Sudan Journal of Medical Sciences
Volume 20, Issue no. 4, https://doi.org/10.18502/sjms.v20i4.19300
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Review Article

Traditional Uses, Phytochemicals, and Pharmacological Effects of *Cichorium intybus*: A Narrative Review

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Abstract

Background: Medicinal plants remain an important source of therapeutic agents worldwide. The review compiles the traditional uses, phytochemistry, and pharmacological effects of *Cichorium intybus* to serve as a valuable guide for researchers and healthcare professionals. This review fills important gaps by bringing together scattered information on *C. intybus*, offering a clearer and more comprehensive reference than previous studies.

Methods: Data were collected from 2000 to 2025 through extensive searches across multiple databases, including Scopus, Web of Science, Google Scholar, PubMed, and Springer Nature, following PRISMA guidelines.

Results: Traditionally, different parts of the *C. intybus* were used to cure conditions like gallstones, jaundice, fever, and diarrhea. Previous literature studies have revealed that multiple pharmacological activities have been explored in different parts of the plant, including antidiabetic, anti-inflammatory, anti-ulcerative, and antioxidant activities. Fifty-one studies met the inclusion criteria, including seventeen on traditional uses and phytochemistry, twenty-eight preclinical investigations, and six clinical trials. The phytochemical analysis indicates that the majority of sesquiterpene lactones found in *C. intybus* are lactucin and lactucopicrin. Moreover, *C. intybus* contains several important caffeic acid derivatives, most notably caftaric acid, along with isochlorogenic acid, cichoric acid, and chlorogenic acid. *Cichorium intybus* has been shown to contain additional pharmacologically active compounds, such as proteins, sugars, terpenoids, hydroxycoumarins, alkaloids, sugars, flavonoids, inulin, steroids, and volatile chemicals.

Conclusion: *C. intybus* is a rich source of various phytochemicals, which are responsible for its therapeutic effects. Future research is necessary to confirm the plant's efficacy, safety, and its potential in therapeutic applications.

Keywords: *Cichorium intybus*; Ethnopharmacology; Health; Phytochemicals; Traditional Medicine

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Received: 2 August 2025
Accepted: 9 October 2025
Published: 12 January 2026

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Editor-in-Chief:
Prof. Nazik Elmalaika Obaid Seid Ahmed Husain, MD, M.Sc, MHPE, PhD.

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1. Introduction

Centuries ago, plants were effectively utilized in traditional medicine across various parts of the world due to the presence of multiple biologically active compounds, which contributed positively to addressing the underlying causes of the problem. Globally, many people still rely on herbal remedies because of their associated benefits and promising outcomes [1]. Some possible advantages of using traditional treatment include cost-effectiveness, accessibility, safety record, and a lower chance of adverse effects. Therefore, these advantages significantly enhance the acceptability of herbal medication even today [2].

Cichorium intybus, commonly known as chicory, is widely used in traditional medicine to treat various disorders. It is an archeophyte of Mediterraneo-Irano-Turanian origin. The name of *C. intybus* most probably derives from several Greek and Latin words. Cichorium is derived from the Latin word "Cichorium," meaning "field," while *intybus* has a counterpart in both languages. The Greek counterpart means "to cut" and pertains to the morphology of the leaves. In turn, the Latin "tubus," meaning "tube," describes the structure of the stem [3]. The Greek word "kichorion," which is frequently found in the writings of ancient physicians, was the source of the Latin name "Cichorium" [4]. It is a bushy, perennial herb that has been an essential part of Ayurvedic and Unani medicine for a long time due to its various health-promoting effects. Various parts of *C. intybus* have been reported to exhibit diverse pharmacological and biological activities, including wound healing, analgesic, antiviral, anti-inflammatory, antidiabetic, antihypertensive, antiprotozoal, hepatoprotective, cytotoxic, and antineurotoxic activities. Because of its rich phytochemical profile, *C. intybus* continues to attract scientific attention as a promising source for developing herbal remedies and functional foods [5–7]. This article attempts to provide comprehensive information on the traditional applications, phytochemistry, and pharmacological properties of *C. intybus*.

1.1. Habitat

Cichorium intybus, a member of the Asteraceae family, is a common herb found in temperate and semi-arid regions worldwide [8]. It is native to Europe and the Mediterranean regions, but is widely distributed and can be found almost anywhere in the world [9]. It is extensively cultivated in the southwestern parts of Asia and other countries, including the United States, Germany, Spain, Turkey, the United Kingdom, northern and central China, Italy, New Zealand, India, and Pakistan. It thrives in all types of soil and is mainly found in Baluchistan, Pakistan. Moreover, it is a tall herb that can grow up to 6000 feet in Pakistan. In India and Pakistan, it begins blooming large, bright flowers from July through October [10].

1.2. Plant description

Cichorium intybus is a bushy, perennial herb that grows erect and tall and may reach a height of up to 40–110 cm. It is a woody plant accompanied by a strong taproot system (Figure **1**) [5, 10–15]. Detailed features are mentioned in Table **1**.

Table 1: Characteristic features of different parts of *Cichorium intybus*.

Plant parts	Characteristic features	References
Stem	It showed that the stems were 2–3 feet tall, angled or grooved, with spreading branches that extended at a significant angle from the central stem. The stems were green on the outside and white on the inside—shaped cylindrical, straight, and branching.	[10–13]
Leaves	The leaves of *C. intybus* are green and form a basal rosette measuring 10–25 cm long. They are typically narrow, oval to oblong-lanceolate, and are most often pinnate or serrated along the edges.	[5]
Flower	In *C. intybus*, the inflorescence comprises numerous multi-flowered anthodia. The florets show a distinct color gradient, with the marginal ones being light blue and the central tubular florets displaying a deeper shade. These anthodia are borne on short, thick peduncles, either singly or in small clusters. The bracts are dimorphic, with the outer ones being small and spreading, while the inner bracts are longer and held erect.	[5]
Root	Well-developed, tapering, and fleshy inside, they are white in color and have a light brown exterior.	[10]
Seeds	The seeds of *C. intybus* are obconical in shape, ranging in color from cream to brown and darker shades. Seeds are 2–4 mm long, 1–2 mm wide, slightly curved, with distinct longitudinal ridges.	[14]
Fruit	The fruit of *C. intybus* is creamish-brown in color, measuring approximately 3 to 3.5 mm long and about 1.25 mm wide. It has an oblong shape, narrowing at the base and wider at the top, topped with a scaly pappus from the accrescent calyx. The surface is smooth, shiny, and features around eight distinct ridges.	[15]



Figure 1: The plant of *Cichorium intybus*.

1.3. Taxonomy

The taxonomy of *C. intybus* places it in the plant kingdom under the family Asteraceae, which is well known for many medicinal herbs. Within this group, it belongs to the genus *Cichorium* and is classified as the species *intybus,* as summarized in Table **2** [11].

1.4. Vernacular names

Punjabi (*Hand*, *Gul*), Hindi (*Kasni*), Arabic (*Hidaba*, *Indyba*), English (Cjicory, Coffee chicory, Belgium endive, French endive, French (*endive*, *endive witloof*, *witloof*), Italian (*Radicchio Cicoria*), and Japanese (*Kiku nigana*) [10].

Table 2: Taxonomy of *Cichorium intybus*.

Taxonomic rank	Classification
Kingdom	Plantae
Phylum	Angiosperms
Class	Magnoliopsida
Order	Asterales
Family	Asteraceae
Subfamily	Cichorioideae
Genus	*Cichorium*
Species	*C. intybus*

1.5. Aim of the review

This review aims to consolidate and organize the existing knowledge about *C. intybus* by examining its extensive history of traditional use, diverse phytochemical profile, and the range of pharmacological activities reported to date. By compiling and connecting these aspects, the review not only highlights the plant's therapeutic potential but also identifies areas where further scientific research could enhance its application in modern medicine.

2. Methods

2.1. Search strategy

A systematic search was conducted in accordance with the PRISMA guidelines (2020). Relevant literature was identified through databases including Scopus, Web of Science, PubMed, Google Scholar, and Springer Nature. The keywords used were "*Cichorium intybus*," "phytochemical," "traditional uses," "pharmacological activities," "toxicity," "human studies", "clinical studies," "in vitro," and "in vivo."

2.2. Inclusion and exclusion criteria

Articles published in English between 2000 and 2025 were considered. Studies were included if they provided information on the traditional uses, phytochemistry, pharmacological properties, or toxicity of *C. intybus*. Non-English articles published before 2000, or those that lacked direct relevance to *C. intybus* (e.g., unrelated species or generalized reviews without plant-specific data) were excluded.

2.3. Data extraction

Data from the studies included were systematically extracted using a structured form. Key information collected included study details (author, year, country, design, and model), plant part and extract type, preparation method, dose or concentration used, comparators or controls, outcomes measured, and key results. In this study, the authors also recorded the phytochemicals identified, the duration of exposure, the limitations reported by the authors, the risk of bias or quality assessment, and any potential conflicts of interest. To assess study quality, we used standard tools: the Cochrane RoB 2.0 for clinical trials and

the SYRCLE tool for animal studies. For *in vitro* and phytochemical work, we applied a tailored checklist emphasizing proper plant authentication, extraction details, replication, assay controls, and analytical validation. Each study was then judged for risk of bias (low, some concerns, or high), and these judgments were summarized across the body of evidence.

3. Results and Discussion

3.1. Selection of studies

A total of 398 records were initially identified from databases, following the PRISMA 2020 guidelines (Figure **2**). After removing 199 duplicates, 80 records deemed ineligible by automated tools, and 8 records for other reasons, 211 records remained for screening. From these, 152 were excluded based on the screening criteria, leaving 59 reports for retrieval. Three reports could not be retrieved, resulting in 56 reports assessed for eligibility. Five reports were excluded because they were published in a language other than English. Ultimately, 51 studies were included in the review, comprising 17 on traditional uses and phytochemistry, 28 preclinical studies, and 6 clinical studies.

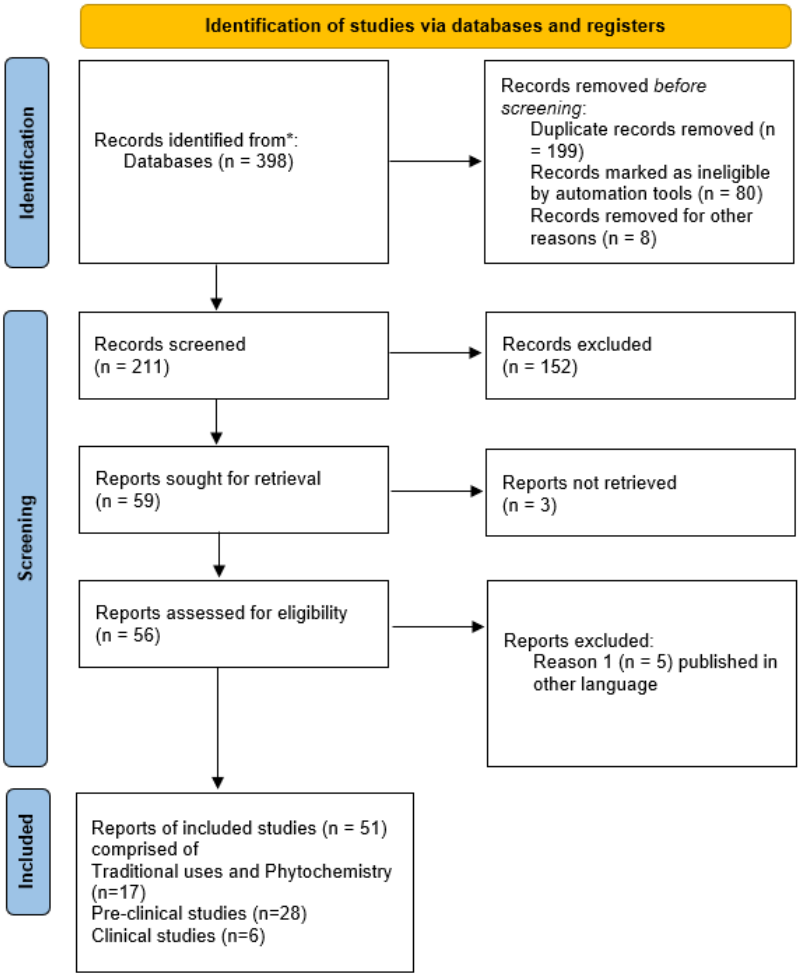


Figure 2: PRISMA flow diagram showing the study selection process.

3.2. Traditional uses

Cichorium intybus has been traditionally used to treat fever, diarrhea, jaundice, and gallstones. It has also been reported that *C. intybus* has antibacterial, anti-inflammatory, antihyperglycemic, and anti-ulcerogenic properties. The traditional uses of the plant are summarized in Table **3**.

3.3. Phytochemical constituents

The phytochemistry of *C. intybus's* roots, stems, seeds, and flowers was analyzed. The gas chromatography mass spectroscopy (GC-MS) technique was used to identify various compounds. Methanolic extracts of the plant parts were employed for phytochemical screening. Outcomes revealed the presence of 109 compounds cumulatively in the root, stem, seeds, and flowers. The flower and leaf are the most studied parts due to their richness in secondary metabolites [16–19]. Principal compounds found in different parts of C. intybus include inulin, chicoric acid, ellagic acid, flavonoids, esculetin, anthocyanins, and caffeoylquinic acid. These compounds are associated with specific pharmacological effects, including antioxidant, anticancer, antimicrobial, anti-inflammatory, and wound-healing activities [20–22]. The list of isolated compounds from different parts of the plant is summarized in Table **4**.

Table 3: Traditional applications of *Cichorium intybus.*

Country	Plant parts	Uses	References
Pakistan	Roots	Diabetes	[10]
Iran	Whole plant	Stomach problems Hypotensive Choleretic Laxative Antipyretic	[10, 11]
Turkey	Leaves Roots Aerial	Wound healing Cancer Kidney problems Urinary disorders	[3]
India	Whole plant Seeds Roots	Diabetes Liver disorders Gout and rheumatism	[3]
Afghanistan	Roots	Malaria	[10]
Italy	Leaves/ Roots	Blood purification Hypotensive Arthritis Digestive problems	[10]
Jordan	Whole plant	Sedation in typhoid Hemorrhage	[10, 13]
Morocco	Whole plant	Kidney disorders Diabetes	[3]
Poland	Roots in form of tea	Digestive disorders Loss of appetite	[3]
South Africa	Stem, leaves, and roots	Jaundice	[3]
Bulgaria	Roots/aerial parts	Diabetes	[10]

Table 4: Phytochemicals found in *Cichorium intybus*.

Plant part	Phytochemical constituents	Reported pharmacological activities	References
Flower	Polyphenols, glucosides, minerals, vitamins, chicorine, flavonoids, saccharides, delphinidin-3,5-di-O-(6-O-malonyl-β-D-glucoside), and delphinidin	Antioxidant, hepatoprotective, and anti-inflammatory activities attributed to flavonoids and delphinidin derivatives	[16–18]
Leaves	Fatty acids, pigments, polyphenols, flavonoids, and phenolic acids (chlorogenic, caffeic acid, caftaric acid, chicoric, quercetin glucuronide, gallic acids)	Antidiabetic, anti-inflammatory, and lipid-lowering effects linked with phenolic acids and flavonoids	[5, 10, 19]
Seed	Flavonoids, saponins, glycosides, oils, carbohydrates, gums, fatty acids, minerals, amino acids, and terpenoids	Antioxidant, hepatoprotective, and antimicrobial properties mainly associated with flavonoids and saponins	[3, 20, 21]
Root	Alkaloids, volatile oils, fatty acids, emodin, flavonoids, triterpenoids, anthracene glycosides, tannins, phenolic compounds, and saponins	Antioxidant, anti-inflammatory, and gastroprotective activities correlated with triterpenoids, emodin, and phenolic compounds	[5, 20, 22]

3.4. Pharmacological activities

Cichorium intybus has a long history of traditional use in managing a variety of health disorders. Over the years, its therapeutic potential has been extensively investigated and validated through a range of experimental approaches, including in vitro, in silico, and in vivo studies. These studies have provided valuable insights into the plant's bioactive compounds and their mechanisms of action. A comprehensive summary of the findings from previous research is presented in Table **5**.

3.5. Antibacterial effect

To date, several investigations have assessed *C. intybus's* antibacterial activity against various microorganisms. One study evaluated the antibacterial effects of different extracts of *C. intybus* [23]. Various alcoholic extracts from different plant parts, including seeds, leaves, and stems, were prepared and evaluated for their antibacterial potential. Moreover, multiple test organisms were selected for the study, which included *Pseudomonas aeruginosa*, *Proteus vulgaris*, Enterobacter species, *Escherichia coli*, *Streptococcus faecalis*, *Staphylococcus aureus*, Klebsiella species, and Lactobacillus species. These microorganisms were previously collected from human lesions and tested against various concentrations of plant extract, such as 25, 50, 100, 200, 400, 800, and 1000 mg/mL. The concentration of methanolic extract from plant leaves that showed the most antibacterial activity against a range of microorganisms was 1000 mg/mL. These organisms included Klebsiella species, *S. faecalis*, *P. vulgaris*, *P. aeruginosa,* and Lactobacillus species, with a zone of inhibition exceeding 12 mm. At the same time, Enterobacter species and *E. coli* emerged with minimum inhibition even at the maximum dose of 1000 mg/mL. To summarize, the study revealed that a high dose of the methanolic extract of *C. intybus* exhibited beneficial antimicrobial effects against various bacterial strains [23].

Another study involved preparing nanocomposites from *C. intybus* root extract [24]. These extracts were incorporated into a chitosan nanofiber system and tested for antibacterial activity against *E. coli* and *S. aureus*. The results showed that the ethanolic extract produced promising antibacterial effects [24]. In a different study, the efficacy of *C. intybus* against various bacterial strains was investigated. A methanolic extract was prepared and tested for its antibacterial potential using

the agar well diffusion method against different bacterial strains. The aerial parts of the plants were incubated on agar plates, which showed antibacterial effects with zones measuring up to 10.62 ± 0.33, 12.62 ± 1.44, 6.81 ± 0.63, 14.84 ± 1.42, 10.28 ± 1.30, 8.32 ± 0.14, and 10.22 ± 1.12 mm for *Salmonella enteritidis*, *K. pneumoniae*, *Enterococcus aerogenes*, *E. coli*, *Bacillus subtilis*, and *Listeria monocytogenes*, respectively. The findings indicate that *C. intybus* possesses notable antibacterial potential; however, it cannot yet be regarded as a substitute for conventional antibiotics. Further *in vivo* and clinical investigations are required to substantiate its efficacy and safety [25].

Cichorium intybus yielded five bioactive fractions, with Fractions I and II isolated from ethyl acetate and Fractions III–V from ethanol. In antibacterial assays, several fractions showed strong effects, sometimes superior to those of standard antibiotics. Fraction I reached 26 mm zones of inhibition against *Neisseria pharyngis* and *Neisseria mucosa* at 200 µg/mL, while Fraction II produced remarkable inhibition of up to 35 mm against *E. corrodens* at 50 µg/mL and 25 mm against *N. pharyngis* at 100 µg/mL. Fraction III had the broadest action, achieving 35 mm inhibition against *N. pharyngis* and *M. cerebrosus* at 100 µg/mL. Fraction IV was more selective, showing 35 mm inhibition against *N. pharyngis* at 100 µg/mL, while Fraction V consistently demonstrated high potency with 35 mm zones against *N. pharyngis* at 100 µg/mL and 30 mm against *N. mucosa* at 200 µg/mL.

In comparison, standard antibiotics like ampicillin and cephriaxim yielded only 12–13 mm or no activity (R). Beyond antibacterial effects, the fractions also showed strong antioxidant capacity. Fractions I and II recorded values of 22.36 at 30 ppm, while Fraction V exhibited the most pronounced activity, rising from 35.65 at 30 ppm to 76.44 at 120 ppm, and continuing to increase at 250 ppm. These results highlight that both the antibacterial and antioxidant potential of *C. intybus* fractions are noteworthy, supporting their possible therapeutic application in combating bacterial infections and oxidative stress [26]. The methanolic extracts of *C. intybus* showed the strongest antibacterial effects, particularly the 80% methanol fraction, which produced inhibition zones of 22 ± 1.14 mm against *S. aureus* and 20 ± 1.21 mm against *E. coli*. Absolute methanol also demonstrated good activity, though slightly lower. Ethanol extracts were moderately effective, while aqueous extracts displayed the weakest inhibition across all tested bacteria. Overall, methanol proved to be the most efficient solvent for extracting antibacterial compounds from the plant [27].

3.6. Antidiabetic effect

A previous study investigated the antidiabetic effects of *C. intybus* [28]. The study used an ethanol extract from the plant's leaves. Four different compounds were selected for further studies after the phytochemical screening of the plant extract. Docking studies were conducted to investigate the anti-diabetic effects of a plant ethanolic extract. The targeted protein was taken as human aldose reductase. The study demonstrated that the plant extract exhibited significant inhibitory potential, with IC_{50} values of 38 µg and 88 µg against α-amylase and α-glucosidase, respectively.

In contrast, acarbose was taken as a standard. Thus, plant ethanol extract showed considerable antidiabetic potential [28]. In another study, researchers experimented to evaluate the antidiabetic effect of *C. intybus* on its *n*-hexane extract

[29]. After preparing the extract, it was assessed for insulin and glycated hemoglobin levels in diabetic neuropathy in animals. Results indicated that hypoglycemic effects were generated in the range of 14.15% to 42.4%. Thus, the extract showed adequate hypoglycemic potential [29].

3.7. Analgesic effect

A study has examined the analgesic effect of *C. intybus* [30]. An *in vivo* study was carried out on mice induced with analgesia. The study was conducted on three compounds obtained from plants: lactucopicrin, lactucin, and 13-dihydrolactucin, at a dose of 30 mg/kg. A tail-flick and hot-plate test apparatus was used for experimentation. Ibuprofen was administered at a standard dose of 60 mg/kg. Test results indicated that these compounds exhibit remarkable pain-relieving activity in mice. Additionally, lactucin and lactucopicrin had sedative effects, decreasing animal locomotor activity [30].

3.8. Anticancer effect

The *in vitro* anticancer effect of the methanolic extract of the root of *C. intybus* on human breast cell lines has been explored. Rahimipour *et al.* used the SKBR3 cell line in their investigation to assess the impact of a plant methanolic extract on survival rate [31]. Dulbecco's Modified Eagle Medium (DMEM) was a culture medium for the human breast SKBR3 cell line. Different dilutions of root extract were added to the culture medium, ranging from 200 to 600 µg/mL. However, the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay was performed at 24, 48, and 72 hours of incubation. Outcomes revealed that the root extract displayed effective cytotoxic potential after the periods mentioned above, with an IC_{50} value of 800 after 24 hours and 400 after 48 hours, while the IC_{50} was concluded to be 300 after 72 hours of study. Thus, the methanolic extract was found to be significantly effective against breast cell lines [31]. Another study revealed the anticancer potential of *C. intybus* [32]. Due to the presence of various potentially important phytochemicals, the plant was assessed for its *in vitro* cytotoxic potential. For this, various hydroalcoholic extracts were employed, and results indicate that the hydroalcoholic extract of the leaf of the plant was found to be effective against prostate cancer, with an IC_{50} value of 3.67 ± 0.12. In contrast, the root extract showed an excellent cytotoxic effect against breast cell lines with an IC_{50} of 12.65 ± 0.26. The dose of plant extract was maintained at 100 µg/mL [32].

3.9. Hepatoprotective effect

Multiple studies have investigated the hepatoprotective potential of *C. intybus* using its various parts. A study was conducted on the hydroalcoholic extract of plant seeds to assess its effect against carbon tetrachloride (CCl_4)-induced hepatotoxicity. An *in vivo* study was done on albino rats. Seeds were used to prepare the hydromethanolic extract for further studies. Animals were given a hepatotoxic dose of CCl_4 at 0.8 mL/kg. For this treatment, seeds were employed through Soxhlet extraction, and the seed extract was administered orally at different doses of 100, 250, and 500 mg/kg. However, silymarin was administered at a standard dose of 25 mg/kg to the animals. After experimentation and dosing of the animals, blood samples were taken from Wistar rats 14 days later.

Furthermore, these samples underwent further examination of biochemical markers for hepatic toxicity. The findings showed that the plant's seed extract, administered at 500 mg/kg, displayed the highest levels of hepatic biomarkers. Levels of catalase, glutathione peroxidase, and superoxide dismutase were remarkably elevated at concentrations of 48.90 μmol, 22.1 mg, and 14.2 units, respectively, while the glutathione level showed a decline to 18.1 μmol. Therefore, plant seed extract was observed to be effective against hepatotoxic effects by providing hepatoprotection [33–36].

Asadi *et al.* assessed the protective effect of *C. intybus* on methotrexate-induced oxidative stress in test animals [37]. Rats were divided into two groups: a positive control and a negative control. The rats in the positive control group received normal saline followed by a single dose of the drug, while the treatment group received a 70% hydroethanolic extract of *C. intybus*, whole plant, orally at doses of 100, 200, and 400 mg/kg. After 11 days, blood samples were collected, and the animals were dissected for histopathological examination. Various liver biomarkers, such as alanine aminotransferase (ALT), aspartate aminotransferase (AST), total bilirubin (TB), alkaline phosphatase (ALP), superoxide dismutase (SOD), and catalase (CAT), were measured. Results showed a significant reduction in biomarkers, especially at a dose of 400 mg/kg. Therefore, hydroethanolic *C. intybus* demonstrated hepatoprotective effects against liver damage [37].

3.10. Antiviral effect

Due to the presence of caffeic acid, *C. intybus* is believed to have an antiviral effect. The literature has extensively studied its antiviral effects against various viruses. *Cichorium intybus* and several other physiologically active plants were tested for their ability to inhibit the coronavirus (SARS-CoV-2) through antiviral activity. Molecular docking was employed to examine the antiviral effects of plants, with docking performed against viral proteins including papain-like protease, RNA-dependent RNA polymerase, and 3-chymotrypsin protease. Results showed that plants exhibited notable targets, such as different components, and were able to normalize body functions by generating therapeutic action in the alleviation of disease [38, 39].

3.11. Antioxidant effect

Antioxidant activity is one of chicory's most notable and significant features. This effect is primarily attributed to the abundance of polyphenolic compounds. In particular, sesquiterpene lactones—especially lactucin—act as potent cyclooxygenase inhibitors, while certain flavonoids further contribute to the pronounced anti-inflammatory activity of this medicinal herb [40, 41]. The flavonoids and phenolic acids found in the leaves of *C. intybus* exhibit strong antioxidant activity, primarily attributed to the hydroxyl groups in their chemical structures. These compounds play a crucial role in protecting the body's defense system against oxidative damage caused by endogenous free radicals [42].

3.12. Antifungal effect

Cichorium intybus has been studied in several investigations to assess its antifungal effects against various strains. A study investigated *the* anti-fungal potential of C. intybus in its crude extract against four fungal strains: *Aspergillus fumigatus*, *Fusarium solani*, *Aspergillus flavus,* and

Aspergillus niger [43]. The test was performed using the standard method for various fractions of crude extract and solvent fractions. The solvent fractions included ethanol, *n*-hexane, ethyl acetate, aqueous, and chloroform. The agar tube dilution method was used to inoculate fungal strains onto Sabouraud dextrose agar, which served as the culture medium. Gentamycin was taken as a standard. Out of various fractions, the ethyl acetate and aqueous fractions emerged with promising outcomes against all four fungal strains. In contrast, the chloroform fraction exhibited the highest antifungal activity against *F. solani*. As a result, *C. intybus* demonstrated its efficacy in treating and curing antifungal infections caused by the strains above [43].

3.13. Hypotensive effect

The effect of the hydroalcoholic leaf extract of *C. intybus* on the blood pressure of rats has been evaluated. An *in vivo* study was conducted by Sedighi and colleagues, who grouped the test animals appropriately [44]. Rats in the control group received normal saline and various doses of the extract (25, 50, and 100 mg/kg). Meanwhile, biochemical parameters were assessed using a PowerLab. Outcomes revealed a considerable decline in diastolic, median, and systolic arterial pressure in the treated group at a dose of 50 mg/kg. Thus, it is concluded that plant extract exhibited a notable cardioprotective effect against high blood pressure [44].

3.14. Effect on the immune system

Karimi and coworkers examined the role of *C. intybus* plant extract in immune-mediated disorders [45]. The study utilized an ethanolic extract from the roots of *C. intybus* and evaluated its impact on the dendritic cells of mice. Thus, low doses of plant extract cause elevated generation of interleukin 12 without altering the liberation of interleukin 10. At the same time, high doses resulted in a decline in allogeneic T cell proliferation by reducing the level of interleukin-4 and elevating the level of γ-TNF [45].

3.15. Anti-inflammatory effect

Previously, *C. intybus* was successfully prescribed for the treatment of skin diseases, including inflammation of mucosal membranes, dermatitis, ulcers, and wounds. It was believed that the floral infusion of the plants could help cure inflamed skin and eyes. The plant was well known for its role in treating eczema and wound healing. It was also involved in managing periocular circulation by reducing puffiness and signs associated with eye tiredness [5, 46].

A study was conducted to validate the anti-inflammatory potential of the root extract of *C. intybus,* based on its ability to inhibit several cytokines and its antioxidant activity. The study used aqueous and ethanolic extracts of *C. intybus* roots to evaluate their anti-inflammatory effects. An *in vivo* experiment was conducted on Wistar rats to assess the anti-inflammatory potential. Furthermore, levels of interleukin 1, interleukin 6, and α-TNF were measured along with glutathione and catalase activity. Findings reported a dose-dependent decline in carrageenan-induced paw edema, while interleukin and α-TNF levels were also reduced. Furthermore, catalase activity was remarkably increased. Thus, the plant's root extract demonstrated remarkable anti-inflammatory properties [41, 42, 47].

3.16. Antineurotoxic effect

Hasannejad *et al.* investigated the antineurotoxic potential of *C. intybus*, which may be due to the presence of numerous glycosides and terpenoids. Mainly, glutamate and GABA are considered potential neurotransmitters involved in neural pathways. Thus, *C. intybus* was found to reduce glutamatergic transmission, thereby elevating GABAergic transmission. The experiment was carried out by inducing neuropathy in rats via intraperitoneal injection of pyridoxine at a dose of 800 mg/kg. After 14 days, behavioral testing was conducted using the foot fault, hot plate, and rotarod tests. Hydromethanolic extract (96%) from the roots of *C. intybus* was employed for the study. Test animals were administered the plant extract at a dose of 50 mg/kg via intraperitoneal injection. Levels of α-TNF were measured by *enzyme-linked immunosorbent assay* (ELISA). Results showed a neuropathic effect in the sciatic nerve and on dorsal root ganglion neurons, as measured by histopathological imaging. The root extract of *C. intybus* caused improvement in behavioral testing and decreased the levels of α-TNF. In this study, picrotoxin was used as a standard. Thus, plant extract showed excellent positive outcomes by modulating the GABAergic system [48].

3.17. Wound healing

Kaçmaz *et al.* investigated the wound-healing potential of various extracts from different parts of *C. intybus*, including the root, stem, flower, and herba. Using *in vitro* scratch and cell migration assays, the extracts were analyzed for efficacy. The stem extracts, except for the hexane extract, showed significant healing effects, with chlorogenic acid identified as the main active component. These results support traditional medicinal uses of chicory for wound treatment. Further research is recommended to understand the active compounds and mechanisms involved [49].

3.18. Effect on fertility

Babenko *et al.* investigated the effects of *C. intybus* extract on male reproductive health and offspring development in rats. Male rats were orally administered the extract at varying doses for 60 days. The extract treatment significantly enhanced sperm quality, seminiferous tubule diameter, spermatogenic index, and testosterone levels. It also reduced embryo pre- and post-implantation loss without affecting normal pup development. The findings suggest CE may be a safe and effective phytodrug for improving male fertility [50].

3.19. Clinical studies

Clinical trials investigating *C. intybus* have explored diverse populations, ranging from osteoarthritis and diabetes to liver disorders and hematological conditions (Table **6**). In patients with knee osteoarthritis, a 3% hydroalcoholic *C. intybus* gel applied topically was found to significantly reduce pain and stiffness, while improving function, with results comparable to those of diclofenac gel. No serious adverse events were reported. Similarly, in type 2 diabetes mellitus, chicory seed extract, when used as an adjunct to metformin, lowered glycated hemoglobin (HbA1c), improved oxidative stress markers, and had a favorable effect on triglyceride levels. However, the relatively small sample size limited the robustness of the findings. In

transfusion-dependent β-thalassemia, the administration of chicory syrup for 8 weeks resulted in a significant reduction in serum ferritin and ALT levels, suggesting potential hepatoprotective and iron-chelating effects. However, results in neonatal jaundice were less encouraging, as consuming chicory aroma water during pregnancy showed no significant impact on bilirubin levels or the need for phototherapy. For non-alcoholic fatty liver disease (NAFLD), chicory seed infusion alone reduced BMI and waist circumference, and in combination with turmeric, improved lipid ratios and liver enzymes. In contrast, brewed chicory leaf initially showed biochemical improvements but led to adverse metabolic effects, necessitating early trial termination. Collectively, these findings indicate chicory's therapeutic promise, though trial quality, sample sizes, and duration varied, with some concerns of bias and safety signals in specific interventions [51–56].

3.20. Risk of bias assessment

The included *in vivo* animal studies were evaluated using SYRCLE's Risk of Bias tool, which considers selection bias, performance bias, detection bias, attrition bias, reporting bias, and other sources of bias. Across the studies, common limitations included a lack of explicit randomization procedures, unclear blinding of outcome assessors, and small sample sizes.

For the *in vitro* and docking studies, no standardized, universal tool exists; therefore, the risk of bias was assessed using adapted criteria that focused on methodological rigor. These criteria included adequacy of control groups, reproducibility of experimental conditions, use of appropriate positive and negative controls, and transparent reporting of results. *In silico* docking studies additionally carried a risk of overinterpretation due to reliance on computational predictions without confirmatory biological validation (Table **5**).

For clinical studies, the Cochrane Risk of Bias 2 (RoB 2) tool was used to assess domains including randomization process, deviations from intended interventions, missing outcome data, measurement of outcomes, and selective reporting. Clinical evidence was generally more reliable than preclinical studies, but risks persisted, particularly due to small sample sizes, short intervention durations, and heterogeneity in outcome measures (Table **6**).

Overall, animal studies raised moderate concerns, primarily due to incomplete reporting of randomization and blinding. In contrast, *in vitro* and docking studies demonstrated a higher risk of bias, owing to limited reproducibility and a lack of standardized validation. Clinical studies, although stronger in methodological design, still raised concerns about sample size limitations and variability in reporting standards.

Table 5: Pharmacological effects of *Cichorium intybus*.

Study	Design & model	Plant part/preparation	Dose/exposure	Key findings	Key limitations/bias	Level of evidence	Reference
Antibacterial activity	*In vitro*	Leaves, seeds, stems; methanolic extracts	25–1000 mg/mL	Strong inhibition (>12 mm) at 1000 mg/mL vs. *Klebsiella*, *S. faecalis*, *P. vulgaris*, *P. aeruginosa*, *Lactobacillus*; weak vs. *Enterobacter*, *E. coli*.	Very high doses; crude extracts; clinical relevance uncertain.	Moderate (*in vitro*)	[23]

Table 5: Continued.

Study	Design & model	Plant part/preparation	Dose/exposure	Key findings	Key limitations/bias	Level of evidence	Reference
	In vitro	Root ethanolic extract in chitosan nanofiber	Not specified	Ethanolic nanocomposites active vs. *E. coli* & *S. aureus*.	No standardized dose; preliminary; lacks toxicity data.	Low (*in vitro* – preliminary)	[24]
	In vitro	Aerial parts; methanolic extract	Not specified	ZOI 6.81–14.84 mm; best vs. *K. pneumoniae* & *E. coli*.	No control drug; only moderate inhibition; MIC not reported.	Moderate (*in vitro*)	[25]
	In vitro (fractionation)	Fractions I–V (ethyl acetate: I–II; ethanol: III–V)	25–200 µg/mL	Fractions II–V showed strong inhibition (up to 35 mm vs. *N. pharyngis*); Fraction V strongest antioxidant (76.44 at 250 ppm).	*In vitro* only; no toxicity/clinical data.	Moderate (*in vitro*)	[26]
	In vitro (solvent comparison)	Whole plant; methanol, ethanol, water	Extracts tested	80% methanol strongest: 22 mm (*S. aureus*), 20 mm (*E. coli*).	MIC not reported; aqueous weak.	Moderate (*in vitro*)	[27]
	In vitro + *in silico*	Leaves; ethanolic extract	IC_{50}: 38 µg (α-amylase), 88 µg (α-glucosidase)	Significant enzyme inhibition vs. acarbose.	No *in vivo* validation.	Low (preliminary *in vitro*/*in silico*)	[28]
Antidiabetic	*In vivo* (rats, diabetic neuropathy)	n-Hexane extract	Not specified	Hypoglycemic effect 14–42%; improved insulin & HbA1c.	Dose not detailed; short-term; animal only.	Moderate (preclinical – animal)	[29]
Analgesic	*In vivo* (mice, analgesic tests)	Lactucopicrin, lactucin, 13-dihydrolactucin	30 mg/kg; ibuprofen control	Strong analgesic effects; sedative effect noted.	Sedation limits therapeutic window; animal model only.	Moderate (preclinical – animal)	[30]
Anti-cancer	*In vitro* (MTT assay)	Root methanolic extract	200–600 µg/mL	Time-dependent cytotoxicity; IC_{50} = 800 µg (24h), 300 µg (72 h).	High IC_{50}; single cell line; no *in vivo* validation.	Low (*in vitro*)	[31]
	In vitro (cytotoxicity)	Hydroalcoholic extracts (leaves, roots)	100 µg/mL	Leaf effective vs. prostate (IC_{50} 3.67), root vs. breast cancer (IC_{50} 12.65).	High extract dose; mechanism unclear.	Low (*in vitro*)	[32]
Hepatoprotective	*In vivo* (rats, hepatotoxicity)	Seeds; hydromethanolic extract	100–500 mg/kg (oral)	500 mg/kg improved catalase, GPx, SOD; reduced GSH; hepatoprotective effect.	High dose; only in rats; short study (14 days).	High (preclinical – animal)	[33–36]
	In vivo (rats, methotrexate hepatotoxicity)	Whole plant; 70% hydroethanolic extract	100–400 mg/kg (oral)	400 mg/kg reduced biomarkers, improved histology.	No long-term follow-up; animal only.	High (preclinical – animal)	[37]
Antiviral	*In silico* (molecular docking)	Whole plant phytochemicals (e.g., caffeic acid)	Docking with SARS-CoV-2 proteases	Showed potential binding to papain-like protease, RdRp, 3CLpro.	No experimental validation; purely computational.	Very low (*in silico* only)	[38, 39]
Antioxidant	*In vitro* (antioxidant assays)	Leaves; flavonoids, phenolic acids	Not specified	Strong free-radical scavenging; lactucin inhibits COX.	*In vitro* only; needs *in vivo* confirmation.	Moderate (*in vitro*)	[40–42]

Table 5: Continued.

Study	Design & model	Plant part/preparation	Dose/exposure	Key findings	Key limitations/bias	Level of evidence	Reference
Antifungal	*In vitro* (antifungal)	Crude extract + solvent fractions (ethyl acetate, aqueous, chloroform, etc.)	Not specified	Ethyl acetate & aqueous active vs. all; chloroform strongest vs. *F. solani*.	No MIC data; crude extracts.	Moderate (*in vitro*)	[43]
Hypotensive	*In vivo* (rats, hypotensive study)	Leaf hydroalcoholic extract	25–100 mg/kg	At 50 mg/kg reduced systolic, diastolic, and mean arterial pressure.	Small animal study; no mechanistic biomarkers.	High (preclinical – animal)	[44]
Immunomodulation	*In vitro* + *in vivo* (mice immune cells)	Root ethanolic extract	Low vs. high dose	Low dose ↑ IL-12; high dose ↓ IL-4, ↑ TNF-γ; suppressed T cell proliferation.	Dose-dependent effects not mechanistically clear.	Moderate (preclinical)	[45]
Anti-inflammatory	*In vivo* (rats, carrageenan paw edema)	Root aqueous/ethanolic extracts	Not specified	Dose-dependent reduction in edema, ↓ IL-1, IL-6, TNF-α; ↑ catalase.	No human validation; mechanism partly inferred.	High (preclinical – animal)	[46, 47]
Antineurotoxic	*In vivo* (rats, pyridoxine neurotoxicity)	Root hydromethanolic (96%) extract	50 mg/kg i.p.	Improved behavior (rotarod, hot plate); ↓ TNF-α; modulated GABAergic pathways.	Small sample; i.p. route less relevant clinically.	Moderate (preclinical – animal)	[48]
Wound healing	*In vitro* (scratch assay, cell migration)	Root, stem, flower, herba extracts	Not specified	Stem extracts (except hexane) accelerated wound closure; chlorogenic acid identified.	Only *in vitro*; no animal/human validation.	Low (*in vitro*)	[49]
Fertility	*In vivo* (rats, fertility)	Whole extract	Oral, 60 days	Improved sperm quality, seminiferous tubule diameter, testosterone; ↓ embryo loss.	Only in male rats; no long-term safety data.	High (preclinical – animal)	[50]

ALT, alanine aminotransferase; AST, aspartate aminotransferase; ALP, alkaline phosphatase; TB, total bilirubin; SOD, superoxide dismutase; CAT, catalase; GPx, glutathione peroxidase; TNF-α, tumor necrosis factor alpha; IL, interleukin; IC50, half maximal inhibitory concentration; DMEM, Dulbecco's Modified Eagle Medium; MTT, 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide assay; CCl_4, carbon tetrachloride; ELISA, enzyme-linked immunosorbent assay; GABA, gamma-aminobutyric acid; SKBR3, human breast cancer cell line; PLpro, papain-like protease; RdRp, RNA-dependent RNA polymerase; 3CLpro, 3-chymotrypsin-like protease; ROS, reactive oxygen species; CE, chicory extract.

Table 6: Clinical studies of *Cichorium intybus*.

Study (Author/Year)	Population & sample size	Intervention (dose, duration)	Comparator	Outcomes	Key findings	Risk of bias	Reference
Topical gel for knee OA (Ansaripour *et al.*, 2025)	150 patients with moderate–severe knee OA	3% hydroalcoholic *C. intybus* gel, fingertip unit/25 cm^2, 3×/day, 6 days	Diclofenac gel & placebo	Pain (VAS), WOMAC (pain, stiffness, function)	Both *C. intybus* and diclofenac gels reduced pain, stiffness, and improved function ($P < 0.001$ vs. placebo). No serious adverse effects.	Low risk	[51]

Table 6: Continued.

Study (Author/Year)	Population & sample size	Intervention (dose, duration)	Comparator	Outcomes	Key findings	Risk of bias	Reference
Seed extract for T2DM (Chandra *et al.*, 2020)	100 T2DM patients on metformin	Aqueous extract of *C. intybus* seeds, 12 weeks	Placebo	HbA1c, inflammation, oxidative stress, lipids	HbA1c ↓ 1.18% vs 0.1% placebo, improved oxidative stress, triglycerides ($P < 0.05$). Safe as adjunct therapy.	Some concerns – small sample	[52]
β-Thalassemia (Ansari *et al.*, 2025)	110 transfusion-dependent β-thalassemia patients	Chicory syrup, 8 weeks	Placebo	Serum ferritin, ALT	Significant ↓ in ferritin (918 vs. 799 ng/ml; $P = 0.04$) and ALT ($P = 0.019$).	Some concerns – short duration	[53]
Neonatal jaundice (Pasalar *et al.*, 2017)	80 pregnant women (to assess neonatal outcome)	Chicory aroma water during pregnancy	Usual diet (control)	Neonatal bilirubin, phototherapy need	No significant benefit on bilirubin or phototherapy ($P > 0.05$).	Low risk	[54]
NAFLD – turmeric + chicory (Ghaffari *et al.*, 2019)	92 NAFLD patients	Chicory seed infusion (9 g/day), turmeric (3 g/day), combo, 12 weeks	Placebo	BMI, WC, liver enzymes, lipid profile	Chicory ↓ BMI/WC, combo ↓ ALP, improved HDL-C, TG/HDL-C ratio.	Low risk	[55]
NAFLD – brewed chicory leaf (Iran)	60 NAFLD patients	Brewed chicory leaf (15 g), 12 weeks (stopped at 6 weeks)	Usual care	Liver enzymes, CBC, metabolic markers	↓ ALT, AST, bilirubin; ↑ RBC, platelets, Hb, FBS, LDL, cholesterol; adverse side effects → trial stopped early.	High risk – terminated early	[56]

OA, osteoarthritis; VAS, Visual Analogue Scale; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index; T2DM, type 2 diabetes mellitus; HbA1c, glycated hemoglobin; ALT, alanine aminotransferase; NAFLD, non-alcoholic fatty liver disease; CAW, chicory aroma water; BMI, body mass index; WC, waist circumference; ALP, alkaline phosphatase; HDL-C, high-density lipoprotein cholesterol; TG, triglycerides; RBC, red blood cells; Hb, hemoglobin; FBS, fasting blood sugar; LDL, low-density lipoprotein; CBC, complete blood count; RoB, risk of bias.

4. Limitations and Recommendations

While this review brings together valuable information on *C. intybus*, it also has some limitations. Most of the available studies focus on basic pharmacological activities, with limited clinical evidence to support their therapeutic use. In addition, the safety profile, standardized dosages, and long-term effects of the plant remain underexplored. Future research should fill these gaps by conducting well-designed clinical trials, conducting deeper mechanistic studies, and further isolating and standardizing its active compounds.

5. Conclusion

Cichorium intybus is a rich source of several phytochemicals, which are responsible for the plant's therapeutic properties, including antibacterial, antidiabetic, anti-inflammatory, cardioprotective, hepatoprotective, antiviral, and antifungal effects. This review adds novelty by bringing together scattered findings on *C. intybus* and presenting them in a more connected way. Among its different parts, the flowers and leaves are the most widely studied and hold the greatest medicinal value.

Acknowledgements

None.

Ethical Considerations

Not applicable.

Competing Interests

The author/editor has no conflicts of interest, financial or otherwise, to declare.

Availability of Data and Materials

The datasets used and/or analyzed in this study are available from the corresponding author upon reasonable request.

Funding

None.

Abbreviations and Symbols

3CLpro: 3-Chymotrypsin-like protease

ALP: Alkaline phosphatase

ALT: Alanine aminotransferase

AST: Aspartate aminotransferase

BMI: Body mass index

CAW: Chicory aroma water

CAT: Catalase

CBC: Complete blood count

CCl_4: Carbon tetrachloride

CE: Chicory extract

DMEM: Dulbecco's Modified Eagle Medium

ELISA: Enzyme-linked immunosorbent assay

FBS: Fasting blood sugar

GABA: Gamma-aminobutyric acid

GPx: Glutathione peroxidase

Hb: Hemoglobin

HbA1c: Glycated hemoglobin

HDL-C: High-density lipoprotein cholesterol

IC50: Half maximal inhibitory concentration

IL: Interleukin

LDL: Low-density lipoprotein

MTT: 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide assay

NAFLD: Non-alcoholic fatty liver disease

OA: Osteoarthritis

PLpro: Papain-like protease

PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses

RBC: Red blood cells

RdRp: RNA-dependent RNA polymerase

RoB: Risk of bias

ROS: Reactive oxygen species

SKBR3: Human breast cancer cell line

SOD: Superoxide dismutase

TB: Total bilirubin

TG: Triglycerides

T2DM: Type 2 diabetes mellitus

TNF-α: Tumor necrosis factor alpha

VAS: Visual Analogue Scale

WC: Waist circumference

WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index

AI Use Disclosure

The authors declare that no generative artificial intelligence (AI) tools were used in the writing, data analysis, figure generation, or editing of this manuscript.

Author Contributions

Concepts, literature search: KA, KAS; Clinical studies, experimental studies: Not applicable; Data acquisition, analysis, statistical analysis: KAS, KA, SAS, AB; Manuscript preparation, editing, review: KAS, KA, SAS, AB. All authors participated equally in this research and approved the final manuscript.

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