week-old male C57BL/6J mice with obesity induced by a high-fat diet were given 200 mg/kg/day of isolated betacyanin by oral gavage for 14 weeks. Betacyanin attenuated hepatic steatosis concomitantly with lower levels of hepatic triglycerides and total cholesterol. Histological analysis revealed that the treatment minimized the increased cell size of both white and brown adipocytes, suggesting the effect

of reducing adipose hypertrophy. Supplementation also induced a significant reduction in serum levels of IL-6, IL-1 β , and TNF- α and an increase in the level of IL-10 in the liver [85].

The effects of adding 5% and 10% of *P. grandifolia* flour to the total energy in a high-calorie diet provided to rats for 4 weeks were also evaluated. Animals that received a diet supplemented with *P. grandifolia* flour showed a reduction in the weight of the liver and a reduction in lipid droplets in the cytoplasm of liver cells, characterizing a reduction in the degree of steatosis to mild [86].

A hepatoprotective effect was also observed for the cactus species *Pachycereus marginatus*. Female Balb/c mice aged 2 months with tumors induced by L5178Y-R/mL lymphoma cells were treated with vincristine or a methanol extract of *P. marginatus* at a fixed dose of 0.2 mL every 3 days, totaling seven doses. The drug vincristine reduced the tumors by 70% but caused liver damage as a side effect. Treatment with the methanol extract of *P. marginatus* reduced the tumors by 27%. Regarding liver function and tissue damage, no changes were observed in relation to the control. Serum levels of total bilirubin, ALT, AST, and alkaline phosphatase were not significantly altered. Histopathological examinations showed no liver damage; in the microscopic analyses, the livers of the control and extract-treated animals showed a normal parenchymal architecture, with no noticeable changes [87]. Table 3 summarizes the in vivo studies, and the main mechanisms and effects promoted by cacti in liver diseases.

Table 3. Studies of the effects of cactus on liver diseases, evaluated in animal models.

Study Design	Product	Dose/Administration Period	Mechanism/Repercussion	Reference
Rat model of thioacetamide-induced liver fibrosis	<i>Opuntia robusta</i> aqueous fruit extracts	800 mg/kg for 5 weeks	Reductions in AST and ALT enzymes; decreased oxidative stress; attenuation of the process of fibrosis	[12]
Rats with metabolic-associated fatty liver disease	<i>Pereskia grandifolia</i> , ethanolic leaf extract	30, 100, and 300 mg/kg for 2 weeks	Reductions in AST and ALT enzymes; decreased oxidative stress and liver injury	[34]
In vivo (adult male Wistar rats)	Fruit juice extracts from <i>Opuntia robusta</i> and <i>Opuntia streptacantha</i>	800 mg/kg body weight for 5 days	Reductions in AST and ALT enzymes; preservation of normal histologic patterns of the liver parenchyma	[53]
Obese male Zucker rats	Dehydrated nopal	4% of the diet	Elevation in the serum concentration of adiponectin and hepatic insulin signaling	[58]
Rodents with steatosis induced by ethanol	<i>Opuntia ficus-indica</i> fruit juice	20 and 40 mL/kg	Reductions in AST and ALT enzymes	[60]
In vivo (obese adult male Wistar rats)	<i>Opuntia ficus-indica</i> (OFI) fruit seeds	250, 500, and 1000 mg/kg for 4 weeks	Reductions in hepatic lipid content and the inflammatory process	[61]
In vivo (obese adult male Wistar rats)	Dehydrated <i>Opuntia ficus-indica</i> cladodes	High-fat diet with the addition of 5% dehydrated cladode nopal for 1 month	Decreased hepatic steatosis and inflammatory processes	[62]
Rats with carbon tetrachloride-induced poisoning	<i>Opuntia ficus-indica</i> , aqueous extract from the cladodes	2 mL/kg and 5 mL/kg for 15 days	Reduction in the enzyme activity of AST	[63]

Table 3. Cont.

Study Design	Product	Dose/Administration Period	Mechanism/Repercussion	Reference
Mice with oxidative damage induced by the mycotoxin zearalenone	Hydroalcoholic extract of cladodes of <i>Opuntia ficus-indica</i>	A single dose of 25, 50, and 100 mg/kg, administered 24 h before administration of ZEN	Total decrease in the oxidative damage induced by ZEN	[64]
Rat fed a high-fat diet	<i>Opuntia ficus-indica</i> fruit vinegars	7 mL/kg for 7 months	Reductions in hepatic triglyceride and LDL levels; reductions in AST and ALT enzymes; increased SOD and hepatic GPx	[65]
In vivo (obese adult male Wistar rats)	Indicaxanthin from <i>Opuntia ficus-indica</i>	0.4 mg/kg indicaxanthin for 4 weeks	Attenuation of oxidative stress and inflammation	[66]
Rat with CCl ₄ -induced liver damage	<i>Opuntia dillenii</i> seed oil	2 mL/kg for 1 week	Attenuation of elevated levels of AST, ALT, and ALP enzymes; reduction in MDA	[67]
Obese rats	Aqueous extract of polysaccharides (rhamnose, arabinose, galactose, glucose, and arabineuronic acid) from <i>Opuntia dillenii</i> Haw	200 mg/kg and 400 mg/kg	Inhibited activity of hepatic HMG-CoA reductase	[68]
Diabetic rats	Polysaccharides, comprising rhamnose, xylose, mannose, and glucose, from <i>Opuntia dillenii</i>	200 mg/kg/day	Resulted in a significant decrease in MDA levels, while increasing the activity of SOD, CAT, and GPx	[69]
Mice with streptozotocin (STZ)-induced diabetes	<i>Opuntia dillenii</i> polysaccharides	50, 100, 200, and 400 mg/kg for 3 weeks	Increased hepatic activity of SOD and GSH-Px; reduced MDA levels	[70]
Mice with liver injury induced by cadmium chloride	<i>Opuntia dillenii</i> polysaccharides	200 mg/kg for varying periods (7, 14, 21, 28, and 35 days)	Improvements in the reduction in AST and ALT enzymes; reduced the inflammatory process; inhibited apoptosis of the cells	[71]
Rabbits	<i>Opuntia monacantha</i>	Extracts at 200, 400, and 600 mg/kg for 1 week	Reductions in levels of ALT, AST, ALP, and total bilirubin and positive histopathological evaluations	[78]
Rat with obesity and non-alcoholic fatty liver disease	Diet supplemented with <i>Opuntia atropes</i> cladodes and <i>Opuntia joconostle</i> fruit flour	Diet supplemented with 39.8%, 41.2% and 42.8% of cactus flour for 12 weeks	Reduction in the Lee index, total lipid content, and triacylglycerols in the liver	[79]

Table 3. Cont.

Study Design	Product	Dose/Administration Period	Mechanism/Repercussion	Reference
In vivo (obese adult male rats)	<i>Pilosocereus gounellei</i> stem aqueous extract	125, 250, or 500 mg/kg for 21 days	Improvements in the alanine aminotransferase and aspartate aminotransferase enzymes; reduced steatosis, inflammation, and collagen deposition; increased superoxide dismutase	[83]
Adult rats, subjected to a diet rich in carbohydrates and fats	Pitaya juice	5% diet	Decrease in liver enzymes after the intervention, probably reflecting the reduction in fat deposition and the degree of necrosis in liver cells	[84]
Mice with alcoholic liver disease	<i>Hylocereus polyrhizus</i> peel extract	500 and 1000 mg/kg for 11 weeks	Improvement in liver injury from accumulation of hepatic fat and hepatic lipid metabolism; reductions in inflammatory markers	[85]
Rats subjected to a hypercaloric diet	<i>Pereskia grandifolia</i> leaf flour	Diet supplemented with 5% and 10% of the total food energy of <i>P. grandifolia</i> flour for 4 weeks	Reduction in liver weight; reduction in lipid droplets in the cytoplasm of liver cells; reduction in the degree of steatosis to mild.	[87]

Abbreviations: ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; MDA, malondialdehyde.

The main mechanisms of action proposed to explain the hepatoprotective effects of cactus in the cited studies were reduced lipogenesis associated with an increase in β -oxidation of fatty acids, reducing the supply of fatty acids for forming triglycerides [61,62]. Another finding in the studies was an association with improved insulin resistance, given that this is one of the causes of hepatic steatosis [62,83].

The data showed that there is scientific evidence to support the beneficial effects of cacti on liver disorders, especially *Opuntia* species. Clinical studies of interventions need to be carried out to confirm this evidence, as well as studies with other species of cacti. Figure 3 shows the potential mechanisms of action of the consumption of cactus in liver diseases and Table 4 shows a summary of the main potential hepatoprotective effects of cactus on health and disease in animal models, since they are the most commonly used models to evaluate such effects.

Table 4. Main potential hepatoprotective effects of cactus (Cactaceae) on health and disease in animal models.

Species/Product	Animal	Anti-Inflammatory	Antioxidant	ALT and AST Enzymes	Minimized Steatosis	Minimized Hepatotoxicity	Reference
<i>Opuntia robusta</i> aqueous fruit extracts	Male rats	+	+	+	–	–	[12]
<i>Opuntia robusta</i> and <i>Opuntia streptacantha</i> extracts	Adult male Wistar rats	–	–	–	–	+	[24]
<i>Opuntia ficus indica</i> seed	Male rats	+	+	–	–	–	[25]

Table 4. Cont.

Species/Product	Animal	Anti-Inflammatory	Antioxidant	ALT and AST Enzymes	Minimized Steatosis	Minimized Hepatotoxicity	Reference
<i>Opuntia ficus indica</i> fruit juice	Male Wistar rats (180–200 g)	–	–	–	–	+	[30]
Aqueous extract of <i>Opuntia robusta</i> fruit	Wistar rats (200–250 g)	–	+	–	–	+	[31]
<i>Opuntia microdasys</i> floral decoction	Adult Wistar rats	–	+	+	–	–	[32]
<i>Opuntia ficus indica</i> Prickly Pear Fruit	Tilapia fish (21–25 g)	–	+	+	–	–	[33]
<i>Pereskia grandifolia</i> extract	Adult male Wistar rats	–	+	+	–	–	[34]
<i>Opuntia robusta</i> and <i>Opuntia streptacantha</i> fruit juice	Male rats	–	–	+	–	–	[53]
Nopal dehydrated	Male Zucker rats	+	–	+	–	–	[58]
<i>Opuntia ficus-indica</i> fruit juice	Male rodents	–	–	+	–	–	[60]
<i>Opuntia ficus-indica</i> (OFI) fruit seeds	In vivo	+	–	–	+	–	[61]
<i>Opuntia ficus-indica</i> cladodes	In vivo	+	–	–	+	–	[62]
Aqueous extract of <i>Opuntia ficus-indica</i> cladodes	Male rats	–	–	–	–	–	[63]
Hydroalcoholic extract of cladodes of <i>Opuntia ficus-indica</i>	Male mice	–	+	–	–	+	[64]
<i>Opuntia ficus-indica</i> fruit vinegars	Male rats	–	+	+	–	–	[65]
Indicaxanthin from <i>Opuntia ficus-indica</i>	Male rats	+	+	–	–	–	[66]
<i>Opuntia dillenii</i> seed oil	Male rats	–	+	+	–	+	[67]
Aqueous extract of <i>Opuntia dillenii</i> Haw	Male rats	–	–	–	+	–	[68]
<i>Opuntia dillenii</i> id fruits	Male rats	+	+	–	–	–	[69]
<i>Opuntia dillenii</i> polysaccharides	Male mice	–	+	–	–	–	[70]
<i>Opuntia dillenii</i> polysaccharide	Male mice	–	–	+	–	–	[71]

Table 4. Cont.

Species/Product	Animal	Anti-Inflammatory	Antioxidant	ALT and AST Enzymes	Minimized Steatosis	Minimized Hepatotoxicity	Reference
Methanolic extract of <i>Pachycereus marginatus</i> cladodes	Female Balb/c mice (22–28 g)	–	+	+	–	+	[72]
<i>Opuntia ficus indica</i> cladodes juice	Male BalbC mice (20–25 g).	–	+	–	–	+	[73]
<i>Opuntia ficus-indica</i> cladode juice	BalbC male mice (20–25 g).	–	+	–	–	–	[74]
<i>Opuntia ficus-indica</i> fruit juice	Male albino mice (25–30 g)	–	+	+	–	+	[75]
<i>Opuntia ficus-indica</i> cladodes	Male mice (38–40 g)	–	–	+	–	+	[76]
<i>Opuntia ficus-indica</i> seed oil	C57BL/6 J male mice (12–16 weeks old)	+	+	–	–	–	[77]
Chloroform or methanol extracts of <i>Opuntia monacantha</i>	Rabbits (1.2–1.5 kg)	–	–	+	–	+	[78]
Diet supplemented with <i>Opuntia atropes</i> cladodes and <i>Opuntia joconostle</i> fruit flour	Male rats	+	+	+	–	+	[79]
<i>Opuntia streptacantha</i> flour	Male rats	–	–	–	+	–	[80]
Betacyanins from <i>Hylocereus undatus</i> peel	C57BL/6 J male mice (4 weeks old)	–	–	+	+	–	[81]
Pulp and juice from <i>Hylocereus undulatus</i> fruit	C57BL/6 J male mice (4 weeks old)	–	–	+	+	–	[82]
Aqueous extract of <i>Pilosocereus gounellei</i> stems	Male rats	+	+	+	+	–	[83]
Pitaya juice	Male rats	–	–	+	–	–	[84]
<i>Hylocereus polyrhizus</i> peel extract	Male mice	+	–	–	+	–	[85]
<i>Pereskia grandifolia</i> leaf flour	Male rats	–	–	–	+	–	[87]

ALT, alanine aminotransferase; AST, aspartate aminotransferase; +, effect present; –, effect not evaluated in the study.

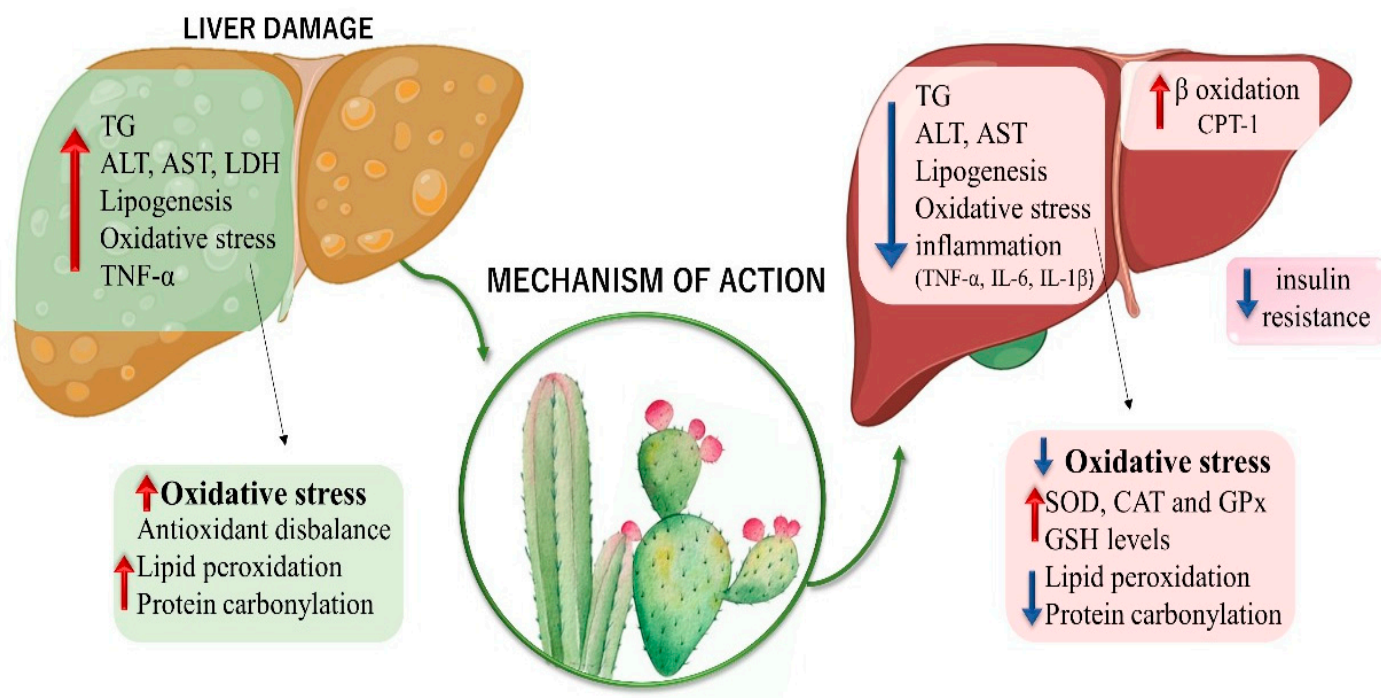


Figure 3. Potential mechanisms of action of the consumption of cactus in liver diseases. ALT, alanine aminotransferase; AST, aspartate aminotransferase; CAT, catalase; CPT-1, carnitine palmitoyltransferase 1; GPx, glutathione peroxidase; GSH, reduced glutathione; IL-1 β , interleukin 1 β ; IL-6, interleukin 6; LDH, lactate dehydrogenase; SOD, superoxide dismutase; TG, triglyceride; TNF- α , tumor necrosis factor α . Blue arrows indicate reduction in evaluated parameters; red arrows indicate increase in evaluated parameters.

5.3. Clinical Studies

Clinical trials with cacti which focus on preventing or treating liver diseases have not yet been conducted. Previous studies have been published on the administration of a beverage based on *Nopalea cochenillifera* and its beneficial effects against Type II diabetes [88], as well as on the administration of steamed nopal cladodes (50–300 g/150 min), fiber tablets (300 mg/12 weeks), and capsules (1.6 g per meal/6 weeks) obtained from *Opuntia ficus-indica*, which demonstrated effects in controlling Type II diabetes, weight loss, and improving cardiovascular parameters, respectively [89–91].

The only record found was an article reporting a case–control study, in which a female child with Prader-Willi syndrome (maternal uniparental disomy) who presented characteristic symptoms of the syndrome such as weight gain, hyperphagia, and extreme eating behavior, received an extract of the Indian cactus *Caralluma fimbriata* over 12 years. The extract was alcoholic (40%) and aqueous (60%), purified, granulated, and encapsulated. The dose was initially 200 mg/day, and at the end of the study, it was 2000 mg/day. Ingestion of the extract resulted in satiety with free access to food and weight control within the normal range. After 12 years of consuming cactus-based supplementation, her liver function was normal, with a reduction in triglycerides. This study highlighted the long-term beneficial effects of the extract in humans with this syndrome; however, the mechanisms involved and whether these outcomes can be predicted in other diseases involving the same symptoms have not yet been elucidated [92].

6. Safety of the Consumption of Cacti and Drug–Drug Interactions

The liver plays an important role in the metabolism and elimination of drugs, and this activity is affected by diseases that affect the hepatic system [93]. Drug interactions among herbal medicines, foods and drugs can be pharmacokinetic (PK) or pharmacodynamic (PD) in nature [94]. PK interactions influence the absorption, distribution, metabolism, or excretion of the drugs, while PD interactions can trigger a direct synergistic or antagonistic effect on the clinical activity of the drugs generally used in treating liver diseases or other diseases [95].

Although changes in the PK and PD properties resulting from medications are common in many liver diseases, as they cause adverse effects [93], drug interactions and an increased risk of drug overdose, or underdosage in general, studies which address the bioactivity of cacti and other potential herbal medicines and foods have not evaluated drug interactions or synergy among these treatments. However, the studies discussed herein provide important information about the doses, duration of administration, and the parts and compounds obtained from the main edible cacti used in different types of studies, as well as the key outcomes for liver health and disease, including toxicity studies. A thorough investigation of the main compounds present in the studied cacti could bring more support to the effects of the administration of cacti on the preservation of liver function and as an adjuvant treatment in diseases that affect the liver.

7. Concluding Remarks and Future Directions

The accumulating evidence from *in vitro* and *in vivo* studies supports the notion that cactus-derived compounds possess hepatoprotective and liver-supporting properties. However, further research, including clinical trials, is warranted to elucidate the specific molecular mechanisms of action, optimal dosages, other life stages, and long-term effects of cactus consumption on liver health in humans as well as animal models. Understanding these mechanisms may unveil novel therapeutic interventions or dietary strategies for liver-related disorders, offering new avenues for preventive healthcare.

Future research should focus on conducting well-designed clinical trials to evaluate the efficacy and safety of cactus-derived compounds or cactus-based formulations in managing liver diseases, such as MASLD, liver fibrosis, and drug-induced hepatotoxicity. Moreover, exploring the synergistic effects of the constituents of cactus with conventional therapies and evaluating drug interactions could pave the way for complementary approaches in the management of liver disease.

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