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Chicory (*Cichorium intybus* L.) as a Multifunctional Medicinal Plant

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Cichorium intybus L., commonly known as chicory, is a widely distributed medicinal plant belonging to the Asteraceae family. It has been traditionally used in folk medicine to treat liver, digestive, inflammatory and metabolic disorders. In recent decades, it has attracted considerable scientific attention due to its rich phytochemical composition and exceptionally broad spectrum of biological activities. This review summarises the latest research on the botanical characteristics, phytochemical diversity and pharmacological properties of *C. intybus*, focusing on its antioxidant, anti-inflammatory, immunomodulatory, antimicrobial, antiviral, antiparasitic, hepatoprotective, antidiabetic, cardioprotective, neuroprotective and antitumour effects. These activities are primarily attributed to polyphenols, flavonoids, phenolic acids, sesquiterpene lactones and inulin, which act synergistically to regulate oxidative stress, inflammatory responses, immune functions and key metabolic pathways. Other minor constituents, such as coumarins, sterols, terpenoids, and volatile compounds, also contribute to the plant's pharmacological profile. Evidence from *in vitro*, *in vivo* and clinical studies suggests that chicory extracts and isolated compounds have significant therapeutic potential in treating various pathological conditions, including diabetes, liver disease, infections, cardiovascular disorders and cancer. Importantly, emerging data also highlight its role in modulating gut health, endothelial function and neuroinflammatory processes, thereby expanding its relevance beyond traditional applications. While the accumulated evidence strongly supports the pharmacological importance of *C. intybus*, further standardised clinical trials, studies to optimise dosage, and investigations into its mechanisms are required to validate its efficacy, safety, and therapeutic potential in evidence-based medicine.

Keywords: chicory; phytochemicals; antioxidant activity; anti-inflammatory effects; hepatoprotection; medicinal plants

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Introduction

Cichorium intybus L., commonly known as chicory, is a perennial herb belonging to the Asteraceae family. It is widely distributed across Europe, Asia, and North America (Street et al., 2013). It has traditionally been used in various folk medicines as a digestive aid, a liver protector, an anti-inflammatory, and a tonic. Different parts of the plant, including the roots, leaves, flowers and seeds, are consumed as food or used in herbal remedies, reflecting its long-standing importance in nutrition and phytotherapy (Bais and Ravishankar, 2001). In recent years, chicory has attracted considerable scientific interest due to its rich phytochemical profile and wide range of biological activities (Street et al., 2013; Perović et al., 2021; Janda et al., 2021; Birsa and Sarbu, 2023).

The pharmacological properties of *C. intybus* are primarily attributed to its diverse array of bioactive compounds, including polyphenols, flavonoids, phenolic acids (such as caffeic acid, chlorogenic acid, and chicoric acid), sesquiterpene lactones, and anthocyanins (Street et al., 2013; Birsa and Sarbu, 2023; Azad et al., 2026). These metabolites are known to exert strong antioxidant effects and play a central role in modulating oxidative stress, inflammation, and cellular signalling pathways. The complexity of its phytochemical composition suggests that its therapeutic effects result from the combined action of multiple constituents rather than from a single active compound (Birsa and Sarbu, 2023; Azad et al., 2026).

Oxidative stress and chronic inflammation are key pathological mechanisms underlying many modern diseases, including cardiovascular disorders, diabetes, liver disease, cancer and neurodegenerative conditions (Liu et al., 2025). In this context, plant-derived antioxidants and anti-inflammatory agents have become important potential preventive and therapeutic tools. Chicory has been extensively investigated in this regard, and numerous studies have confirmed its ability to scavenge free radicals, inhibit lipid peroxidation, and modulate pro-inflammatory mediators, including cytokines and enzymes involved in inflammatory cascades (Rizvi et al., 2014; Janda et al., 2021).

In addition to its antioxidant and anti-inflammatory properties, chicory exhibits notable immunomodulatory activity. Experimental studies have demonstrated its ability to regulate innate and adaptive immune responses by influencing cytokine production, lymphocyte proliferation and macrophage activity (Karimi et al., 2014; Rizvi et al., 2014). These effects suggest that *C. intybus* may help maintain immune homeostasis and enhance resistance to infections and inflammatory disorders (Janda et al., 2021; Azad et al., 2026). Furthermore, its antimicrobial, antiviral and antiparasitic properties reinforce its relevance in the management of infectious diseases (Street et al., 2013; Perović et al., 2021; Janda et al., 2021; Birsa and Sarbu, 2023).

Another important area of research into *C. intybus* is its metabolic and organ-protective effects. The plant has demonstrated hepatoprotective activity against various toxic agents, as well as antidiabetic and cardioprotective properties in experimental models (Street et al., 2013; Perović et al., 2021; Janda et al., 2021; Birsa and Sarbu, 2023). These effects are largely associated with enhanced antioxidant defences, regulated glucose and lipid metabolism, and reduced inflammatory responses. Emerging evidence suggests that *C. intybus* has antitumour, neuroprotective, antihypertensive and gastroprotective properties, indicating a broad pharmacological spectrum (Tote and Ahmed, 2025; Janda et al., 2021; Azad et al., 2026).

This review aims to provide an overview of the current knowledge regarding the biological activities of *C. intybus*, with a particular focus on its antioxidant, anti-inflammatory, immunomodulatory, antimicrobial, antiparasitic, antitumour, hepatoprotective and metabolic effects. By integrating findings from *in vitro*, *in vivo*, and selected clinical studies, this article highlights the therapeutic potential of chicory and emphasises the need for further research to improve our understanding of its mechanisms of action and translate these findings into evidence-based medical applications.

Botanical characteristics, distribution, and taxonomy

Cichorium intybus, commonly known as chicory, is a herbaceous species belonging to the Asteraceae family (formerly Compositae) (Figure 1). It may occur as an annual, biennial or perennial plant. It is winter-hardy, typically reaching 20–120 cm in height, though it may grow up to 150 cm or more in favourable conditions. It is considered an archaeophyte of Mediterranean-Irano-Turanian origin and was introduced to Central Europe in ancient times. The oldest records in Poland date back to the Roman period (Simmonds et al., 2016; Mirek et al., 2020; Mederska, 2022; Sudnik-Wójcikowska, 2023). In Poland, *C. intybus* is widely distributed across lowlands and lower mountain regions, where it is a synanthropic species associated with anthropogenically transformed habitats (Janda et al., 2021).

Figure 1 *Cichorium intybus* L., commonly known as chicory: A – general view of the inflorescence; B – typical habitats
Dębnica Kaszubska (54° 22′ 43″ N 17° 09′ 38″ E), near Słupsk, Pomeranian Voivodeship, Poland
Photo by Natalia Brzeska

The natural distribution range of *C. intybus* extends from Europe and North Africa to Southwest Asia and the Ural region. Due to its ecological adaptability, the species has spread to other continents, including Australia, New Zealand, and the Americas. It commonly inhabits open, sunlit environments such as roadsides, field margins, meadows, fallows, pastures, wastelands and railway areas, particularly thriving in disturbed and nutrient-poor soils (Street et al., 2013; Janda et al., 2021).

Morphologically, *C. intybus* is characterised by its well-developed, thick taproot system, which has a robust, spindle-shaped structure. Its erect, stiff and branched stem is often ribbed and hollow, with sparse foliage and occasional reddish pigmentation. The stem may be covered with short, coarse hairs, particularly in the lower parts. The basal leaves form a rosette measuring approximately 10–25 cm in length, exhibiting considerable variability in shape, ranging from narrowly oval or oblong to lanceolate. They are usually pinnately lobed or serrated, and may be glabrous or pubescent, particularly along the midrib or across the entire surface. The stem leaves are sessile with an arrow-shaped or cordate base and serrated margins. The upper leaves are smaller and often ciliate (Mederska, 2022; Sudnik-Wójcikowska, 2023).

The inflorescence consists of numerous capitula (anthodia) measuring 2–4 cm in diameter. These are borne on short peduncles either singly or in small clusters in the axils of the upper leaves or at the ends of the stems and branches. The ligulate flowers are usually bright blue, though pink or white forms may also occur. The bisexual flowers open primarily under sunny conditions, providing a rich source of nectar and pollen. The corolla is fused at the base into a tube and terminates in a five-toothed ligule. The androecium comprises five stamens and the gynoecium consists of a single pistil. The fruit is an achene measuring 2–3 mm in length. It is triangular or pentagonal in shape and is topped with a reduced pappus in the form of a crown of scales. The species flowers from July to September (Mederska, 2022; Sudnik-Wójcikowska, 2023).

Major classes of bioactive compounds

C. intybus is a rich source of structurally diverse bioactive compounds found in all parts of the plant, such as the roots, leaves, flowers and aerial tissues. Phytochemical analyses have identified a wide range of constituents, including carbohydrates (particularly inulin), phenolic acids, flavonoids, coumarins, terpenoids, sesquiterpene lactones, alkaloids, steroids, essential oils, vitamins and other secondary metabolites. Phenolic compounds and fructans are considered the dominant classes responsible for many of the plant's biological activities (Street et al., 2013; Janda et al., 2021; Birsa and Sarbu, 2023).

Inulin, a major storage carbohydrate in chicory roots, is one of the most abundant and well-characterised compounds in *C. intybus*. It is a linear fructan composed of β-(2→1)-linked fructose units, typically terminated by a glucose residue (Gupta et al., 2019). As the second most prevalent storage polysaccharide in nature after starch, inulin has attracted considerable interest due to its functional and health-promoting properties (Wan et al., 2020). Chicory roots may contain up to 40–60% inulin, with even higher levels reported in dried material (up to approximately 98%) (Nwafor et al., 2017). Due to its moderate degree of polymerisation and favourable physicochemical properties, inulin is widely used in food, cosmetic and biomedical applications (Ahmed and Rashid, 2019; Canazza et al., 2025), and its chemical modifications have been explored to enhance its antioxidant potential (Karimi et al., 2025).

Phenolic acids are another important group of bioactive compounds found in chicory, with caffeic acid derivatives particularly abundant. These include chlorogenic acid (3-CQA), isochlorogenic acids (e.g. 3,5-diCQA), caftaric acid, ferulic acid and dicaffeoyltartaric acid (also known as chicoric acid) (Nwafor et al., 2017; Puhlmann and de Vos, 2020). Chicoric acid, a derivative of caffeic acid and tartaric acid, is recognised as the primary phenolic compound in *C. intybus*. It exhibits strong antioxidant activity, which is attributed to its catechol moiety (Yang et al., 2022; Birsa and Sarbu, 2023). Its high concentration in chicory tissues and its ability to form biologically active metal complexes further highlight its pharmacological relevance (Iqbal et al., 2021). Additionally, caffeoylquinic acid derivatives contribute to antioxidant and antimicrobial properties and serve as *intermedia*tes in lignin biosynthesis (Chen et al., 2025). The distribution of these compounds varies among plant organs: tartaric acid esters are predominantly located in the aerial parts of the plant, while dicaffeoylquinic acids are more concentrated in the roots (Innocenti et al., 2005; Bahri et al., 2012).

Flavonoids are another important class of phytochemical found in chicory. They include derivatives of quercetin, kaempferol and myricetin, as well as flavanones and glycosylated forms (Carazzone et al., 2013; Abbas et al., 2015). These compounds significantly contribute to the plant's antioxidant capacity, particularly in red or purple varieties where high levels of flavonoids, such as quercetin-3,4-O-diglucoside, have been associated with enhanced biological activity (Carazzone et al., 2013; Yook et al., 2015). The flowers and leaves also contain anthocyanins, which are responsible for the characteristic blue colour of the perianth, as well as additional phenolic constituents such as gallic and ellagic acids (Nørbaek et al., 2002).

Coumarins, including aesculetin and its derivatives, umbelliferone and scopoletin, are also present in *C. intybus* and exhibit notable anti-inflammatory and antioxidant properties (Sharifi-Rad et al., 2021). In particular, aesculetin has been shown to mitigate oxidative stress and inflammation in experimental models, suggesting its potential therapeutic relevance (Garg et al., 2022). Furthermore, chicory contains various organic acids (e.g. malic, quinic, shikimic and succinic acids), the amino acid L-tryptophan and other minor metabolites that contribute to its overall biochemical profile (Birsa and Sarbu, 2023).

Terpenoids and sesquiterpene lactones are another important group of compounds, particularly in the roots. These include germacranolides (e.g. lactucin, lactucopicrin and 8-deoxylactucin) and guaianolides, which give chicory its characteristic bitter taste (Häkkinen et al., 2021). Additional triterpenes, such as taraxasterol, as well as phytosterols including β-sitosterol, campesterol, and stigmasterol, have also been identified (Krebsky et al., 1999; Süntar et al., 2012). The plant also contains trace amounts of alkaloids, saponins, tannins, cardiac glycosides and other bioactive constituents (Birsa and Sarbu, 2023).

Although they are present at relatively low concentrations, essential oils and volatile compounds contribute to the biological activity of *C. intybus*. Identified volatile constituents include aliphatic hydrocarbons (e.g. octane and nonadecane), aldehydes, ketones and terpenoid derivatives such as β-elemene and (E)-caryophyllene (Judžentienė and Būdienė, 2008). The qualitative and quantitative composition of these compounds varies depending on the part of the plant, its developmental stage and environmental conditions. Despite the limited number of studies on

chicory essential oils, the available evidence suggests potential antimicrobial and antiparasitic activities (Afzal et al., 2014).

Table 1 presents the major classes of bioactive compounds found in *C. intybus*, along with their key representatives, distribution within different plant parts and principal biological activities. These include primary metabolites such as inulin, as well as a wide range of secondary metabolites including polyphenols, terpenoids, flavonoids and volatile compounds.

Thus, the phytochemical profile of *C. intybus* reflects a complex, organ-specific distribution of bioactive compounds, with phenolic derivatives, inulin and terpenoids playing a central role in its biological and pharmacological properties.

Biological activities of *Cichorium intybus*

C. intybus is a multifunctional medicinal plant whose diverse biological activities are supported by a wide range of experimental and clinical studies. In recent decades, it has attracted considerable scientific interest due to its rich and diverse phytochemical composition, which includes polyphenols, flavonoids, sesquiterpene lactones and phenolic acids. These bioactive compounds are responsible for a wide variety of pharmacological effects that have been demonstrated in both experimental and clinical studies. Available evidence suggests that *C. intybus* exhibits pronounced antioxidant, anti-inflammatory, immunomodulatory, antimicrobial, antiviral, antiparasitic, hepatoprotective, antidiabetic and antitumour activities, highlighting its multifunctional therapeutic potential (Janda et al., 2021). Its pharmacological effects are closely linked to its complex phytochemical composition, making it a promising source of natural therapeutic agents. However, further well-designed clinical studies are needed to confirm its efficacy and safety in humans, and to establish standardised therapeutic applications.

Antioxidant, anti-inflammatory, and immunomodulatory activities of *Cichorium intybus*

The biological activity of *C. intybus* is largely attributed to its high polyphenol and other bioactive compound content, which gives it a strong antioxidant potential. The radical scavenging activity of polyphenol-rich fractions has been demonstrated using the DPPH assay, confirming their strong antiradical properties (Heimler et al., 2009). Studies in chemical and biological systems

Table 1 Major classes of bioactive compounds in *Cichorium intybus* L. and their characteristics

Class of compounds	Main representatives	Plant parts (distribution)	Key biological/functional properties
Carbohydrates (fructans)	inulin (β-(2→1)-linked fructose polymer)	mainly roots	prebiotic activity, metabolic health benefits, functional food ingredient
Phenolic acids	chlorogenic acid, caffeic acid derivatives, chicoric acid, ferulic acid	roots, leaves, aerial parts (organ-dependent distribution)	strong antioxidant, antimicrobial, metal-chelating, lignin biosynthesis precursor role
Flavonoids	quercetin, kaempferol, myricetin derivatives, flavonoid glycosides	leaves, flowers, aerial parts	antioxidant, anti-inflammatory, contribution to pigmentation (anthocyanins in flowers)
Anthocyanins and related phenolics	anthocyanins, gallic acid, ellagic acid	flowers, leaves	pigmentation (blue colour), antioxidant activity
Coumarins	aesculetin, umbelliferone, scopoletin	whole plant	anti-inflammatory, antioxidant, cytoprotective effects
Terpenoids and sesquiterpene lactones	lactucin, lactucopicrin, 8-deoxylactucin, β-elemene, caryophyllene	mainly roots	bitter taste, anti-inflammatory, antimicrobial, antiparasitic activity
Steroids and triterpenes	β-sitosterol, campesterol, stigmasterol, taraxasterol	whole plant (especially roots)	membrane modulation, anti-inflammatory activity
Alkaloids, saponins, tannins, glycosides	minor constituents	whole plant (low concentration)	contribute to overall bioactivity, synergistic effects
Essential oils and volatiles	octane, nonadecane, aldehydes, ketones, β-elemene, caryophyllene	aerial parts, variable by development stage	antimicrobial, antiparasitic potential
Organic acids and amino acids	malic, quinic, shikimic, succinic acids; L-tryptophan	whole plant	metabolic roles, contribute to biochemical profile

have shown that water-soluble *C. intybus* var. *silvestre* compounds exhibit significant antioxidant activity in the linoleic acid–β-carotene model. Interestingly, certain components initially displayed pro-oxidant activity, which decreased over time or after thermal treatment; however, the overall antioxidant capacity of raw juice and its fractions remained stable (Papetti et al., 2006). Further fractionation studies indicated that antioxidant activity is associated with specific molecular weight ranges of compounds present in chicory extracts.

The antioxidant properties of chicory have also been demonstrated in biological models. For example, in the microsomal membranes of rat hepatocytes that were exposed to carbon tetrachloride-induced oxidative stress, chicory extracts were found to significantly reduce lipid peroxidation, as evidenced by decreased hydroperoxide formation. Similarly, chicory juices enhanced bacterial survival in bacterial cultures of *Staphylococcus aureus* exposed to oxidative damage, indicating protective antiradical activity (Gazzani et al., 2000; Papetti et al., 2006). Furthermore, red chicory (*Cichorium intybus* var. *silvestre*) demonstrated robust antioxidant capacity in chemical assays and enzyme-based systems involving xanthine oxidase, myeloperoxidase and diaphorase. A significant correlation was observed between total phenolic content and antioxidant activity, with chicory phenolics showing comparable efficiency to Trolox in scavenging synthetic radicals (Lavelli, 2008). Furthermore, aqueous-alcoholic extracts were found to inhibit xanthine oxidase activity in a dose-dependent manner (Pieroni et al., 2002). Additional studies demonstrated hydrogen peroxide scavenging and ferrous ion chelation properties (El and Karakaya, 2004). Li et al. (2018) investigated the effect of different drying methods and thermal treatment on enzyme inactivation, phenolic content and antioxidant activity in *C. intybus* leaves. The results showed that hot air and freeze drying were the most effective at preserving phenolic compounds and antioxidant capacity. Higher phenolic content was found to strongly correlate with stronger radical scavenging activity.

Migliorini et al. (2019) demonstrated that anthocyanin-rich extracts obtained from red chicory leaves exhibit strong chemical and biological antioxidant activity. Under optimized extraction conditions (64.2 °C, 25 min, pH 2.5), a high anthocyanin content was achieved, and the extract showed significant free radical scavenging capacity in the DPPH assay (EC_{50} = 0.363). Moreover, the extract effectively inhibited lipid peroxidation and protected erythrocytes against hemolysis, indicating its cytoprotective properties. Importantly, *in vitro* studies using human cell lines (HepG2, HCT8, and Caco-2) revealed low cytotoxicity alongside antiproliferative effects, without any procarcinogenic activity. The extract also modulated reactive oxygen species (ROS) generation, further confirming its role in oxidative stress regulation.

In addition to its antioxidant properties, *C. intybus* exhibits notable anti-inflammatory effects. Chicory root extracts have been shown to inhibit tumour necrosis factor-α (TNF-α)-mediated cyclooxygenase-2 (COX-2) expression and reduce prostaglandin E2 (PGE2) production in human colon carcinoma (HT-29) cells in a dose-dependent manner (Cavin et al., 2005). Further support for these findings comes from *in vivo* studies, which show that chicory root extracts significantly reduce carrageenan-induced paw oedema in rats and decrease circulating levels of pro-inflammatory cytokines, including TNF-α, IL-6 and IL-1. These effects were accompanied by reduced lipid peroxidation (malondialdehyde levels) and enhanced antioxidant enzyme activities, such as catalase (CAT) and glutathione peroxidase (GPx) (Rizvi et al., 2014).

The immunomodulatory properties of *C. intybus* have also been widely documented. Extracts of chicory roots have been shown to influence immune cell function, particularly by modulating cytokine production and lymphocyte activity. In murine models, ethanolic extracts inhibited the proliferation of allogenic T cells at higher concentrations, while at lower concentrations, they altered cytokine profiles by decreasing interleukin-4 (IL-4) levels and increasing interferon-γ (IFN-γ) levels (Karimi et al., 2014). Furthermore, chicory extracts have been shown to protect against ethanol-induced immunotoxicity in mice by restoring various immune parameters, including antibody production, phagocytic activity, natural killer (NK) cell function and leukocyte counts. Improvements were also observed in delayed-type hypersensitivity responses and interferon-γ production (Kim et al., 2002).

Further evidence of immunomodulatory activity has been provided by studies using mitogen proliferation assays and mixed lymphocyte reactions. In these studies, aqueous-alcoholic root extracts were found to inhibit lymphocyte proliferation in response to phytohemagglutinin, whilst simultaneously stimulating mixed lymphocyte responses (Amirghofran et al., 2000). These findings suggest a complex regulatory effect on immune function that could contribute to the therapeutic relevance of chicory in immune-mediated disorders. In addition to its systemic effects,

C. intybus has long been used in traditional medicine for topical applications. Preparations such as compresses and flower infusions are used to treat dermatological conditions including dermatitis, eczema, wounds and inflammatory skin and mucous membrane disorders. These effects are attributed to the plant's antiseptic, anti-inflammatory and soothing properties, as well as its ability to promote tissue regeneration and improve local circulation (Janda et al., 2021).

Figure 2 summarises the key biological activities of *C. intybus*, highlighting its antioxidant, anti-inflammatory and immunomodulatory effects, which are driven by a diverse range of bioactive compounds, particularly polyphenols. It shows how these mechanisms translate from molecular and cellular actions into systemic protective effects, which are supported by both experimental evidence and traditional therapeutic applications.

These findings suggest that *C. intybus* exhibits a wide range of biological activities, including antioxidant, anti-inflammatory, and immunomodulatory effects. These activities are closely linked to the plant's diverse phytochemical composition, supporting its traditional and potential therapeutic applications.

Antimicrobial, antiviral, and antiparasitic activities of *Cichorium intybus*

The antibacterial potential of chicory has been demonstrated in multiple studies using extracts derived from various parts of the plant. For example, extracts rich in organic acids from fresh red chicory (*C. intybus* var. sylvestre) have been shown to inhibit the growth of periodontopathic bacteria, including *Streptococcus mutans*, *Actinomyces naeslundii*, and *Prevotella intermedia*. Identified compounds, including oxalic, succinic, quinic, and shikimic acids, have been shown to reduce bacterial adhesion and biofilm formation whilst promoting disruption of biofilms and detachment of dead cells (Gazzani et al., 2000).

A wide range of chicory extracts, including aqueous, methanolic, ethanolic, chloroform, hexane and ethyl acetate fractions, have demonstrated activity against both Gram-positive and Gram-negative bacteria, as well as fungi. Reported susceptible microorganisms include *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Escherichia coli*, *Salmonella typhi*, *Micrococcus luteus*, *Bacillus subtilis*, *Klebsiella pneumoniae*, *Enterobacter cloacae* and *Streptococcus pyogenes*, as well as the yeast *Candida albicans* (Petrovic et al., 2004; Nandagopal

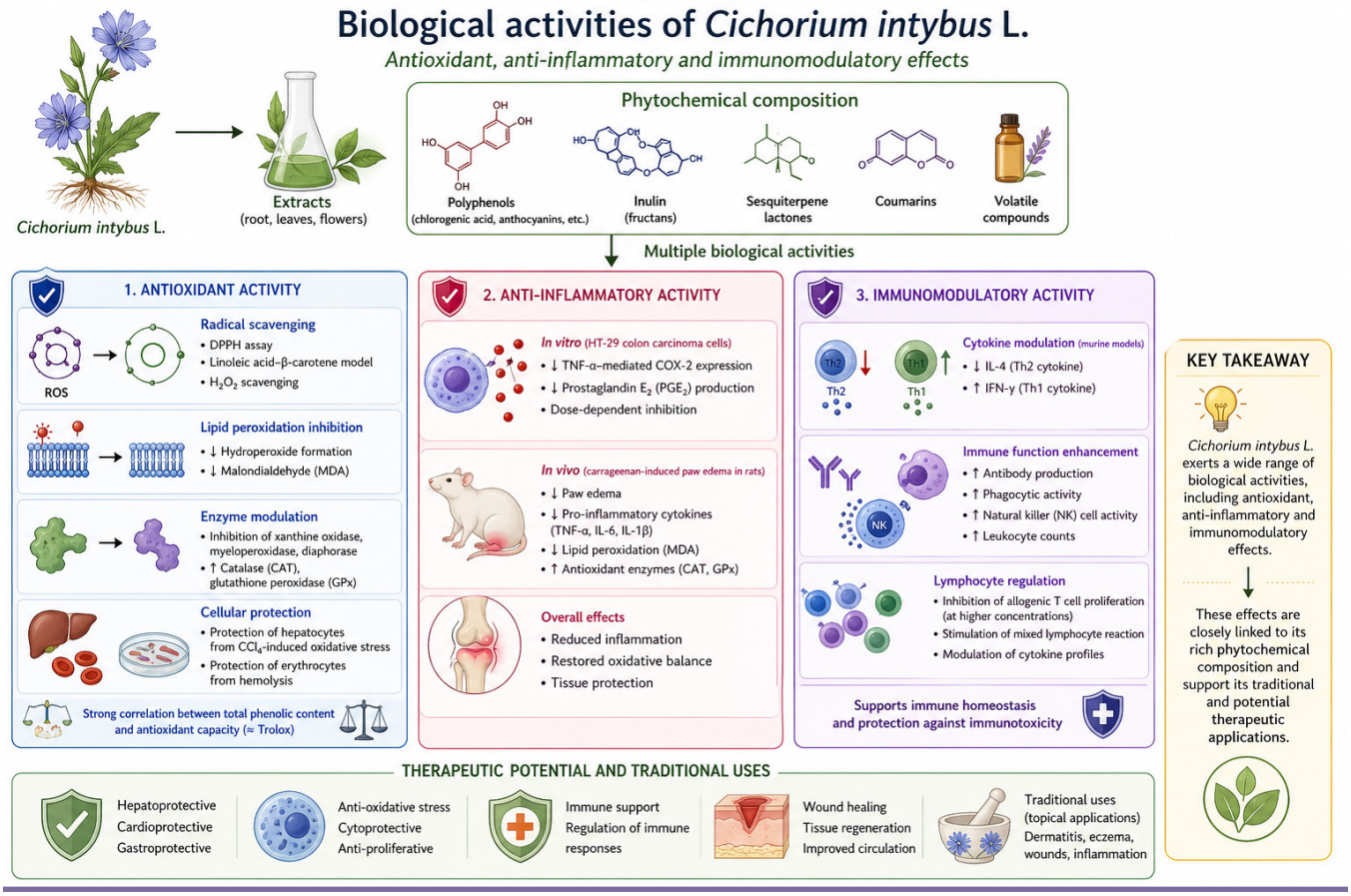

Figure 2 Integrated antioxidant, anti-inflammatory, and immunomodulatory mechanisms of *Cichorium intybus* L.

and Ranjitha Kumari, 2007; Liu et al., 2013; Khan et al., 2018; Jasim, 2018). Several studies have shown that methanolic and ethyl acetate extracts exhibit broader or stronger antimicrobial effects than aqueous extracts. However, water extracts have sometimes demonstrated higher activity against specific pathogens, such as *S. aureus* and *S. epidermidis* (Jasim, 2018; Rahimullah, 2019). Seed extracts were also found to possess significant antibacterial properties, with aqueous fractions producing the largest inhibition zones (Rahimullah, 2019). Additionally, leaf extracts showed activity against multidrug-resistant *S. typhi* (Rani and Khullar, 2004).

The study of Shabani et al. (2023) examined the antibacterial and antibiofilm properties of *C. intybus* extract, both on its own and when combined with cold atmospheric-pressure argon plasma, against multidrug-resistant strains of *P. aeruginosa* and *E. coli.* The results showed that chicory extract reduced bacterial metabolic activity. However, when combined with plasma treatment, it produced a strong synergistic effect, significantly enhancing biofilm disruption and membrane damage. This suggests that it could be a promising green strategy for combating resistant bacterial infections. Another study (Hernández-Álvarez et al., 2024) investigated the antioxidant, antimicrobial and phytochemical properties of various parts of *C. intybus*. The results showed that all of the extracts that were tested displayed measurable antibacterial activity. The most susceptible strains were *E. coli* and *P. aeruginosa*, as indicated by the largest inhibition zones. Non-polar seed extracts exhibited the strongest overall antimicrobial effects against most of the tested bacteria, with the exception of *Bacillus subtilis*, against which only moderate activity was observed. By contrast, root aqueous extracts were mainly effective against *B. subtilis* and *E. coli,* while leaf extracts showed pronounced activity, particularly against *P. aeruginosa* and *E. coli.*

Chicory also exhibits significant antifungal properties. Root extracts rich in guaianolides have been shown to inhibit anthropophilic fungi, including *Trichophyton tonsurans*, *T. rubrum* and *T. violaceum* (Mares et al., 2005). Furthermore, the sesquiterpenoid phytoalexin cichoric acid demonstrated potent antifungal activity against *Pseudomonas cichorii* (Monde et al., 1990). These findings emphasise the importance of sesquiterpene lactones and similar substances in a plant's defence mechanisms against fungal pathogens. The study of Häkkinen et al. (2021) showed that *C. intybus* extracts, particularly those obtained using supercritical fluid extraction, exhibit broad-spectrum antimicrobial activity against bacterial and fungal pathogens. Ethyl acetate fractions generally demonstrated stronger antibacterial and antifungal effects than aqueous extracts. Importantly, multidrug-resistant strains such as MRSA and ampicillin-resistant *P. aeruginosa* were also inhibited by the extracts. Additionally, the presence of sesquiterpene lactones in chicory contributed to its antibiofilm activity against *Candida albicans*. The overall cytotoxicity of the extracts was low, suggesting that chicory compounds could be promising candidates in the development of safe and effective antimicrobial agents. Another study (Badakhasann and Bhatnagar, 2019) examined the antifungal properties of *C. intybus* extract against various *Candida* species, including *C. albicans*, *C. glabrata*, *C. famata*, *C. tropicalis* and *C. krusei*. The results showed that the extract was particularly effective against *C. krusei* and *C. glabrata*; *C. krusei* was found to be the most susceptible species, as indicated by the largest inhibition zone. By contrast, *C. albicans* displayed the lowest sensitivity to the extract of all the species tested.

In addition to its antibacterial and antifungal properties, *C. intybus* exhibits antiviral activity. Extracts of the plant have shown strong activity against herpes simplex virus type 1 (HSV-1) and moderate effects against adenoviruses at higher concentrations (Ziai et al., 2007). Cichoric acid, the main phenolic compound in chicory, has been investigated for its anti-hepatitis B virus (HBV) activity using various *in vitro* models, including hepatocyte cultures and HBV-transfected cell lines. The results confirmed its protective and antiviral effects, suggesting its potential as a lead compound for the development of antiviral drugs (Zhang et al., 2014). In their study, Ávila-Gálvez et al. (2022) investigated the potential antiviral properties of *C. intybus* against SARS-CoV-2, with a particular focus on its sesquiterpene lactones. The study demonstrated that chicory extract and its major sesquiterpene compounds can inhibit key viral enzymes (Mpro and PLpro), which are involved in the replication of coronaviruses, by binding effectively to their active sites. These results imply that chicory-derived compounds could be valuable for developing antiviral strategies that target SARS-CoV-2, though more research is needed.

Recent in silico studies have further highlighted the potential of *C. intybus* in the context of emerging viral infections. Molecular docking and network pharmacology analyses identified chicory as a plant with promising activity against SARS-CoV-2 due to the presence of bioactive compounds, such as caffeic acid derivatives, which are capable of interacting

with key viral enzymes including 3CLpro, PLpro and RNA-dependent RNA polymerase (RdRp) (Shawky et al., 2020; Bahramsoltani and Rahimi, 2020; Thota et al., 2020). While these findings are preliminary and require experimental validation, they imply a potential multi-target antiviral mechanism.

The antiparasitic and anthelmintic activities of *C. intybus* have been extensively studied, particularly in relation to livestock. Animals grazing on chicory have been shown to have an improved health status and reduced gastrointestinal nematode infections. These effects are mainly attributed to condensed tannins and sesquiterpene lactones (Miller et al., 2011). Experimental studies have demonstrated that chicory extracts reduce the number of abomasal helminths in lambs and inhibit the motility of larval parasites such as *Dictyocaulus viviparus* and other gastrointestinal nematodes in a dose-dependent manner (Marley et al., 2003; Molan et al., 2003). Furthermore, extracts rich in sesquiterpene lactones inhibited the hatching of *Haemonchus contortus* eggs (Foster et al., 2011).

Chicory has also traditionally been used as an antimalarial and anti-protozoal remedy. Bitter sesquiterpene lactones, such as lactucin and lactucopicrin, which are found in root extracts, have been shown to exhibit strong inhibitory activity against the parasite *Plasmodium falciparum* (HB3 clone). These lactones were found to completely suppress parasite growth at concentrations of 10 and 50 µg·mL^{-1}, respectively (Leclercq, 1984; Bischoff et al., 2004). Furthermore, recent studies have demonstrated antiparasitic effects against *Cryptosporidium parvum*, although this activity may not depend solely on the content of sesquiterpene lactones (Woolsey et al., 2019). The study conducted by Peña-Espinoza et al. (2022) investigated the anti-protozoal activity of *C. intybus* against *Trypanosoma cruzi*, the causative agent of Chagas disease. Different leaf and root extracts were examined using metabolomic and molecular networking analyses. All extracts exhibited dose-dependent trypanocidal effects, with leaf extracts demonstrating greater selectivity and lower cytotoxicity than root extracts. Leaf extracts were also found to significantly reduce parasite infection in mammalian cells. The bioactive compounds identified included sesquiterpene lactones, such as lactucin, as well as flavonoid and fatty acid derivatives. This suggests that chicory could be a promising source of new anti-parasitic agents.

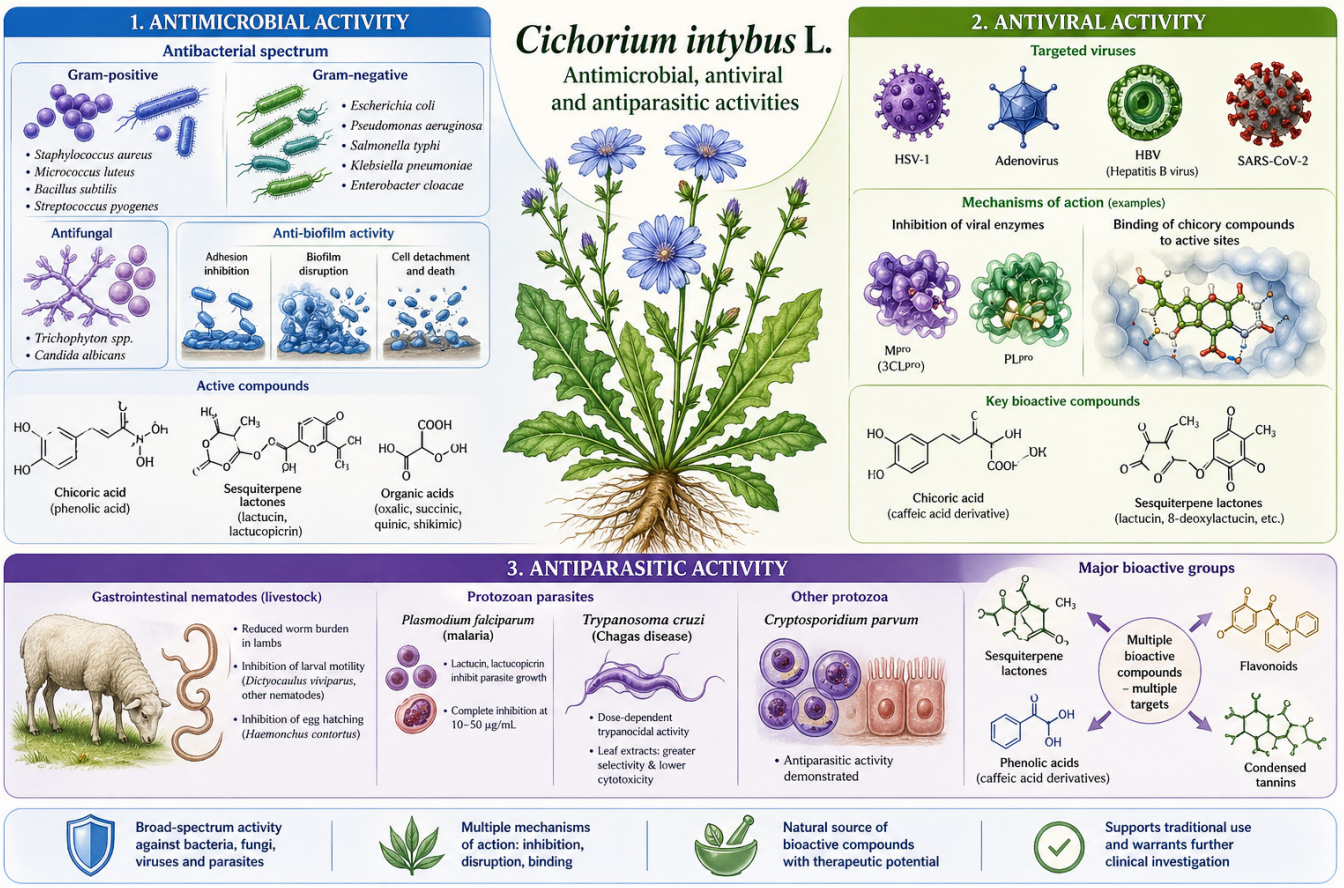

Figure 3 Antimicrobial, antiviral and antiparasitic activities of *Cichorium intybus* L.

Figure 3 provides an overview of the antimicrobial, antiviral and antiparasitic properties of chicory, emphasising its broad-spectrum biological activity against bacteria, fungi, viruses and parasitic organisms. The most susceptible microbial strains are summarised, including Gram-positive and Gram-negative bacteria, pathogenic fungi, and clinically important viruses such as HSV-1, HBV, and SARS-CoV-2.

Thus, *C. intybus* exhibits significant antimicrobial, antiviral and antiparasitic properties, which supports its traditional use and highlights its potential as a source of natural therapeutic agents. Its susceptibility to a wide range of microorganisms and parasites, combined with multiple mechanisms of action, highlights the pharmacological relevance of this species and warrants further investigation in clinical settings.

Antitumor and cytotoxic activities of *Cichorium intybus* L.

There is accumulating evidence that *C. intybus* has notable anti-tumour and cytotoxic properties, primarily due to its diverse range of bioactive secondary metabolites. Early *in vivo* studies demonstrated that crude ethanolic extracts of chicory roots significantly inhibited tumour growth in experimental models. In mice bearing Ehrlich tumour carcinoma, intraperitoneal administration of the extract (500–700 $mg \cdot kg^{-1} \cdot day^{-1}$) resulted in a significant reduction in tumour progression and an increase in lifespan of up to 70% (Hazra et al., 2002). These findings highlight the potential of root-derived compounds in modulating tumour development and improving survival outcomes.

In vitro studies further support the antiproliferative effects of *C. intybus*. Aqueous-alcoholic macerates of chicory leaves have been shown to suppress the proliferation of amelanotic melanoma C32 cell lines (Conforti et al., 2008). Furthermore, chicory extracts exhibit cytotoxic activity against various human cancer cell lines, including those from breast (MCF-7), prostate (LNCaP), renal (ACHN), melanoma (C32) and leukaemia (Khan et al., 2020). These effects suggest a broad spectrum of anticancer activity across different tumour types.

Specific phytochemicals isolated from *C. intybus* have also demonstrated potent anti-tumour effects. *Magnolia*lide, for example, is a 1β-hydroxyeudesmanolide derived from chicory roots that has been reported to inhibit the growth of multiple tumour cell lines and induce the differentiation of human leukaemia HL-60 and U-937 cells into monocyte- or macrophage-like phenotypes (Lee et al., 2000). This differentiation-inducing capacity is particularly relevant as it may contribute to the suppression of malignant cell proliferation and restoration of normal cellular function.

Phytochemical investigations have identified numerous compounds that are potentially responsible for the observed cytotoxic effects. These include guaianolides, eudesmanolides, germacranolides, flavonoids (e.g. 6-methoxyflavone), polyacetylenes, sterols, anthocyanins (such as delphinidin) and phenolic derivatives (Imam et al., 2019). Many of these metabolites have exhibited significant cytotoxic activity *in vitro* and antitumour efficacy *in vivo*. In some cases, they have progressed to clinical evaluation. Structure-activity relationship analyses further support the contribution of these compounds to the anticancer potential of chicory (Imam et al., 2019). Rasul et al. (2023) conducted a study in which they used computational methods to screen 110 compounds of *C. intybus* for their ability to inhibit the mTOR protein, a key target in breast cancer. Several phytochemicals, including taraxerone, stigmasterol and rutin, demonstrated strong and consistent binding to mTOR. This suggests that they could be used as the basis for developing future anti-cancer drugs, pending experimental validation.

Thus, the available data suggest that *C. intybus* is a promising source of bioactive compounds with cytotoxic and anti-tumour properties. The observed effects, including tumour growth inhibition, cancer cell differentiation induction, and cell proliferation suppression, highlight its potential in the development of novel anticancer agents. However, further studies, particularly well-designed clinical trials, are required to confirm its efficacy and safety in humans.

Hepatoprotective properties of *Cichorium intybus*

The hepatoprotective properties of *C. intybus* have been extensively documented in experimental and clinical studies, confirming its traditional use in managing liver disorders. Extracts derived from different parts of the plant, such as the seeds, roots and leaves, have demonstrated significant protective effects against chemically induced liver damage. In animal models, aqueous and methanolic chicory seed extracts administered to mice with liver injury induced by acetaminophen or carbon tetrachloride reduced mortality rates and significantly lowered serum levels of hepatic enzymes such as alkaline phosphatase (ALP), aspartate aminotransferase (AST) and alanine aminotransferase (ALT) (Gilani and Janbaz, 1994).

Similar hepatoprotective effects were observed with alcoholic seed extracts and aqueous extracts of roots and root callus. These extracts improved biochemical parameters, including bilirubin levels, and alleviated histopathological signs of liver damage (Zafar and Mujahid Ali, 1998; Ahmed et al., 2003; Elgengaihi et al., 2016). Li et al. (2014) demonstrated that an ethyl acetate extract of chicory has hepatoprotective effects against carbon tetrachloride-induced hepatic fibrosis in rats. The highest efficacy was observed at a dose of 54 $g \cdot kg^{-1} \cdot day^{-1}$, which significantly reduced AST and ALT and reduced fibrosis-related markers, including hexadecenoic acid, laminin, and hydroxyproline. Neha et al. (2014) also found that flavonoids from hydroalcoholic leaf extracts may contribute to hepatoprotection. Meanwhile, Kostić et al. (2013) emphasised the traditional use of chicory flowers in the treatment of skin diseases, diabetes, and liver disorders, thus supporting the anti-hepatotoxic potential of chicory.

The protective mechanisms of *C. intybus* are closely associated with its antioxidant activity. Studies have shown that chicory supplementation restores the balance of oxidative stress markers by increasing the activity of endogenous antioxidant enzymes, such as superoxide dismutase (SOD), catalase (CAT) and glutathione peroxidase (GPx), while reducing lipid peroxidation, as indicated by decreased malondialdehyde (MDA) levels (Pushparaj et al., 2007; Rezagholizadeh et al., 2016). For instance, in a study of methotrexate-induced hepatotoxicity in rats, pretreatment with chicory extracts normalised liver enzyme levels (AST, ALT and ALP), increased glutathione content and decreased total bilirubin and MDA levels, indicating attenuation of oxidative damage (Asadi et al., 2018). Comparable protective effects have also been reported in models of toxicity induced by 4-tert-octophenol.

Further experimental evidence supports the protective role of chicory against various toxic agents in hepatocytes. Extracts and their fractions – particularly the methanol- and water-soluble components – have been shown to significantly reduce serum transaminase and bilirubin levels in models of carbon tetrachloride- and paracetamol-induced hepatotoxicity. *In vitro* studies using rat hepatocytes exposed to galactosamine and thioacetamide also confirmed the protective action of chicory extracts against cellular injury (Gadgoli and Mishra, 1997). This hepatoprotective activity has been attributed to specific phytochemicals such as esculetin (a phenolic compound) and cichotyboside (a guaianolide sesquiterpene glycoside), which have demonstrated significant anti-hepatotoxic effects (Gilani et al., 1998; Ahmed et al., 2008).

The beneficial effects of *C. intybus* also extend to metabolic liver disorders. Phenolic acid-rich seed extracts have been shown to reduce hepatic steatosis in both *in vitro* and *in vivo* models. In HepG2 cells treated with oleic acid, chicory extract decreased intracellular lipid accumulation and increased glycerol release, indicating enhanced triglyceride breakdown. These effects were associated with the modulation of key genes involved in lipid metabolism, including the upregulation of SREBP-1c and PPAR-α. In diabetic rat models, treatment with chicory seed extract significantly reduced hepatic fat deposition and fibrosis (Ziamajidi et al., 2013). The clinical relevance of this is further supported by studies in patients with non-alcoholic fatty liver disease (NAFLD), in which supplementation with chicory seeds (in combination with turmeric) was found to improve lipid profile markers, including reductions in the TG/HDL-C and LDL-C/HDL-C ratios (Ghaffari et al., 2019). The meta-analysis conducted by Maleki et al. (2023) showed that chicory supplementation may exert potential hepatoprotective effects in patients with NAFLD. The randomised, double-blind clinical trial evaluated the effects of *C. intybus* in patients with second- and third-degree burns (Keshavarzi et al., 2024). Although there were no statistically significant differences in liver enzyme levels between the treatment and control groups, both groups showed a decrease in liver enzyme concentrations from day 1 to day 15 of the study.

The hepatoprotective potential of *C. intybus* is reflected by its inclusion in traditional and modern polyherbal formulations. For example, it is a key ingredient in Liv-52, a widely used hepatoprotective preparation that has been shown to reduce liver enzyme levels and improve clinical parameters, such as Child-Pugh scores and ascites, in patients with cirrhosis (Huseini et al., 2005). Another formulation containing chicory leaves, Jigrine, has shown protective effects against galactosamine-induced hepatopathy in rats by lowering transaminase levels, increasing glutathione content and reducing inflammatory changes in liver tissue (Najmi et al., 2005, 2010). At the molecular level, chicory extracts have been shown to protect against free-radical-mediated DNA damage. A fraction obtained from ethanolic leaf extracts significantly reduced the oxidative degradation of deoxyribose in a dose-dependent manner, further confirming its antioxidant and cytoprotective properties (Sultana et al., 1995).

Figure 4 illustrates the hepatoprotective properties of *C. intybus*, highlighting its bioactive compounds

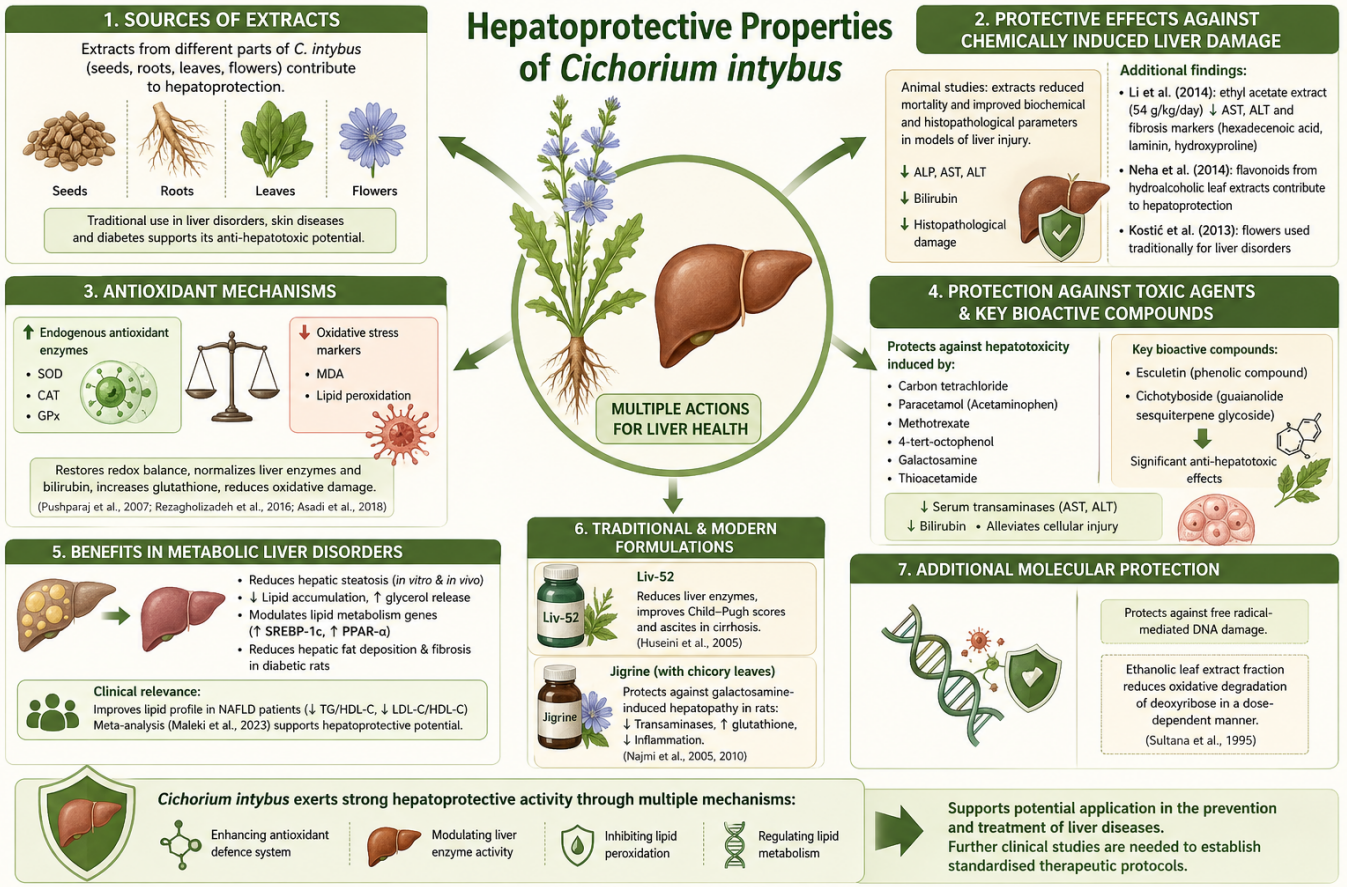

Figure 4 Hepatoprotective properties of *Cichorium intybus* L.

and their role in reducing oxidative stress, inflammation and liver damage. It summarises the main molecular and cellular mechanisms involved in protecting the liver, including enhancing the body's antioxidant defences and modulating hepatocellular injury pathways.

Thus, *C. intybus* exhibits strong hepatoprotective activity through multiple mechanisms, including enhancing the antioxidant defence system, modulating liver enzyme activity, inhibiting lipid peroxidation and regulating lipid metabolism. These findings support its potential application in the prevention and treatment of liver diseases, although further clinical studies are needed to establish standardised therapeutic protocols.

Antidiabetic and cardioprotective effects of *Cichorium intybus*

There is a substantial body of experimental evidence supporting the antidiabetic potential of *C. intybus*, particularly in streptozotocin (STZ)-induced diabetes models. In one study utilising diabetic rats, the administration of a whole-plant ethanolic extract at a dose of 125 mg·kg^{-1} body mass resulted in significant reductions in serum glucose, cholesterol and triglyceride levels. This treatment was also associated with decreased hepatic glucose-6-phosphatase (Glc-6-Pase) activity compared with the control group, suggesting reduced hepatic glucose output. Comparable hypoglycaemic effects were observed following the administration of an aqueous seed extract, regardless of whether the diabetes was in the early or late phase. Notably, the extract also prevented body weight loss in the treated animals (Street et al., 2013). Similarly, Pushparaj et al. (2007) demonstrated that the daily administration of a 125 mg·kg^{-1} alcoholic extract of the whole plant for 14 days reduced serum glucose by 20%, triglycerides by 91%, and total cholesterol by 16% in STZ-induced diabetic rats. Importantly, no changes in insulin levels were observed, indicating that the hypoglycaemic effect was not mediated by stimulation of pancreatic β-cell insulin secretion. Instead, a significant decrease in hepatic Glc-6-Pase activity was reported, which may contribute to reduced endogenous glucose production and improved glycemic control (Pushparaj et al., 2007). Furthermore, a 28-day treatment with an ethanolic seed extract containing 9.6% caffeoylquinic acids improved glycaemia, reduced the atherogenic index and enhanced antioxidant status in Wistar rats (Jurgoński et al., 2012).

Further investigations have expanded the scope of *C. intybus* activity to include protection against diabetic complications. Sharma et al. (2019) evaluated the effects of chicory seed extract in a rat model of diabetic cardiomyopathy, induced by STZ (40 mg·kg^{-1}) in combination with a high-energy diet. Oral administration of the extract (at doses of 250 and 500 mg·kg^{-1}) for three weeks significantly restored blood glucose levels and modulated oxidative stress and inflammatory parameters. Specifically, following STZ treatment, levels of aspartate aminotransferase, lactate dehydrogenase, superoxide dismutase, 2-thiobarbituric acid reactive substances, glutathione, TNF-α and IL-6 were elevated, while catalase levels were reduced. These alterations were normalised upon treatment with *C. intybus*. Furthermore, histopathological examination revealed that extensive necrotic changes in cardiac tissue induced by STZ were markedly attenuated, indicating a cardioprotective effect mediated by inhibition of oxidative stress and pro-inflammatory cytokine release (Sharma et al., 2019).

The antidiabetic activity of *C. intybus* is also attributed to its high content of phenolic compounds. Caffeic acid and chlorogenic acid, which are widely distributed throughout the plant, have been shown to enhance glucose uptake in muscle cells and stimulate insulin secretion. Similarly, cichoric acid exhibits insulin-sensitising properties and improves glucose tolerance in a dose-dependent manner. Furthermore, whole-plant methanolic extracts have been reported to enhance glucose transport without promoting adipogenesis, indicating a favourable metabolic profile (Azay-Milhau et al., 2013). Chandra et al. (2020) demonstrated that aqueous seed extract significantly reduced serum glucose and triglyceride levels in diabetic rats, and subsequent clinical observations in 150 patients with type 2 diabetes mellitus confirmed reductions in inflammation, oxidative stress and hypertriglyceridaemia following ingestion of chicory seed preparations. The aqueous seed extract demonstrated similar efficacy in early- and late-stage diabetes models induced by STZ-niacinamide and STZ alone, respectively. Treatment prevented weight loss and excessive increases in fasting blood glucose, normalising key biochemical parameters including alanine aminotransferase, triacylglycerol, total cholesterol and glycosylated haemoglobin. In early-stage diabetes, an increase in insulin levels was observed, suggesting an insulin-sensitising mechanism of action (Ghamarian et al., 2012).

An additional study provides further mechanistic insight into the antidiabetic activity of *C. intybus*, with a particular emphasis on the synergistic role of its main phenolic constituents. Ferrare et al. (2018) investigated a natural, chicoric acid-rich extract (NCRAE) derived from chicory roots, in which chicoric acid and chlorogenic acid constituted around 84% of the total composition. Using *in vivo* and *in vitro* models, the authors demonstrated that the subchronic administration of NCRAE to streptozotocin-induced diabetic rats significantly improved glucose tolerance and reduced basal hyperglycaemia after six days of treatment. A comparative formulation consisting solely of synthetic chicoric acid and chlorogenic acid (SCCAM) also improved glucose tolerance, albeit with less efficacy in lowering basal glycaemia. This suggests that the full phytochemical matrix of the extract contributes to its biological activity. *In vitro* experiments using L6 muscle cells confirmed enhanced glucose uptake and protective effects against oxidative stress, as well as notable antioxidant capacity (DPPH and ORAC assays). These findings suggest that the combined action of chicoric and chlorogenic acids, supported by other minor constituents, is responsible for the insulin-sensitising and anti-hyperglycaemic effects of *C. intybus*, thereby reinforcing its therapeutic potential in the management of diabetes (Ferrare et al., 2018).

Furthermore, dietary supplementation with *C. intybus* leaf powder reduced blood glucose levels to near-normal values and improved oxidative stress markers in diabetic Wistar rats by decreasing malondialdehyde levels and increasing glutathione content. Additional neuroprotective effects were indicated by the restoration of anticholinesterase activity, a reduction in brain lipopolysaccharide levels and increased catalase activity (Ahmad et al., 2009). The bioactive compounds responsible for these effects – caffeic acid, chlorogenic acid and chicoric acid – have been identified as key contributors due to their ability to enhance insulin secretion and improve insulin sensitivity (Tousch et al., 2008). These findings emphasise the multifaceted antidiabetic properties of *C. intybus*, including glycemic control, lipid regulation, antioxidant defence and protection against diabetes-related complications.

Sedighi et al. (2021) investigated the cardioprotective effects of a hydroalcoholic extract of *C. intybus* in a rat model of ischaemia-reperfusion injury. The results showed that pre-treatment with chicory improved cardiac function, reducing both infarct size and oxidative stress markers. It also enhanced the activity of antioxidant enzymes. These results imply that the cardioprotective effects of chicory may be mediated,

at least in part, by upregulation of chemokine receptor type 4 and by antioxidant mechanisms.

Figure 5 illustrates the multidirectional antidiabetic activity of *C. intybus*. This includes the regulation of blood glucose levels, the improvement of lipid metabolism and the activation of antioxidant and anti-inflammatory mechanisms. It also protects organs, particularly the heart and liver, against diabetes-associated complications.

Thus, *C. intybus* has strong antidiabetic properties, including reducing blood glucose levels, improving lipid profiles and protecting against metabolic complications such as diabetic cardiomyopathy and oxidative stress. These effects are not associated with the direct stimulation of insulin secretion, but rather with the inhibition of hepatic glucose production (e.g. via decreased glucose-6-phosphatase activity), improved insulin sensitivity and pronounced antioxidant and anti-inflammatory properties. Key phenolic compounds, such as chlorogenic, caffeic, and chicoric acids, work together to maintain glucose homeostasis and protect tissues from damage associated with diabetes.

Additional pharmacological activities of *Cichorium intybus*

In addition to its well-documented hepatoprotective and antidiabetic properties, *C. intybus* exhibits a wide range of pharmacological activities. These include antihypertensive, neuroprotective, antiulcerogenic, analgesic, antiallergic and wound-healing effects. These diverse biological actions highlight the plant's therapeutic versatility. Evidence of the antihypertensive potential of *C. intybus* has been demonstrated in experimental animal models. Sedighi et al. (2021) reported that ethanol extracts of chicory leaves protect against hypertension in male Wistar rats. Animals treated with the extract at doses of 25, 50 and 100 mg·kg^{-1} for two weeks showed a significant reduction in mean arterial pressure (MAP), systolic arterial pressure (SAP) and diastolic arterial pressure (DAP). The most pronounced effects were observed at the 50 mg·kg^{-1} dose, compared to both the control group and the group that received a higher dose. These findings suggest a dose-dependent vascular regulatory effect of chicory leaf extracts.

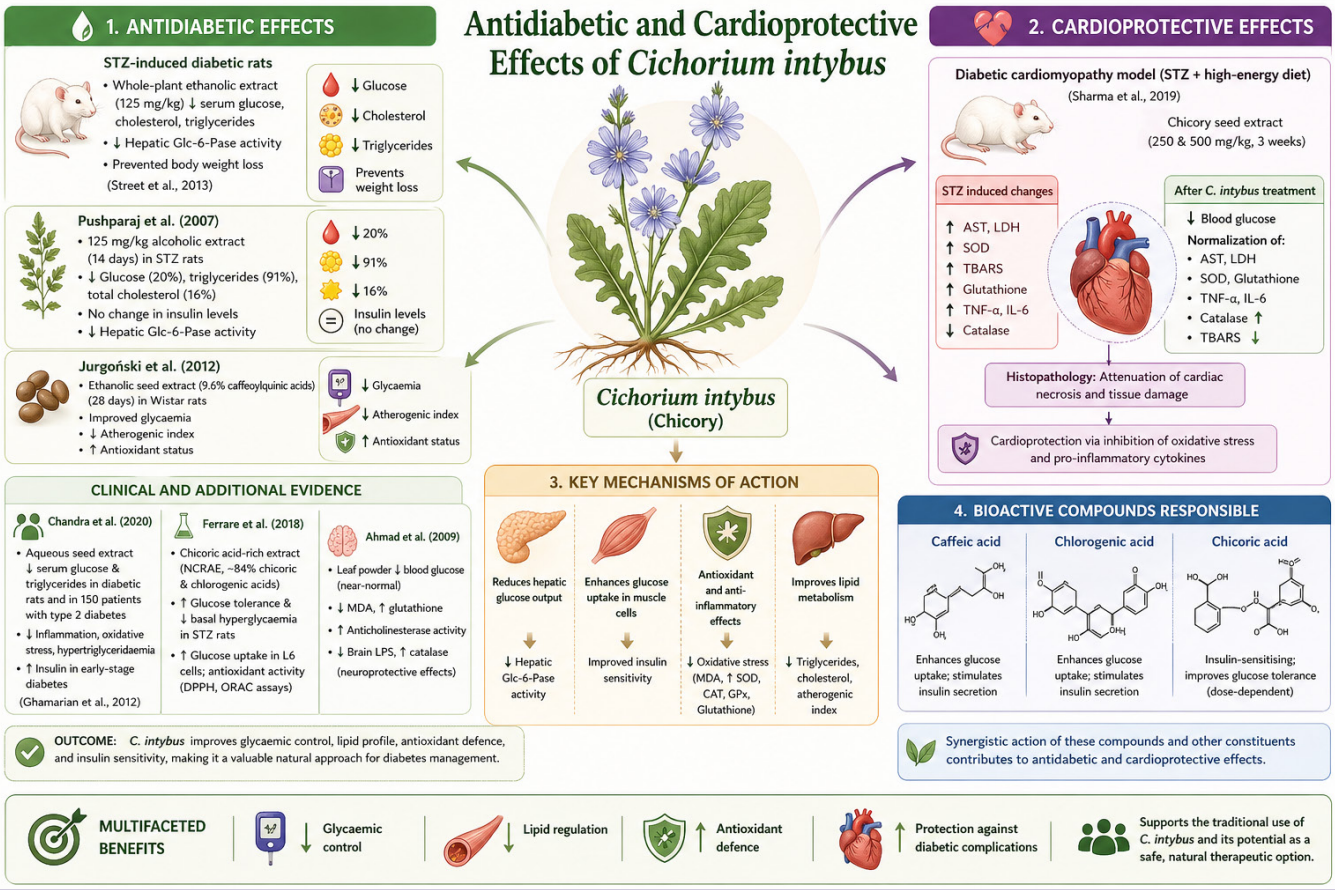

Figure 5 Antidiabetic and cardioprotective effects of *Cichorium intybus* L.

The neuroprotective effects of *C. intybus* have also been investigated, particularly in the context of peripheral neuropathy. The plant contains glycosides and triterpenoids that can modulate neurotransmission by inhibiting glutamatergic pathways and enhancing GABAergic activity. In a pyridoxine-induced peripheral neuropathy model (800 mg·kg^{-1} intraperitoneally for 14 days), chicory extract demonstrated beneficial effects in male rats. The observed neuroprotection was associated with modulation of the GABAergic system, potentially mediated through tumour necrosis factor-alpha (TNF-α), indicating an interaction between inflammatory and neurotransmitter pathways (Hasannejad et al., 2019).

The traditional medicinal use of *C. intybus* is supported by experimental data confirming its antiulcerogenic activity. In a study based on Turkish ethnopharmacological practices, an aqueous chicory root decoction administered to Sprague-Dawley rats 15 minutes prior to ethanol-induced ulcerogenesis resulted in over 95% inhibition of gastric ulcer formation. This pronounced protective effect suggests strong cytoprotective action on the gastric mucosa (Gürbüz et al., 2002).

Several sesquiterpene lactones isolated from *C. intybus*, including lactucin, lactucopicrin and 11β,13-dihydrolactucin, have also demonstrated significant analgesic and sedative properties. In murine models using hot plate and tail-flick tests, these compounds exhibited notable antinociceptive effects, with lactucopicrin identified as the most potent. At a dose of 30 mg·kg^{-1}, their analgesic efficacy was comparable to ibuprofen at 60 mg·kg^{-1}. Furthermore, lactucin and lactucopicrin reduced spontaneous locomotor activity, indicating additional sedative effects (Wesołowska et al., 2002).

The antiallergic activity of *C. intybus* has also been investigated. Aqueous extracts were shown to inhibit mast cell-mediated immediate hypersensitivity reactions *in vitro* and *in vivo*. In murine models, the extract suppressed systemic anaphylactic responses in a dose-dependent manner and significantly inhibited passive cutaneous anaphylaxis induced by anti-dinitrophenyl IgE in rats. This effect was accompanied by decreased plasma histamine levels, reduced histamine release from rat peritoneal mast cells, and increased intracellular cAMP levels. This suggests the stabilisation of mast cells and modulation of allergic mediators (Kim et al., 1999).

Moreover, specific phytochemicals present in *C. intybus* contribute to its vascular and enzymatic regulatory activities. Chicoric acid has demonstrated vasorelaxant effects against norepinephrine-induced contractions in isolated rat aortic strips (Sakurai et al., 2003). Additionally, dichloromethane extracts of chicory roots exhibited significant anticholinesterase activity in assays using Ellman's reagent. Among the active constituents, sesquiterpene lactones such as 8-deoxylactucin and lactucopicrin showed dose-dependent inhibition of acetylcholinesterase (Rollinger et al., 2005).

Further evidence extends the pharmacological profile of *C. intybus* to include respiratory protection. A recent *in vivo* and *in vitro* study demonstrated that a 70% methanolic–aqueous extract of the whole plant significantly alleviates acute lung injury (ALI) induced by cigarette smoke. In a murine model exposed to cigarette smoke for ten consecutive days, the oral administration of the extract (100–300 mg·kg^{-1}) reduced the infiltration of macrophages and neutrophils, lung oedema (as indicated by lung weight coefficient and albumin exudation) and improved histopathological alterations, as well as hypoxaemia. These protective effects were accompanied by marked suppression of pro-inflammatory mediators including IL-6, IL-1β and KC, as well as attenuation of oxidative stress markers. Significantly, the extract inhibited the activation of the NF-κB signalling pathway *in vivo* and in cigarette smoke extract-stimulated macrophages, suggesting that modulation of inflammatory and oxidative pathways underlies its protective action. These findings suggest that *C. intybus* could be a promising therapeutic option for managing smoke-induced pulmonary injury (Hussain et al., 2023).

Finally, the wound-healing potential of *C. intybus* has been attributed to methanolic extracts, with β-sitosterol identified as a key active compound. This effect is likely mediated through its anti-inflammatory and antioxidant properties, as well as its ability to inhibit hyaluronidase and collagenase, enzymes involved in tissue degradation (Süntar et al., 2012). These findings underscore the wide-ranging pharmacological profile of *C. intybus*, supporting its traditional uses and indicating its potential for the development of multifunctional therapeutic agents.

Thus, in addition to its well-established hepatoprotective and antidiabetic properties, *C. intybus* exhibits a remarkably broad pharmacological spectrum. This includes antihypertensive, neuroprotective, antiulcerogenic, analgesic, antiallergic, vasorelaxant, anticholinesterase, pulmonary protective and wound healing activities. Consistent experimental evidence from *in vivo* and *in vitro* models confirms the plant's

multi-target mechanisms of action, supporting its traditional medicinal use and highlighting its potential as a source of multifunctional therapeutic agents.

The safety profile of *Cichorium intybus*

C. intybus is widely accepted as safe for human consumption. Its extracts, along with inulin derived from chicory, have been classified as 'Generally Recognised as Safe' (GRAS) by the US Food and Drug Administration (FDA, 2018) and are listed in the 'Everything Added to Food in the United States' (EAFUS) database. This safety profile is supported by toxicological studies. For example, Schmidt et al. (2007) used the Ames assay and a four-week sub-chronic toxicity study in Sprague-Dawley rats to demonstrate that chicory root extract containing sesquiterpene lactones exhibits no toxic or mutagenic effects at doses of up to 1,000 mg·kg^{-1}·day^{-1}. Similarly, Chandra et al. (2018) confirmed that aqueous seed extracts of chicory were well tolerated in both subacute and chronic toxicity evaluations, with no adverse effects observed. At the same time, these extracts lowered serum glucose and triglyceride levels and reduced oxidative stress in experimental diabetic models.

Further clinical investigations underline the beneficial role of chicory-derived compounds in metabolic regulation. Improvements in glucose tolerance and glycated haemoglobin (HbA1c) levels have been reported (Nowrouzi et al., 2017), as have positive outcomes in the management of osteoarthritis (Olsen et al., 2010). Furthermore, inulin and oligofructose obtained from chicory have been demonstrated to reduce postprandial glycemic responses (Lightowler et al., 2018) and improve various metabolic parameters, such as glucose and calcium homeostasis, liver function, blood pressure and haematological risk markers, in patients with type 2 diabetes mellitus (Farhangi et al., 2016). These findings align with the stance of the European Food Safety Authority (EFSA), which has approved health claims asserting that indigestible carbohydrates derived from chicory, including fructooligosaccharides (FOS), can mitigate postprandial glycemic responses when employed as sugar substitutes (EFSA Panel on Dietetic Products,

Table 2 Additional pharmacological activities of *Cichorium intybus* L.

Pharmacological activity	Experimental model/ system	Plant extract/ compound	Main observed effects	Key reference
Antihypertensive	Male Wistar rats	ethanolic leaf extract (25–100 mg·kg^{-1})	reduced MAP, SAP, and DAP (dose-dependent effect)	Sedighi et al., 2021
Neuroprotective (anti-neuropathic)	pyridoxine-induced peripheral neuropathy in rats	chicory extract (glycosides, triterpenoids)	modulation of GABAergic system; reduced neurotoxicity via TNF-α pathways	Hasannejad et al., 2019
Antiulcerogenic	ethanol-induced gastric ulcer in rats	aqueous root decoction	>95% inhibition of ulcer formation; strong gastroprotective effect	Gürbüz et al., 2002
Analgesic and sedative	murine hot plate and tail-flick tests	sesquiterpene lactones (lactucin, lactucopicrin, 11β,13-dihydrolactucin)	strong antinociceptive and sedative effects (lactucopicrin most potent)	Wesołowska et al., 2002
Antiallergic	*n vitro* and *in vivo* murine models	aqueous extract	inhibition of mast cell degranulation, reduced histamine release, ↓ IgE-mediated responses	Kim et al., 1999
Vascular regulation/ vasorelaxant	isolated rat aortic strips	chicoric acid	inhibition of norepinephrine-induced contractions	Sakurai et al., 2003
Anticholinesterase	enzymatic assays (Ellman's method)	sesquiterpene lactones (e.g., lactucopicrin, 8-deoxylactucin)	dose-dependent inhibition of acetylcholinesterase	Rollinger et al., 2005
Pulmonary protection (anti-inflammatory)	cigarette smoke-induced acute lung injury (mice)	70% methanolic–aqueous whole-plant extract	reduced inflammation, oxidative stress, NF-κB inhibition, improved lung histology	Hussain et al., 2023
Wound healing	experimental wound models	methanolic extract (β-sitosterol)	anti-inflammatory, antioxidant effects; inhibition of hyaluronidase and collagenase	Süntar et al., 2012

Nutrition and Allergies, 2014). Furthermore, the EFSA has recognised that consuming 12 g of native chicory inulin daily can positively impact normal bowel function (Theis, 2018).

In the European Union, a herbal medicinal product containing *C. intybus* as the sole active ingredient has been officially registered, although several combination products containing chicory are available on the market. One such product is Liv-52, a multi-herbal preparation containing *Mandur bhasma*, *Tamarix gallica* and extracts from *Capparis spinosa*, *Cichorium intybus*, *Solanum nigrum*, *Terminalia arjuna* and *Achillea millefolium*. Its efficacy has been evaluated in the context of liver cirrhosis. In a six-month, placebo-controlled clinical study involving 36 patients, treatment with Liv-52 improved liver-related outcomes, indicating a hepatoprotective effect. These benefits are likely due to the combined diuretic, anti-inflammatory, antioxidant and immunomodulatory properties of its herbal constituents (Huseini et al., 2005).

Despite its well-established safety profile, allergic reactions to *C. intybus* are rare. Most cases have occurred in adults with occupational exposure, with only one case reported in a child following ingestion of inulin. Depending on the individual and type of exposure (contact, inhalation, ingestion, or rarely intravenous inulin), symptoms can range from mild local reactions (e.g. contact dermatitis, rhinoconjunctivitis) to severe systemic effects such as asthma and anaphylaxis. The underlying allergens are unclear, but they may include plant proteins, inulin–protein complexes or sesquiterpene lactones. Sensitisation may occur via repeated exposure or cross-reactivity with birch pollen or lettuce. Therefore, individuals with Asteraceae allergies, birch pollen sensitivity, or atopic dermatitis should exercise caution when using chicory products (Denisow-Pietrzyk et al., 2019; Puhlmann and de Vos, 2020).

Conclusions

Cichorium intybus is a highly valuable medicinal plant with a remarkably broad spectrum of biological and pharmacological activities. Its therapeutic potential is closely associated with its complex phytochemical profile, which is dominated by phenolic compounds, flavonoids, sesquiterpene lactones and inulin. Accumulated experimental and clinical evidence demonstrates its significant antioxidant, anti-inflammatory, immunomodulatory, antimicrobial, antiviral, antiparasitic, hepatoprotective, antidiabetic, cardioprotective and antitumour effects. Chicory's multifunctional activity is largely the result of synergistic interactions between its bioactive constituents, which influence oxidative stress, inflammatory pathways, immune regulation, and metabolic homeostasis. These mechanisms support its traditional medicinal use and highlight its potential as a source of natural therapeutic agents. Despite substantial progress in understanding its pharmacological properties, further well-designed clinical trials and mechanistic studies are necessary to elucidate its full efficacy, safety profile, and clinical applicability. Standardisation of extracts and identification of active compounds will be crucial for translating preclinical findings into evidence-based therapeutic strategies.

Conflicts of interest

The authors have no competing interests to declare.

Ethical statement

This article does not include any studies that would require an ethical statement.

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