

Phytochemical profile and pharmacological activities of *Opuntia ficus-indica* cladodes: bioactive compounds and mechanisms of action – A review

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ABSTRACT

Introduction

Opuntia ficus-indica cladodes are widely used in food systems and traditional medicine across Africa, Latin America, and the Mediterranean. Their high content of bioactive compounds has attracted increasing scientific attention due to reported pharmacological properties, including antioxidant, anti-inflammatory, antimicrobial, and antidiabetic activities. However, current evidence remains fragmented and heterogeneous, limiting clear understanding of the relationships between phytochemicals and their mechanisms of action.

Purpose

This study provides a critical and integrative review of the phytochemical composition, pharmacological activities, and mechanisms of action of *O. ficus-indica* cladodes.

Methods

A structured literature review was conducted using ScienceDirect, PubMed, Google Scholar, and WHO reports. Keywords included “*Opuntia ficus-indica* cladodes,” “phytochemical composition,” “bioactive compounds,” and “pharmacological activity.” Peer-reviewed articles and reports published between 2014 and 2025 were included, while studies focusing on non-cladode plant parts were excluded. References were managed using Zotero.

Results

Cladodes contain diverse phenolic compounds, including p-coumaric acid (14.08–16.18 mg/100 g), narcissin (14.69–137.10 mg/100 g), rutin (2.36–26.17 mg/100 g), isoquercetin (2.29–39.67 mg/100 g), isorhamnetin derivatives, and nicotiflorin (2.89–146.50 mg/100 g), which significantly contribute to their bioactivity. Major phytosterols identified include β -sitosterol (16.17 mg/kg), stigmasterol (16.53 mg/kg), Δ^7 -avenasterol (13.40 mg/kg), and campesterol (11.60 mg/kg). Carbohydrates such as glucose (153.15 ± 6.50 μ g/mg), xylose, and mannose, along with minerals including calcium (5.64–316.95 mg/100 g), iron, zinc, and manganese, further enhance their functional potential. Antioxidant and anti-inflammatory activities were reported in 91% of studies, while antimicrobial effects were documented in 69%.

Conclusion

The phytochemical richness of *O. ficus-indica* cladodes provides a strong scientific basis for their traditional and modern uses. Their pharmacological effects arise from synergistic interactions among multiple bioactive compounds acting through diverse mechanisms. Overall, cladodes represent a promising multifunctional resource for nutraceutical and therapeutic applications. However, further clinical studies are required to bridge the gap between preclinical findings and human applications.

INTRODUCTION

Opuntia ficus-indica (OFI), commonly known as cactus or nopal, is a xerophytic plant belonging to the Cactaceae family and widely distributed in arid and semi-arid regions of North Africa and Latin America (Nefzaoui, 2019). Native to Mexico and Central America, it was introduced into Europe—particularly Spain and Italy—at the beginning of the 16th century and subsequently spread to North and sub-Saharan Africa, where it has become well adapted to harsh climatic conditions (Maiuolo et al., 2024). In these environments, OFI plays important ecological and socio-economic roles. Its cladodes, traditionally consumed by humans (Brahmi et al., 2024) and widely used in animal feeding systems, have recently attracted increasing scientific attention due to their rich phytochemical composition and emerging therapeutic potential (Alghamdi et al., 2023; Aparicio-Ortuño et al., 2024; Shoukat et al., 2023).

For decades, OFI cladodes have been used in traditional medicine, supported by indigenous knowledge transmitted across generations. They are commonly employed in the management of digestive disorders, including gastric hyperacidity and ulcers, as well as in the regulation of blood glucose levels, reduction of inflammation, and treatment of mild burns and superficial wounds (Ahmed et al., 2024; Silva et al., 2021). Additional uses include the management of mild respiratory conditions, alleviation of fatigue, and nutritional supplementation during periods of food scarcity. While these traditional applications have stimulated numerous scientific investigations, current evidence remains fragmented, with studies often focusing on isolated biological effects rather than providing an integrated understanding of therapeutic potential (Adjafre et al., 2024; Alqudah et al., 2024; Ammam et al., 2023; Amrane-Abider et al., 2023; Aparicio-Ortuño et al., 2024). This fragmentation partly explains the growing yet insufficiently structured interest in cladode valorization (Sethatho et al., 2025).

Recent studies have reported that cladodes, as specialized photosynthetic and water-storage organs, contain a wide range of bioactive compounds (Martins et al., 2023). These include flavonoids, polyphenols, carotenoids, vitamins, and dietary fibers, which are associated with multiple

biological activities such as antioxidant, anti-inflammatory, antidiabetic, antimicrobial, cardioprotective, and potential anticancer effects (Adjafre et al., 2024; Alghamdi et al., 2023; Galati et al., 2003; Hikal et al., 2021; Hwang et al., 2017; Kabengele et al., 2020; Maiuolo et al., 2024; Shoukat et al., 2023; Xavier et al., 2024; Zourgui et al., 2022).

However, the relationship between phytochemical composition and biological activity is not always consistently established, particularly due to variations in extraction methods, plant origin, and experimental models.

Despite these limitations, the wide availability, low production cost, and ecological resilience of OFI make it a promising candidate for pharmacological applications (Benramdane et al., 2025) as well as nutritional research (Silva et al., 2021; Souza et al., 2025). Several authors have therefore recommended its incorporation into functional foods and nutraceutical formulations (Aparicio-Ortuño et al., 2024).

The juice extracted from OFI cladodes represents a specific and increasingly studied form of utilization, although it remains less systematically investigated. This juice is characterized by a slightly viscous texture, a color ranging from pale to dark green, and a neutral to mildly vegetal taste (Elsheawy et al., 2023). It contains soluble fibers (mucilages), antioxidants (flavonoids and polyphenols), vitamins (C, A, E, B6, and B2), essential minerals (calcium, potassium, and magnesium), and amino acids (Rodrigues et al., 2023). It is consumed as a natural beverage in arid regions, often blended with fruit juices, and is increasingly incorporated into dietary supplements, nutraceuticals, and cosmetic formulations.

Beyond nutritional applications, OFI mucilage has demonstrated potential in reducing oxidative damage in spermatozoa during semen cryopreservation (Ramírez-Chequer et al., 2025) and as a multifunctional additive in construction materials (Berhanu & Khshen, 2025). Nevertheless, scientific evidence regarding the specific pharmacological effects of cladode juice remains fragmented and insufficiently synthesized.

Therefore, this review aims to provide a critical and integrative synthesis of current scientific evidence on *Opuntia ficus-indica* cladodes. Specifically, it seeks to: (i)

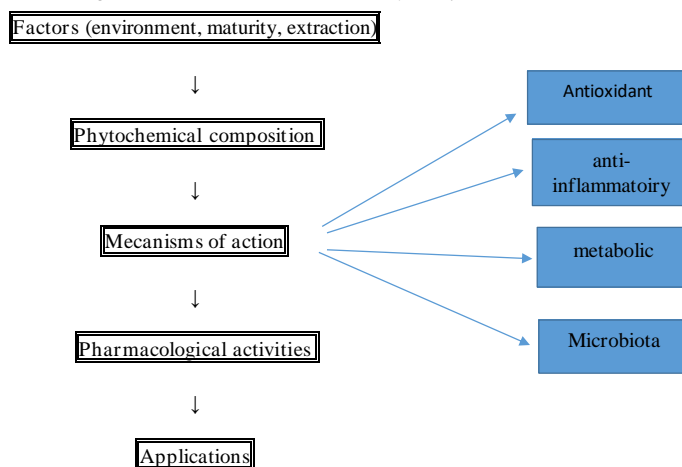
analyze the qualitative and quantitative phytochemical composition of cladodes; (ii) examine the relationship between bioactive compounds and reported in vitro and in vivo biological activities, with particular attention to cladode juice; and (iii) evaluate potential applications in health, pharmaceutical, agri-food, and environmental sectors. By addressing these objectives, this review bridges fragmented evidence and provides a coherent framework for future research and valorization of this multifunctional plant resource.

CONCEPTUAL FRAMEWORK

The conceptual framework of this review is based on an integrative approach linking the phytochemical composition of *Opuntia ficus-indica* cladodes to their pharmacological activities through specific mechanisms of action. This framework structures the analysis of existing evidence and guides future research directions. Phytochemical composition is influenced by environmental, physiological, and technological factors, which ultimately determine biological activity and potential applications.

Figure 1:

Conceptual framework illustrating the relationships between environmental and processing factors, phytochemical composition, mechanisms of action, pharmacological activities, and applications of *Opuntia ficus-indica* cladodes.



METHODS

A comprehensive literature search was conducted using ScienceDirect, PubMed, Google Scholar, and Google, as well as reports from international organizations. Keywords included “*Opuntia ficus-indica* cladodes,” “phytochemical composition,” “bioactive compounds,” and “pharmacological activity.”

Studies published between 2014 and 2025 were included. Eligible sources comprised peer-reviewed journal articles and scientific reports focusing specifically on cladodes. Studies on other plant parts were excluded.

Reference management and screening were performed using Zotero. A structured qualitative synthesis approach was applied to analyze phytochemical composition, biological activities, and mechanisms of action.

PRESENTATION OF THE THEMES OF ANALYSIS

Botanical and Ecophysiological Data of Opuntia ficus-indica (OFI)

Taxonomic Classification and Geographical Distribution

Opuntia ficus-indica is a plant cultivated under arid conditions, particularly in Mediterranean regions and Central America. In these regions, *Opuntia ficus-indica* (spineless or nearly spineless) and *Opuntia megacantha* (spiny) are commonly found and are often collectively referred to as *Opuntia ficus-indica* (*Opuntia* spp.) (Mylo et al., 2021). The absence of spineless forms in wild populations is attributed to long-term agricultural selection processes (Mohamed & Sbaghi, 2023).

Several taxa have been proposed as putative ancestors of *O. ficus-indica*, notably *O. megacantha* and *O. streptacantha*. However, these taxa are often difficult to distinguish due to ambiguous descriptions and the absence of well-defined reference specimens (FAO, 2018).

The lectotype of *O. ficus-indica* is characterized by spineless or nearly spineless morphology; however, spine presence is not considered a reliable taxonomic criterion. Consequently, both spiny and spineless forms are regarded as phenotypic variants of the same species (Aalaoui & Sbaghi, 2023). Taxonomic classification thus facilitates understanding of phylogenetic relationships and ecological adaptation.

According to the Linnaean system, *O. ficus-indica* (L.) belongs to:

- i. **Kingdom:** Plantae
- ii. **Subkingdom:** Tracheobionta
- iii. **Division:** Magnoliophyta
- iv. **Class:** Magnoliopsida
- v. **Subclass:** Caryophyllidae

- vi. **Order:** Opuntiales
- vii. **Family:** Cactaceae
- viii. **Subfamily:** Opuntioideae
- ix. **Tribe:** Opuntieae
- x. **Genus:** *Opuntia*
- xi. **Subgenus:** *Platyopuntia*
- xii. **Species:** *O. ficus-indica* (L.)

Semi-arid regions of Mexico harbor the greatest cactus diversity globally, with nearly 300 *Opuntia* species, many producing edible stems and fruits. These regions exhibit high genetic diversity among cultivated and wild cactus species (Mylo et al., 2021). Numerous *Opuntia* species have been introduced into Australia, South Africa, Madagascar, and the Mediterranean basin (Mohamed & Sbaghi, 2023). The species was introduced into Mediterranean Europe during the late 15th and early 16th centuries as a food resource and is now widely cultivated in arid and semi-arid regions worldwide (Quintero-García et al., 2021).

Plant Morphology and Cladode Anatomy

O. ficus-indica exhibits a tree-like growth form characterized by fleshy, oval, paddle-shaped stems that may reach 3–4 meters in height. Cladodes typically measure 30–40 cm in length, 15–25 cm in width, and 1.5–3 cm in thickness. They are green, interconnected, and form branched structures (Aalaoui & Sbaghi, 2023).

The cladodes are covered by a waxy cuticular layer that reduces transpiration and provides protection while performing photosynthetic functions in place of leaves. With age, basal cladodes become lignified and form a trunk-like structure. The plant produces abundant flowers and fruits (Mylo et al., 2021).

Flowers develop on upper cladode regions and measure 4–10 cm in diameter, with colors ranging from yellow to orange or red. They are edible, as are the fruits, which are ovoid berries covered with a spiny epidermis. Flowering occurs between April and May in temperate climates, while fruit harvesting takes place from late July to September. In hot and dry climates, fruiting may occur twice annually (Mohamed & Sbaghi, 2023).

The fruit, commonly known as prickly pear, contains pulp ranging from pale yellow to deep red, with a sweet and

pleasant flavor. Seeds are rich in nutrients and are used for oil extraction.

Figure 2:

Morphology of *Opuntia ficus-indica* showing cladodes, areoles, spines, glochids, and fruits



Mechanisms of Drought Adaptation in *O. ficus-indica*

O. ficus-indica has adapted to diverse ecosystems ranging from deserts to mountainous and tropical regions. Its drought resistance relies on physiological, anatomical, and morphological adaptations.

Crassulacean acid metabolism (CAM) enables nocturnal stomatal opening, significantly reducing water loss through transpiration (Martins et al., 2023). Additionally, leaves are modified into spines, reducing transpiring surface area, while cladodes function as water storage organs. The shallow but extensive root system facilitates rapid uptake of surface moisture following rainfall. A thick waxy cuticle further reduces water loss and protects against solar radiation. Together, these adaptations confer exceptional drought tolerance (Mylo et al., 2021).

Phytochemical Composition of *Opuntia ficus-indica* Cladodes

Cladodes of *O. ficus-indica* contain diverse bioactive compounds with nutritional and pharmacological relevance. Major groups include carbohydrates, fibers, mucilages, phenolic compounds, minerals, and phytosterols.

Major Constituents (Carbohydrates, Dietary Fibers, and Mucilages)

Cladodes contain high levels of dietary fibers, including cellulose and hemicellulose, as well as mucilages composed of hydrophilic polysaccharides responsible for their gelling, moisturizing, and digestive regulatory properties. Aparicio-Ortuño et al. (2024) reported that cladode powder contains approximately 54.89% dietary fiber.

Simple carbohydrates, soluble sugars, and structural polysaccharides are also present and contribute to the nutritional and functional properties of the plant.

Micronutrients

Opuntia ficus-indica cladodes exhibit high water content, a characteristic feature of succulent plants that explains their ecological adaptation to arid environments. They also contain essential vitamins, including vitamin C, vitamin B1, and vitamin B2, as well as mineral elements such as calcium, magnesium, and potassium (Razzak et al., 2024). Their high water and mucilage content further contributes to their hydrating properties and formation of mucilaginous protective barriers, which support gastrointestinal and dermal functions.

Phenolic Compounds

Phenolic compounds represent the most biologically active secondary metabolites in *O. ficus-indica* cladodes and are primarily responsible for their antioxidant, anti-inflammatory, and antimicrobial activities. Shoukat et al. (2023) confirmed the high polyphenolic richness of cladodes, supporting their pharmacological relevance.

Rodrigues et al. (2023) identified several flavonoid glycosides, including kaempferol, quercetin, and isorhamnetin derivatives. Similarly, Aparicio-Ortuño et al. (2024) quantified approximately 2,050 mg gallic acid equivalents (GAE) per 100 g of cladode powder, indicating a high total phenolic content. In addition, isovitexin 7-O-xyloside-2"-O-glucoside, polyhydroxypregnane glycoside, and neohancoside C were reported for the first time in *Opuntia* cladode extracts (Aruwa et al., 2019).

Table 1:
Principal Components of *Opuntia ficus-indica* Cladodes

Component	Content (g/100 g dry matter)	Content (g/100 g fresh weight)	References
Water	—	88–95	Rodrigues et al., 2023; Shoukat et al., 2023; Silva et al., 2021
Carbohydrates	64–71	3–7	Ramírez-Chequer et al., 2025; Silva et al., 2021; Razzak et al., 2024
Ash	19–23	1–2	Rodrigues et al., 2023
Dietary fiber	3–50	1–2	Razzak et al., 2024; Shoukat et al., 2023; Aparicio-Ortuño et al., 2024
Proteins	2–10	0.5–1	Sethatho et al., 2025; Silva et al., 2021; Tesoriere et al., 2004
Lipids	1–4	0.2	Rodrigues et al., 2023; Shoukat et al., 2023

Note: MS = dry matter; FW = fresh weight.

Bioactive Pigments (Betalains and Carotenoids)

Although pigments are more extensively studied in fruits, *O. ficus-indica* cladodes also contain appreciable levels of bioactive pigments, mainly carotenoids such as β -carotene, lutein, and xanthophylls, and, in some varieties, betalains (Razzak et al., 2024). While several studies report their presence, quantitative data remain limited and inconsistent (Shoukat et al., 2023).

From a pharmacological perspective, carotenoids significantly contribute to the antioxidant capacity of cladode extracts and provide protection against photo-oxidative stress, thereby enhancing their therapeutic potential.

Lipophilic Compounds (Phytosterols, Terpenoids, and Related Constituents)

Opuntia ficus-indica cladodes contain phytosterols and other lipophilic compounds, although their quantitative characterization remains limited and underexplored in comparison to other plant parts. Nevertheless, their presence has been consistently reported (Maiuolo et al., 2024).

Ethanollic extracts have led to the identification of terpenoid compounds, although detailed profiling and quantification remain scarce (Msaddak et al., 2017). Importantly, most phytosterol analyses have focused on seeds, fruits, or oils rather than cladodes specifically (Alqudah et al., 2024).

From a pharmacological standpoint, phytosterols contribute to cholesterol-lowering effects, terpenoids exhibit anti-inflammatory and antimicrobial activities, and carotenoids provide antioxidant protection. Together, these compounds enhance the value of cladodes as functional raw materials for pharmaceutical, nutraceutical, and cosmetic applications.

Cladode composition is influenced by environmental conditions, plant maturity, geographic origin, soil-climate factors, and extraction methods (Mokrani et al., 2025). Post-harvest processing techniques such as drying, cooking, and extrusion may further modify phytochemical content and bioavailability (Pérez-Viveros et al., 2024).

Table 2:
Composition of Cladodes in Carbohydrates, Organic Acids, and Mineral Elements

Carbohydrates (µg/mg)	Organic Acids (mg/100 g FW)	Minerals (mg/100 g DW)
Rhamnose: 7.13 ± 1.28	Oxalic acid: 35	Calcium: 5.64–316.95
Fructose: 0.74 ± 0.11	Malic acid: 985 (6 h); 95 (18 h)	Calcium oxalate: 4.3–11.5
Xylose: 18.64 ± 0.84	Citric acid: 178 (6 h); 31 (18 h)	Sodium: 0.3–18.7
Mannose: 13.64 ± 0.81	Malonic acid: 36	Iron: 0.09–25.5
Galactose: 33.69 ± 2.89	Succinic acid: traces	Zinc: 0.08–12.6
Glucose: 153.15 ± 6.5	Tartaric acid: traces	Manganese: 0.19–37.29
–	–	Copper: 0.01; Magnesium: 63.4; Potassium: 2.35–108.2; Phosphorus: 0.2–2.6

Sources: Shoukat et al., 2023; Wang et al., 2024; Rodrigues et al., 2023; Razzak et al., 2024.

Pharmacological Effects and Mechanisms of Action of *Opuntia ficus-indica* Cladode Juice

Recent studies have demonstrated that *O. ficus-indica* cladodes exhibit antioxidant, anti-inflammatory, antidiabetic, hypolipidemic, gastroprotective, antimicrobial, and wound-healing activities. These effects are primarily attributed to polyphenols, flavonoids (quercetin, isorhamnetin), vitamins C and E, carotenoids, soluble fibers, mucilages, and bioactive polysaccharides.

Antioxidant Activity

The antioxidant activity of *O. ficus-indica* cladodes is largely attributed to their high content of phenolic compounds, flavonoids, vitamin C, β-carotene, and mucilaginous polysaccharides (Adjafre et al., 2024; Arias Gorman et al., 2025; Elshewy et al., 2023). These compounds neutralize reactive oxygen species (ROS) and reduce oxidative stress, a key pathological mechanism involved in cardiovascular diseases, diabetes, cancer, and aging (Benramdane et al., 2025; Aruwa et al., 2019).

Polyphenols and flavonoids act as free radical scavengers and inhibit pro-oxidant enzymes, as demonstrated through DPPH, ABTS, FRAP, and ORAC assays (Luna-Sosa et al., 2022; Zeghibib et al., 2022). Vitamin C and carotenoids further enhance antioxidant defense by regenerating endogenous antioxidant systems (Shoukat et al., 2023), while mucilages and dietary fibers protect intestinal mucosa against oxidative injury (Caminiti et al., 2024).

Table 3:
Amino acid, fatty acid, and vitamin composition of *Opuntia ficus-indica* cladodes

Amino acids	Content (mg/100 g DW)	Fatty acids	Content (mg/100 g DW)	Vitamins	Content (mg/100 g)
Alanine	4.75	C12:0	1.33	Vitamin C	2–22
Arginine	6.63	C14:0	1.96	Niacin	0.46
Asparagine	36.12	C16:0	13.87	Thiamine	0.14
Aspartic acid	10.42	C16:1	0.24	Riboflavin	0.60
Glutamic acid	21.68	C18:0	3.33	Pyridoxine	–
Glutamine	Trace	C18:1	11.16	Folic acid	–
Cysteine	0.37	C18:2	34.87	Vitamin K1	–
Histidine	3.11	C18:3	33.23	Vitamin K1	–
Isoleucine	6.20	C20:0	–	Total tocopherols	2.18
Leucine	9.94	C22:0	–	α-Tocopherol	1.76
Lysine	6.79	C22:1	–	β-Tocopherol	–
Methionine	0.70	C24:0	–	γ-Tocopherol	–
Phenylalanine	5.25	–	–	σ-Tocopherol	–
Serine	8.46	–	–	–	–
Threonine	1.53	–	–	–	–
Tyrosine	3.09	–	–	–	–
Tryptophan	Trace	–	–	–	–
Valine	6.02	–	–	–	–
α-Aminobutyric acid	Trace	–	–	–	–
Carnosine	Trace	–	–	–	–
Citrulline	Trace	–	–	–	–
Ornithine	Trace	–	–	–	–
Proline	Trace	–	–	–	–
Taurine	Trace	–	–	–	–
Glycine	5.06	–	–	–	–

Sources: Shoukat et al., 2023; Silva et al., 2021; Rodrigues et al., 2023; Ahmed et al., 2024; Liu et al., 2025; Wang et al., 2024.

Anti-inflammatory Activity

Anti-inflammatory activity of medicinal plants is commonly mediated through modulation of inflammatory mediators, including cytokines, prostaglandins, and enzymes such as COX-2, via suppression of NF-κB

signaling and reduction of TNF- α , IL-1 β , IL-6, and nitric oxide (Razzak et al., 2024; Rodrigues et al., 2023).

O. ficus-indica cladodes have long been used in traditional medicine to alleviate inflammatory conditions (Xavier et al., 2024). Their pharmacological activity is attributed to flavonoids, polysaccharides, phytosterols, phenolic acids, and antioxidant vitamins (Elsheawy et al., 2023).

Experimental studies show inhibition of TNF- α , IL-1 β , COX-2, and NO production in macrophages (Tahri-Joutey et al., 2022). Flavonoids such as quercetin and isorhamnetin inhibit NF- κ B and MAPK signaling pathways (Filannino et al., 2016). Polysaccharides also reduce edema and promote wound healing in vivo (Liu et al., 2025). Consistent findings from RAW 264.7 macrophage models confirm dose-dependent anti-inflammatory effects (Zeghibib et al., 2022).

Table 4:
Polyphenol, flavonoid, and phytosterol composition of *Opuntia ficus-indica* (OFI) cladodes

Polyphenols & flavonoids	Content (mg/100 g)	Phytosterols & related compounds	Content (mg/kg)
Gallic acid	0.64–2.37	Betalains	16.17
p-Coumaric acid	14.08–16.18	β -Sitosterol	16.53
3,4-Dihydroxybenzoic acid	0.06–5.02	Stigmasterol	13.4
4-Hydroxybenzoic acid	0.5–4.72	Δ 7-Avenasterol	11.6
Ferulic acid	0.56–34.77	Campesterol	5.7
Salicylic acid	0.58–3.54	Campestanol	6.4
Isoquercetin	2.29–39.67	Saponins (g/kg)	8.72
Isorhamnetin-3-O-glucoside	4.59–32.21	–	–
Nicotiflorin	2.89–146.5	–	–
Rutin	2.36–26.17	–	–
Narcissin	14.69–137.1	–	–
Kaempferol	–	–	–

Sources: Iftikhar et al., 2023; Razzak et al., 2025; Shoukat et al., 2023; Zeghibib et al., 2022; Mokrani et al., 2025; Wang et al., 2024; Rodrigues et al., 2023.

Hypoglycemic and Hypolipidemic Activity

Cladode extracts reduce postprandial glycemia due to their high soluble fiber content, which inhibits α -glucosidase activity and slows carbohydrate absorption, improving insulin sensitivity (Elsheawy et al., 2023; Hwang et al., 2017).

Clinical and preclinical studies confirm reduced postprandial glucose and insulin peaks in both healthy

and diabetic subjects (López-Romero et al., 2014). In diabetic rat models, aqueous extracts significantly reduced blood glucose levels (Hwang et al., 2017). Nopal supplementation improved glucose tolerance and gut microbiota composition (Sánchez-Tapia et al., 2017). Combined administration with empagliflozin enhanced glycemic control (Alqudah et al., 2024).

Hypolipidemic effects are mediated through pancreatic lipase inhibition, reduced fat absorption, and enhanced bile acid excretion. Polyphenols and fibers reduce LDL cholesterol and triglycerides (Padilla-Camberos et al., 2015; Msaddak et al., 2017).

Gastroprotective Effect

Cladodes have long been used traditionally to treat gastric disorders such as ulcers, acid reflux, and heartburn (Santos et al., 2018; FAO, 2024). Their mucilages exert protective effects on gastrointestinal mucosa by forming a soothing and protective barrier.

Experimental studies show protection against acid and non-acid reflux in esophageal cells (Lehner et al., 2024). Anti-ulcer activity has also been confirmed in multiple independent studies (Ahmed et al., 2024).

Immunomodulatory and Wound-Healing Properties

Traditional uses include immune support, wound treatment, and skin repair. Cladodes promote fibroblast proliferation, collagen synthesis, and anti-inflammatory activity in macrophages (Hikal et al., 2021; Razzak et al., 2024).

Polysaccharides regulate immune responses and support tissue regeneration (Liu et al., 2025). Clinical supplementation increased total antioxidant capacity in humans by 48.1% (Zaman et al., 2025).

Topical formulations accelerate wound closure and enhance keratinocyte migration (Mohamed et al., 2024; Galati et al., 2003).

Antimicrobial Activity

Antibacterial Activity

Traditional use of cladodes for infections is supported by modern evidence showing activity against both Gram-positive and Gram-negative bacteria (Lamia et al., 2022; Abba et al., 2022). Activity is attributed to flavonoids,

phenolics, alkaloids, and essential oils (Rodrigues et al., 2023).

Cladode extracts inhibit pathogens including *E. coli*, *S. aureus*, *Salmonella typhi*, *P. aeruginosa*, and *K. pneumoniae* (Hikal et al., 2021). Activity varies by maturity stage, with immature cladodes often showing higher potency.

Antifungal Activity

Cladode extracts inhibit phytopathogenic fungi such as *Fusarium oxysporum*, *Rhizoctonia solani*, and *Alternaria* spp., with inhibition rates exceeding 80% in some cases (Mokrani et al., 2025). These findings support potential applications in biopesticide development.

Anthelmintic Activity

Ethanol and methanol extracts show dose-dependent anthelmintic activity comparable to albendazole (Pulate et al., 2024). Effects include paralysis and mortality of helminths such as *Eudrilus eugeniae* and *Pheretima posthuma*. Additional in vivo studies confirm inhibitory effects on gastrointestinal parasites (Santos et al., 2018).

Anticancer properties

Cladode extracts of *Opuntia ficus-indica* have demonstrated dose-dependent cytotoxic effects against several cancer cell lines, including colon, breast, hepatocellular, prostate, and leukaemia models, although the majority of evidence remains confined to in vitro studies, with limited in vivo and clinical validation (Liu et al., 2025; Öncül et al., 2024; Wang et al., 2024). These activities are attributed to phytoconstituents such as flavonoids, phenolic acids, and carotenoids, which exert their effects through multiple mechanisms, including induction of apoptosis, cell cycle arrest, modulation of Bcl-2/Bax expression, and elevation of intracellular reactive oxygen species (ROS) levels (Wang et al., 2024).

Notably, in vitro-derived cladode cultures treated with benzyladenine (BA, 2 mg/L) and kinetin (Kin, 1 mg/L) exhibited higher total phenolic and kaempferol contents than in vivo-derived extracts (total phenolics: 156.5 vs. 86 mg/g DW; kaempferol: 2.807 vs. 1.304 mg/g DW), with corresponding enhancement in anticancer activity against prostate (PC3) and breast (MCF-7) cancer cell lines in terms of reduced viability, proliferation, and migration (Heikal et al., 2021).

Further evidence from recent reviews indicates both preventive and therapeutic potential of *O. ficus-indica* against multiple cancer types (Talal Ahmedah, 2023). While Nam et al. (2023) primarily emphasised antioxidant and anti-inflammatory pathways, their findings also support anticancer activity mediated through oxidative stress modulation and apoptosis induction. In addition, pro-apoptotic effects of both spiny and spineless cladode extracts have been demonstrated in K562 human myeloid leukaemia cells, with spiny extracts showing greater cytotoxic potency. Complementary in silico analyses further support apoptosis-related mechanisms, reinforcing the anticancer potential of these extracts (Öncül et al., 2024).

CRITICAL SYNTHESIS, KNOWLEDGE GAPS AND FUTURE RESEARCH DIRECTIONS

The reviewed literature consistently indicates that *Opuntia ficus-indica* cladodes contain a rich spectrum of bioactive compounds, including polyphenols, flavonoids, mucilage, phytosterols, and related secondary metabolites, which underpin diverse biological activities, including anthelmintic effects. These findings support increasing interest in plant-based alternatives to synthetic anthelmintics, particularly in the context of rising drug resistance in parasites.

Several studies report significant anthelmintic activity of *O. ficus-indica* extracts. For example, Pulate et al. (2024) observed dose-dependent paralysis and mortality of helminths, suggesting direct toxic effects on parasite physiology. Similarly, Santos et al. (2018) reported inhibition of egg hatching and larval development in gastrointestinal nematodes, supporting their antiparasitic potential. Kabengele et al. (2020) further highlighted that plant-derived compounds may disrupt parasite metabolic processes, reinforcing these findings.

Despite these promising results, important limitations persist. Most available evidence is based on in vitro assays, which may not accurately reflect in vivo efficacy due to host metabolism, bioavailability, and environmental influences (Liu et al., 2025). In addition, variability in extraction techniques, plant material, and concentrations contributes to inconsistent findings across studies,

limiting reproducibility and comparability (Wang et al., 2024).

Beyond direct anthelmintic effects, antioxidant and anti-inflammatory properties of *O. ficus-indica* (Iftikhar et al., 2023) may indirectly enhance host resistance to parasitic infections by improving immune function (Rodrigues et al., 2023). However, the precise mechanisms underlying antiparasitic activity remain insufficiently characterised, although membrane disruption and enzymatic inhibition have been suggested (Razzak et al., 2024). Environmental and agronomic factors further influence phytochemical profiles and biological activity (Zeghib et al., 2022).

Overall, the evidence supports strong anthelmintic potential, but highlights critical gaps in standardisation, mechanistic understanding, and in vivo validation. Future research should prioritise controlled animal studies and clinical validation, alongside molecular investigations using metabolomics, transcriptomics, and gene expression profiling. Standardised extraction protocols are also essential to ensure reproducibility. Additionally, nano-formulation approaches may improve stability and bioavailability of active compounds, while integrated parasite management strategies and socio-economic evaluations are needed to support real-world adoption.

CONCLUSION

This review demonstrates that *Opuntia ficus-indica* cladodes represent a highly valuable botanical resource rich in diverse bioactive compounds, including polyphenols, flavonoids, carotenoids, phytosterols, mucilages, polysaccharides, and organic acids. Collectively, these constituents underpin a wide range of pharmacological activities, including antioxidant, anti-inflammatory, antidiabetic, hypolipidemic, antimicrobial, gastroprotective, immunomodulatory, wound-healing, and anticancer effects.

The compiled evidence from in vitro and in vivo studies strongly supports the ethnopharmacological relevance of *O. ficus-indica* and highlights its potential for development into functional foods, nutraceuticals, and phytopharmaceutical products. Its adaptability to arid environments further enhances its value as a sustainable and locally accessible resource, particularly in regions facing food insecurity and limited healthcare access.

However, the current body of evidence is largely preclinical, with limited clinical validation. Methodological variability in extraction procedures, plant maturity, and environmental conditions further limits comparability across studies. Additionally, insufficient standardization of bioactive preparations remains a major barrier to reproducibility and translational application.

Future research should prioritize well-designed clinical trials, mechanistic molecular studies, and standardized extraction protocols. Advanced approaches such as metabolomics, transcriptomics, and nano-formulation strategies may further enhance understanding and improve the bioavailability and stability of bioactive compounds. Socio-economic and field-based studies are also essential to evaluate feasibility, scalability, and acceptance in real-world applications, particularly in low-resource and arid regions.

In conclusion, *Opuntia ficus-indica* cladodes hold strong promise as a multifunctional natural resource with significant health and industrial applications. Bridging the gap between experimental findings and clinical validation will be essential for their full integration into evidence-based therapeutic and nutritional strategies.

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