REVIEW PAPER **UDK: 615.322:582.991.42**
DOI: 10.5937/hralsh2401001B

Cichorium intybus L., Asteraceae: taxonomy, chemical composition and pharmacological activity

Filip Balaz[1,2], Ana Tomas[1], Nevena Grujic[1], Emilia Gligoric[1], Branislava Teofilovic[1]

[1]Faculty of Medicine, University of Novi Sad, Novi Sad, Serbia

[2]Krka-Farma d.o.o, Belgrade, Serbia

Corresponding author:
Branislava Teofilović
Department of Pharmacy, Faculty of Medicine, University of Novi Sad,
Hajduk Veljkova 3, 21000 Novi Sad, Serbia
Phone: + 381 21 422 760
E-mail address: branislava.teofilovic@mf.uns.ac.rs

Received 27. 12. 2024.
Revised 14. 02. 2025.
Accepted 25. 02. 2025.

Abstract

Cichorium intybus L. (chicory), Asteraceae, is extensively recognized for its historical and modern uses in healthcare, agriculture, and dietary practices. This study highlights the taxonomy, bioactive compounds, and therapeutic properties of chicory. The species is rich in bioactive substances, such as inulin, phenolic acids (e.g., chlorogenic and caffeic acids), sesquiterpene lactones, and flavonoids (e.g., quercetin and luteolin). These phytochemicals are key to free radical scavenging, inflammation-modulating compounds, hepatoprotective action, microbial growth inhibition, anthelmintic action, and blood sugar regulation. Inulin serves as a prebiotic fiber, promoting gut health and metabolic regulation, while phenolic acids exhibit potent antioxidant and anticancer activities. Sesquiterpene lactones contribute to anti-inflammatory and antimicrobial effects, whereas flavonoids enhance the plant's therapeutic potential by modulating key biological pathways. Chicory's pharmacological applications extend to liver protection, glucose metabolism regulation, and immune modulation, underscoring its potential in managing chronic diseases. Despite its extensive therapeutic profile, further clinical studies are necessary to confirm its efficacy, establish optimal dosages, and explore its long-term safety. This work supports the integration of chicory into functional foods and pharmaceutical formulations, leveraging its diverse health benefits to address global health challenges.

Key words: *chicory; inulin; phenolic compounds; sesquiterpene lactons; pharmacological activity.*

INTRODUCTION

Cichorium intybus L., widely recognized globally by the name chicory, this plant is a member of the Asteraceae family. Due to its exceptional significance spanning centuries, this plant holds a prominent position in traditional medicine and various industries such as culinary arts and agriculture [1]. The ancient Egyptians recognized its benefits in blood purification, treatment of liver disorders, and as an adjunct in digestive ailments [2]. On the other hand, during classical antiquity, renowned Greek and Roman scholars utilized chicory as an anti-inflammatory agent and for treating skin diseases and gastrointestinal issues. Examination of chicory roots has highlighted their remarkable fiber content, comprising nearly 90% of the plant when dried. European monographs note that chicory root has been traditionally utilized to ease symptoms associated with mild digestive issues, including bloating and sluggish digestion, as well as to address temporary appetite loss. Renowned for its striking blue flowers and sturdy root system, chicory is also valued for its remarkable adaptability to diverse environmental conditions [3]. Chicory is a perennial plant characterized by a branched stem structure and can grow to a height ranging from 30 to 150 cm. It often thrives in open fields and along roadsides for its sake high Resistance to water scarcity and poor soil conditions. The plant develops a strong, fleshy root that penetrates deep into the soil, measuring as long as 75 cm and plays a crucial role in nutrient storage. Its basal leaves, measuring 15–30 cm in length, resemble dandelion leaves and contain a milky sap, a characteristic feature of this plant family. The young leaves are edible and possess a slightly bitter taste as a result of the availability of sesquiterpene lactones. The flowers are typically light blue, although white and pink variations occasionally occur. Each flower head has a diameter of 2–4 cm. The flowers open in the morning and close in the afternoon, responding to sunlight. Chicory usually blooms from late summer to early autumn (June to October in temperate climates), with pollination carried out by insects such as bees and butterflies [4,5].

Figure 1. Botanical ilustration of chicory.

Chemical composition

Chicory is a plant species rich in phytochemicals that are of exceptional importance for maintaining proper physiological functions. Inulin is one of the primary compounds present in the plant, along with others such as phenolic compounds (caffeic acid, chlorogenic acid, and chicoric acid), sesquiterpene lactones (8-deoxylactucin, lactucopicrin, lactucin), and flavonoids (luteolin, quercetin, and kaempferol). The plant is also a provider of vital vitamins, including vitamin C and vitamin K, together with minerals including calcium, potassium, and magnesium, which play a key role in overall health. Additionally, minor components such as alkaloids, saponins, tannins, and sterols, including β-sitosterol, further enhance its nutritional and therapeutic value [6,7].

INULIN

Inulin is a natural polysaccharide and one of the most significant bioactive components found in chicory. It is a fructooligosaccharide composed of linear chains of fructose units ending with a single glucose molecule, characterized by β-(2,1) bonds. These connections provide inulin with its distinctive structure and physiological characteristics, allowing it to resist breakdown by digestive enzymes and saliva in the human small intestine. The majority of fructans classified as inulin types typically have an average degree of polymerization between 10 and 12, with chain lengths varying from 2 to 60 units in their molecular distribution [8].

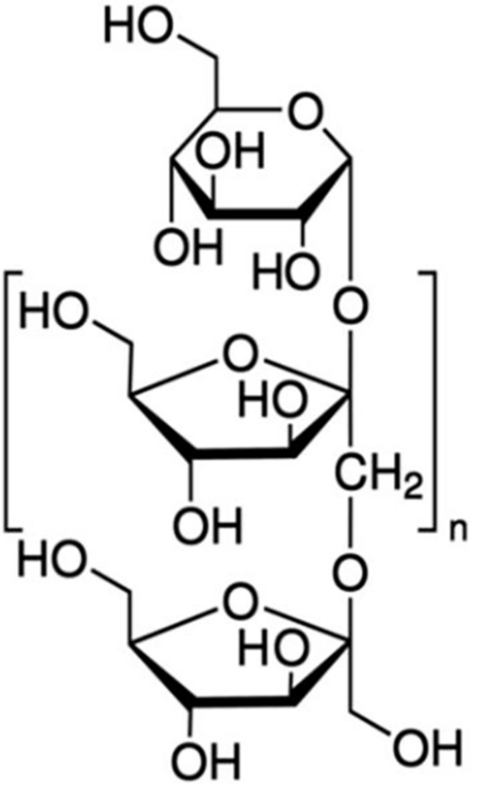

Figure 2. Structure of inulin.

Inulin serves as the primary storage carbohydrate in chicory root, accounting for approximately 40–60% of the root's dry weight. This compound has gained considerable attention in nutrition and medicine due to its prebiotic properties, low caloric value, and functional applications in the food industry. As a prebiotic, inulin selectively promotes the proliferation of advantageous gut microbes, including bifidobacteria and lactobacilli while inhibiting the proliferation of pathogenic microorganisms. It resists digestion in the upper part of the digestive system and reaches the colon unchanged, where it undergoes fermentation through the action of intestinal microbiota. This breakdown activity results in the formation of short-chain fatty acids (SCFAs), such as acetate, propionate, and butyrate, which contribute to improved gut health, enhanced immune function, and a lower likelihood of developing colorectal cancer [9]. The multiple hydroxyl (-OH) groups in inulin's structure enhance its hydrophilic nature, contributing to its solubility and water-binding capacity. Furthermore, the presence of a terminal glucose unit and a fructose-based backbone defines its caloric value and functional role as a low-calorie sugar substitute. The unique structural properties of chicory-derived inulin make it a multifunctional dietary fiber with applications in nutrition, health, and food technology [10].

Phenolic compounds

Phenolic compounds comprise a varied category of secondary metabolites distinguished by the existence of one or more hydroxyl groups (-OH) bonded to an aromatic benzene ring. This fundamental structure allows for significant chemical diversity, as variations in the quantity and arrangement of hydroxyl groups along with substitutions such as methoxy, glycosyl, or acyl groups, create different subclasses of phenols, including simple phenols, phenolic acids, flavonoids, tannins, lignans, and stilbenes. Their structural variability determines their physical, chemical, and biological properties. Chicory serves as an abundant source of biologically active phenolic substances, particularly caffeic acid, chlorogenic acid, and chicoric acid, which significantly aid in its health benefits and therapeutic potential. Phenolic acids, such as caffeic and chlorogenic acids, are defined by a carboxylic acid functional group linked to the phenolic ring, commonly derived from benzoic or cinnamic acid [11]. These phenolic acids are secondary metabolites that play a key role in plant defense mechanisms and offer numerous biological functions, such as antioxidant, anti-inflammatory, and antimicrobial attributes making chicory a valuable plant for various applications. Caffeic acid, a hydroxycinnamic acid widely found in chicory roots and leaves, has a structure made up of a phenolic ring and an acrylic side chain. This unique structure enables it to effectively scavenge free radicals, contributing to its potent antioxidant activity [12].

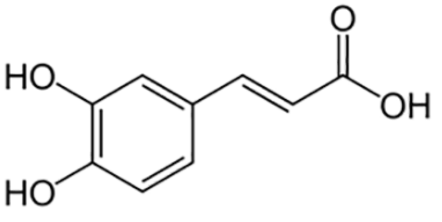

Figure 3. Structure of caffeic acid.

Chlorogenic acid is a phenolic compound classified as a derivative of hydroxycinnamic acid, characterized by an ester bond between caffeic acid and quinic acid. Its molecular structure consists of a phenolic ring with hydroxyl groups, which contribute to its antioxidant properties, and a carboxyl group derived from quinic acid, enhancing its solubility and bioactivity. The hydroxyl groups on the phenolic structure allow chlorogenic acid to provide hydrogen atoms that neutralize free radicals, making it an effective antioxidant.

Chlorogenic acid is among the most plentiful phenolic compounds in chicory and is essential for the plant's bitter taste, with particularly high concentrations found in the root. It is a potent antioxidant, renowned for its ability to chelate metal ions and prevent lipid peroxidation [13].

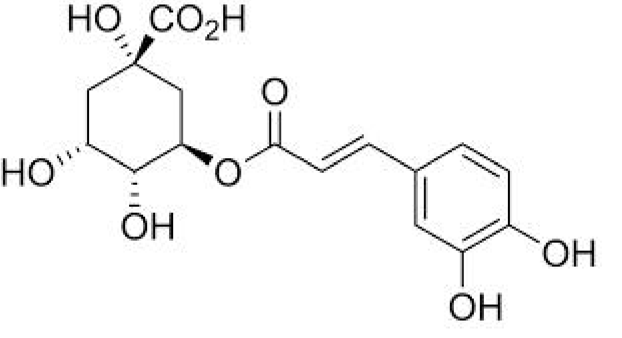

Figure 4. Structure of chlorogenic acid.

Chicoric acid, a dicaffeoyl derivative of tartaric acid, is a significant phenolic compound predominantly located in chicory leaves. Structurally, it comprises two caffeic acid groups esterified to a central tartaric acid molecule, which imparts potent antioxidant properties. Chicoric acid is recognized for its capacity to neutralize free radicals and lower oxidative stress, making it valuable in preventing cell damage caused by oxidative stress [14].

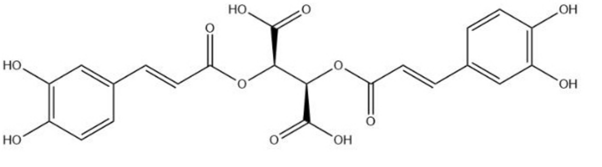
Figure 5. Structure of chicoric acid.

Sesquiterpene lactones

Sesquiterpene lactones represent a category of bioactive compounds primarily located within the Asteraceae family, including chicory. These compounds, particularly lactucin, lactucopicrin, and 8-deoxylactucin, contribute to the characteristic bitterness of chicory and demonstrate a range of pharmacological activities, including analgesic, anti-inflammatory, antioxidant, and antimicrobial properties. Biosynthetically derived from the mevalonate pathway, sesquiterpene lactones in chicory serve an essential function in the plant's protective measures and hold significant therapeutic potential for human health. Lactucin is a bitter sesquiterpene lactone with a core structure comprising a lactone ring fused to a sesquiterpene backbone. Found in the roots and leaves of chicory, lactucin is renowned for its analgesic and sedative properties. Studies suggest that lactucin exerts its effects by modulating the central nervous system, particularly through interactions with opioid receptors, thereby alleviating pain. Lactucopicrin, a derivative of lactucin, is one of the most bitter sesquiterpene lactones in chicory. Its bitterness is associated with its structural features, including an esterified lactone group, which enhances its bioactivity. Lactucopicrin is primarily recognized for its anti-inflammatory and antioxidant activities. 8-Deoxylactucin, another prominent sesquiterpene lactone in chicory, shares structural similarities with lactucin but lacks a hydroxyl group at the eighth carbon position, giving it distinct biological properties. This compound has demonstrated significant anti-inflammatory and analgesic activities [15,16,17].

Flavonoids

Flavonoids are among the most prevalent secondary metabolites found in plants, and chicory is a significant source of these compounds. Flavonoids belong to a category of polyphenolic substances characterized by a core structure based on a 15-carbon skeleton, composed of two aromatic rings (A and B) linked by a three-carbon chain that creates a heterocyclic pyran ring (C). This structure, denoted as C6-C3-C6, underpins their diverse chemical properties and biological activities. Variations in hydroxylation, methoxylation, glycosylation, and conjugation patterns on the A, B, and C rings lead to different flavonoid subclasses, including flavones, flavonols, flavanones, flavanols, anthocyanins, and isoflavonoids. The A-ring, derived from the acetate pathway, typically contains hydroxyl or methoxy groups that contribute to antioxidant activity. The B-ring, originating from the shikimate pathway, is crucial for interactions with enzymes and proteins, underlying the inflammation-reducing and anticancer qualities of flavonoids. The degree of saturation of the C-ring and the binding position of the B-ring further define the subclass and influence bioactivity. Among the flavonoids present in chicory, luteolin, quercetin, and kaempferol stand out for their diverse pharmacological characteristics, such as inflammation-reducing, free radical scavenger, cancer-preventive, and heart-protective effects. These flavonoids are derived from the phenylpropanoid pathway and contribute to the plant's protective responses [18]. Luteolin, a yellow crystalline flavonoid part of the flavone subclass, is commonly located in the leaves and flowers of chicory. Structurally, it features a hydroxylated B-ring, which is critical for its potent antioxidant activity. Quercetin, a flavonol with a distinct hydroxylated framework, is another prominent flavonoid in chicory. Known for its strong antioxidant capacity, quercetin neutralizes free radicals and enhances the activity of endogenous antioxidant enzymes [19].

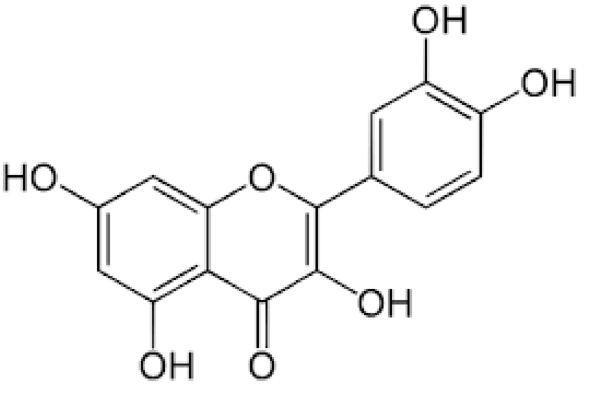

Figure 6. Structure of quercetin.

PHARMACOLOGICAL ACTIVITY

Antimicrobial activity

Antibacterial activity has been extensively studied, highlighting chicory's effectiveness as a natural pathogen inhibitor against various pathogenic bacteria. This activity is associated with its rich content of biochemical agents, such as phenolic acids, flavonoids, sesquiterpene lactones, and inulin. Phenolic acids such as caffeic and chlorogenic acids play a critical role in disrupting bacterial cell walls and membrane structures, leading to increased permeability and eventual apoptosis [20]. Flavonoids like quercetin and luteolin have been shown to inhibit bacterial enzymes and proteins essential for cell replication and metabolism, thereby exhibiting bacteriostatic effects [21]. Chicory exhibits antibacterial activity against a range of bacteria, including both Gram-positive and Gram-negative strains. Studies have demonstrated its effectiveness against common Gram-positive bacteria, like *Staphylococcus aureus* and *Bacillus subtilis*, along with Gram-negative pathogens, such as *Escherichia coli* and *Pseudomonas aeruginosa* [22]. This broad-spectrum activity is particularly significant given the increasing resistance of bacteria to synthetic antibiotics. Sesquiterpene lactones, such as lactucin and lactucopicrin, are believed to contribute to this antimicrobial potential by disrupting bacterial membrane integrity and interfering with DNA replication processes [23]. Phenolic compounds also act as antioxidants, reducing oxidative stress in tissues and indirectly enhancing the immune response to bacterial infections. Additionally, inulin, a prebiotic fiber predominantly found in chicory roots, supports the growth of beneficial gut bacteria, further enhancing its role in combating bacterial pathogens.

Anthelmintic activity

The anthelmintic activity of chicory has received considerable attention owing to its capability as a natural remedy against parasitic nematode infections. This activity is ascribed to multiple bioactive substances found in chicory, including sesquiterpene lactones, phenolic acids, flavonoids, and inulin, which collectively disrupt the life cycle and physiological processes of helminths. Sesquiterpene lactones, such as lactucin and lactucopicrin, are particularly notable for their toxic effects on parasitic worms, including disruption of their neuromuscular systems and interference with energy metabolism [24]. Studies have demonstrated the efficacy of chicory against various gastrointestinal nematodes, such as *Haemonchus contortus*, *Trichostrongylus colubriformis*, and *Teladorsagia circumcincta*, which are major parasites affecting grazing livestock. The bioactive compounds in chicory act by damaging the nematode cuticle, reducing their motility, and impairing their ability to infect host tissues. Furthermore, the antiparasitic effects are enhanced when chicory is included in the diet, as its secondary metabolites remain active in the gastrointestinal tract, contributing to a reduction in worm burden [25]. In addition to its direct effects on adult helminths, chicory has been shown to disrupt the reproductive systems of parasites. The bioactive compounds in chicory reduce the fertility of female nematodes and inhibit the development of eggs and larvae, thereby decreasing environmental contamination and the risk of reinfection. Inulin, a prebiotic fiber, also plays an indirect role by promoting the growth of beneficial gut microbiota. This supports the host's immune response, further aiding in the control of parasitic infections [26]. Promising results from studies on chicory's role in treating parasitic infections underscore its high potential for application. However, further research is needed to standardize dosing, optimize formulations, and assess long-term effects on both humans and animals. Nevertheless, its natural origin and multiple health benefits position chicory as a valuable alternative or complement to conventional anthelmintic drugs.

Hepatoprotective activity

The hepatoprotective activity of chicory is well-documented, making it a promising natural remedy for liver diseases. The benefits of chicory are primarily due to its diverse profile of biologically active substances, including phenolic acids (like caffeic and chlorogenic acid), sesquiterpene lactones (such as lactucopicrin and lactucin), flavonoids, and inulin. These compounds collectively exert antioxidants, inflammation reducers, and effects that prevent apoptosis, which are essential for reducing liver harm resulting from toxins, oxidative pressure, and inflammation [27]. Chicory demonstrates significant antioxidant activity, primarily through its phenolic content. Compounds such as chlorogenic acid neutralize free radicals, preventing lipid peroxidation and protecting the structural integrity of hepatocyte membranes. This antioxidant effect protects the liver from oxidative stress induced by toxic agents such as carbon tetrachloride (CCl4) and acetaminophen, known to cause severe liver injuries. The flavonoids in chicory also enhance the role of endogenous enzymes with antioxidant properties, including glutathione peroxidase (GSH-Px) and superoxide dismutase (SOD), thereby bolstering the liver's defense system [28]. The inflammation-reducing effects of chicory aid in its hepatoprotective impacts. Sesquiterpene lactones, such as lactucin, suppress the secretion of pro-inflammatory cytokines such as IL-6 and TNF-α, which are essential in liver inflammation and fibrosis. By suppressing inflammatory signaling routes, like NF-κB, chicory prevents the progression of long-term liver diseases encompassing non-alcoholic fatty liver disease (NAFLD) and alcoholic liver disease (ALD) [29]. Chicory's hepatoprotective potential extends to its ability to enhance liver detoxification. Inulin, a prebiotic fiber, promotes the growth of beneficial gut microbiota, which helps reduce endotoxins that may enter the liver via the portal vein. This modulation of the gut-hepatic link reduces liver inflammation and supports liver regeneration. Furthermore, chicory extract has been shown to regulate liver enzymes, like aspartate transaminase (AST) and alanine transaminase (ALT), restoring their levels to reference ranges in cases of liver injury [30]. Studies have also highlighted chicory's role in preventing fibrosis and cirrhosis, severe complications of chronic liver damage. Sesquiterpene lactones and phenolic acids inhibit the activation of liver stellate cells, a primary factor in fibrosis, and reduce collagen deposition in liver tissues. These effects suggest that chicory not only protects the liver but may also reverse damage at the cellular level [31]. Additionally, chicory exhibits hepatoprotective effects against liver injuries induced by drugs, chemotherapeutic agents, and antibiotics. Its bioactive compounds mitigate mitochondrial dysfunction and apoptosis in hepatocytes, reducing the severity of drug-associated liver toxicity. Despite its promising hepatoprotective properties, additional clinical research is needed to set up optimal dosages, formulations, and long-term safety. Nevertheless, chicory offers a natural and cost-effective alternative to synthetic hepatoprotective drugs, providing multiple benefits for liver health. Its integration into functional foods and nutritional products holds great potential for preventing and managing liver diseases across diverse populations [29].

Antidiabetic activity

The antidiabetic activity of chicory is well-researched, demonstrating its capability as a natural therapeutic agent for addressing diabetes and its associated issues. Phytochemicals in chicory, such as inulin, phenolic acids (like chlorogenic and caffeic acids), flavonoids (quercetin and luteolin), sesquiterpene lactones, and other secondary metabolites, contribute to antihyperglycemic and antioxidant properties while enhancing insulin sensitivity. These effects work together to regulate glucose metabolism, increase insulin sensitivity, and prevent oxidative stress-induced cellular damage, which are critical points for diabetes regulation [28]. Inulin, a prebiotic fiber abundantly found in chicory roots, plays a key role in improving glucose metabolism. It helps lower postprandial glucose levels by delaying the digestion and absorption of carbohydrates in the intestines. Furthermore, inulin promotes the growth of beneficial gut microbiota, which are known to influence metabolic pathways and improve glucose tolerance. By enhancing the gut microbiome, inulin also supports the synthesis of short-chain fatty acids (SCFAs), which modulate insulin secretion [32]. Phenolic acids, particularly chlorogenic acid, are crucial factors in the anti-diabetic effects of chicory. Chlorogenic acid inhibits glucose-6-phosphatase, an enzyme found in the liver involved in gluconeogenesis, thereby reducing glucose production. It also increases glucose uptake in peripheral tissues by regulating the expression of glucose transporter protein 4 (GLUT-4) [33]. Additionally, phenolic acids in chicory inhibit the enzymes α-amylase and α-glucosidase in the digestive tract, slowing carbohydrate breakdown and absorption, which leads to better postprandial glucose control [30]. Flavonoids such as quercetin and luteolin further enhance the antidiabetic potential of this plant. These compounds improve insulin signaling by activating key pathways such as PI3K/Akt, which enhance glucose absorption and glycogen formation in skeletal muscle. They also exhibit strong antioxidant properties, reducing oxidative damage in pancreatic β-cells and preserving their function. This is significant since oxidative stress is one of the main factors contributing to β-cell dysfunction and insulin resistance in diabetes [21]. Sesquiterpene lactones, a secondary set of bioactive substances in chicory, aid in its antidiabetic effects by modulating inflammatory pathways. Continuous mild inflammation is a notable trait of type 2 diabetes and compounds like lactucin and lactucopicrin have been shown to inhibit cytokines that promote inflammation, including IL-6 and TNF-α. Through its anti-inflammatory effects, chicory enhances insulin sensitivity and prevents the progression of diabetes-related complications [34]. Diabetes is often linked to elevated levels of reactive oxygen species (ROS), which may harm cellular structures, including proteins, DNA, and lipids. The phenolic compounds in chicory effectively neutralize ROS and regulate endogenous enzymes with antioxidant properties, including GSH-Px and SOD. This dual antioxidant mechanism helps protect vital organs, including the liver, kidneys, and pancreas, from diabetes-related damage [35]. In addition to glucose regulation, chicory offers protective effects against diabetes complications. For example, its phenolic compounds exhibit vasodilatory effects and improve endothelial function, which is beneficial in preventing cardiovascular complications. Modulation of lipid profiles through chicory, such as reducing LDL cholesterol and triglycerides, also contributes to better metabolic health [28].

Anti-inflammatory activity

The inflammation-reducing properties of chicory are attributed to the phytochemicals present in this plant species, particularly sesquiterpene lactones, phenolic acids, and flavonoids. These compounds exert a synergistic effect to inhibit pro-inflammatory pathways, reduce oxidative stress, and modulate the immune response, making chicory a potential natural treatment for multiple inflammatory disorders. Chronic inflammation is a significant factor in many illnesses, such as arthritis, cardiovascular disorders, nervous system degenerative diseases, and diabetes. Chicory's ability to mitigate inflammatory processes positions it as a valuable therapeutic agent. Sesquiterpene lactones, like lactucopicrin and lactucin, are among the most potent anti-inflammatory compounds in chicory. These molecules suppress the activation of nuclear factor-kappa B (NF-kB), an essential transcription factor involved in the production of pro-inflammatory cytokines, including interleukin-6 (IL-6), interleukin-1 beta (IL-1β) and tumor necrosis factor-alpha (TNF-α). By suppressing NF-kB signaling, sesquiterpene lactones help alleviate inflammatory responses and prevent tissue damage [36]. Phenolic acids also inhibit cyclooxygenase (COX) enzymes, particularly COX-2, thereby reducing the synthesis of pro-inflammatory prostaglandins. This mechanism is similar to that of non-steroidal anti-inflammatory drugs (NSAIDs) but without the linked detrimental effects [28]. Flavonoids such as quercetin and luteolin contribute to the anti-inflammatory activity by modulating key signaling pathways, including mitogen-activated protein kinase (MAPK) and PI3K/Akt. These mechanisms regulate the synthesis of cytokines and chemokines as part of inflammation. Quercetin and luteolin also support mast cell stability, which stops the release of histamine and other inflammatory agents, thereby reducing allergic and inflammatory responses [28].

Antioxidant activity

An imbalance between ROS and the body's antioxidant defenses leads to oxidative stress, which is a critical element in the pathogenesis of various diseases, including diabetes, cardiovascular issues, cancer, and neurodegenerative disorders. Chicory's antioxidant properties are primarily linked to its phenolic acids (like caffeic and chlorogenic acids), flavonoids (such as quercetin and luteolin), sesquiterpene lactones, and other secondary metabolites. Flavonoids in chicory, including quercetin and luteolin, further contribute to its antioxidant activity. These compounds not only scavenge ROS but also modulate important signaling pathways, including the pathway associated with nuclear factor erythroid 2-related factor 2 (Nrf2), which controls the expression of genes related to antioxidants and detoxification. For instance, quercetin enhances the expression of heme oxygenase-1 (HO-1), an enzyme that protects cells from oxidative damage, while luteolin prevents the oxidation of DNA and proteins, thereby preserving cellular integrity [28]. Sesquiterpene lactones, such as lactucin and lactucopicrin, complement the antioxidant effects of phenolic acids and flavonoids by reducing ROS formation and inhibiting the activation of pro-oxidative enzymes such as NADPH oxidase. These lactones also mitigate oxidative damage to mitochondria, the primary site of ROS production, thereby improving energy balance and cellular sustainability. Numerous studies support the ability to act as an antioxidant chicory both in laboratory and in living organisms. Chicory extracts have demonstrated significant free radical scavenging activity in laboratory tests, such as the DPPH and ABTS assays. In animal models, chicory supplementation reduces biomarkers of oxidative stress, like malondialdehyde (MDA), and increases levels of antioxidant enzymes. Although limited, studies in humans suggest that the antioxidant compounds in chicory help reduce oxidative stress in patients with metabolic disorders [37].

Anti-cancer activity

The most prevalent phytochemicals present in chicory have demonstrated anti-cancer properties by modulating crucial pathways associated with cancer development, including cell growth and programmed cell death, angiogenesis, and metastasis. The natural bioactive components of chicory have shown potential in both laboratory and live organism research, positioning it as a promising candidate for integrative cancer therapy. Lactucin and lactucopicrin have a vital impact on the anticancer impacts of chicory. These compounds induce cellular apoptosis in malignant cells by stimulating intrinsic and extrinsic pathways of apoptosis characterized by increased caspase activity and mitochondrial dysfunction. Moreover, sesquiterpene lactones inhibit the nuclear factor-kappa B (NF-kB) pathway, which is often overactive in cancer, contributing to decreased expression of survival and pro-inflammatory genes. Quercetin and luteolin enhance the anticancer properties of chicory through their antioxidant, antiproliferative, and pro-apoptotic activities. These compounds suppress key oncogenic cellular signaling routes, such as the phosphoinositide 3-kinase/Akt (PI3K/Akt) and mitogen-activated protein (MAP) kinase pathways, thereby reducing cancer cell growth and promoting apoptosis. They also exhibit anti-angiogenic effects by decreasing vascular endothelial growth factor (VEGF), thereby disrupting neoplasm blood vessel formation [38, 39].

CONCLUSION

Cichorium intybus is a crop recognized for its historical significance in traditional healing and its present-day applications in food and medical care. Its therapeutic potential arises from significant biologically active components, like sesquiterpene lactones, phenolic acids, flavonoids, and inulin, which collectively contribute to its anti-inflammatory, antioxidant, hepatoprotective, anthelmintic, antidiabetic, and anticancer properties. The natural compounds in chicory act synergistically to modulate key biological pathways, such as reducing oxidative stress, inhibiting inflammatory mediators, enhancing digestive health, and strengthening immunity. These attributes make chicory a valuable resource for avoiding and management of long-term conditions, such as diabetes, heart-related disorders, hepatological disorders, and malignancy. In addition to its medicinal benefits, chicory holds significant nutritional value, serving as a source of fiber, vitamins, and minerals. Despite its numerous advantages, further clinical studies are required to confirm the efficacy and protection of chicory-derived compounds in human populations and to explore optimal dosages. As interest in natural and sustainable remedies grows, chicory possesses enormous potential for creating functional foods and pharmaceutical items.

REFERENCES

1. Stephens JM, *Chicory--Cichorium Intybus L*. University of Florida Cooperative Extension Service, Institute of Food and Agriculture Sciences, EDIS, 1994.
2. Amer Ahmed M, Antimicrobial effects of Egyptian local chicory, Cichorium endivia subsp. pumilum. International Journal of Microbiology 2018;6475072.
3. Lucchin M, et al. Chicory and endive, Vegetables I: Asteraceae, Brassicaceae, Chenopodicaceae, and Cucurbitaceae 2008;3-48.
4. Barcaccia G, Andrea G, and Margherita L, Current advances in genomics and breeding of leaf chicory (Cichorium intybus L.), Agriculture 2016:50.
5. Cadalen, T, et al. Development of SSR markers and construction of a consensus genetic map for chicory (Cichorium intybus L.), Molecular Breeding 2010;25:699-722.
6. Janda K, Gutowska I, Geszke-Moritz M, Jakubczyk K, The Common Cichory (*Cichorium intybus* L.) as a Source of Extracts with Health-Promoting Properties–A Review, Molecules 2021;26:1814.
7. Varotto S, Margherita L, Paolo P, Immature embryos culture in Italian red chicory, Plant Cell, Tissue and Organ Culture 2000;62(1):75-77.
8. Das S, Vasudeva N, Sharma S, Cichorium intybus: A concise report on its ethnomedicinal, botanical, and phytop-

harmacological aspects, Drug Development and Therapeutics 2016; 7(1):1.
9. Niness KR, Inulin and oligofructose: what are they? Journal of Nutrition 1999;129:1402S-6S.
10. Roberfroid MB, Introducing inulin-type fructans, British Journal of Nutrition 2005;93(S1):S13-S25.
11. Shahidi F, Yeo J, Bioactivities of Phenolics by Focusing on Suppression of Chronic Diseases: A Review, International Journal of Molecular Sciences 2018;19(6):1573.
12. Minatel IO, Borges CV, Ferreira MI, Gomez HAG, Chen CYO, Lima GPP, Phenolic Compounds: Functional Properties, Impact of Processing and Bioavailability [Internet]. Phenolic Compounds – Biological Activity. InTech; 2017.
13. Nguyen V, Taine EG, Meng D, Cui T, Tan W, Chlorogenic Acid: A Systematic Review on the Biological Functions, Mechanistic Actions, and Therapeutic Potentials, Nutrients 2024; 16(7):924.
14. Duda Ł, Kłosiński KK, Budryn G, Jaśkiewicz A, Kołat D, Kałuzińska-Kołat Ż, Pasieka ZW, Medicinal Use of Chicory (*Cichorium intybus* L.), Scientia Pharmaceutica 2024;92(2):31.
15. Chadwick M, Trewin H, Gawthrop F, Wagstaff C, Sesquiterpenoids Lactones: Benefits to Plants and People, International Journal of Molecular Sciences 2013;14(6):12780-12805.
16. Matos MS, Anastácio JD, Nunes Dos Santos C, Sesquiterpene Lactones: Promising Natural Compounds to Fight Inflammation, Pharmaceutics 2021;13(7):991.
17. Zorrilla JG, Innangi M, Cala Peralta A, Soriano G, Russo MT, Masi M, Fernández-Aparicio M, Cimmino A, Sesquiterpene Lactones Isolated from *Centaurea cineraria* L. subsp. *cineraria* Inhibit the Radicle Growth of Broomrape Weeds, Plants 2024;13(2):178.
18. Liga S, Paul C, Péter F, Flavonoids: Overview of Biosynthesis, Biological Activity, and Current Extraction Techniques, Plants 2023;12(14):2732.
19. Özsoy S, Soykut G, Becer E, Quercetin: A Phytochemical with Pro-Apoptotic Effects in Colon Cancer Cells, Cyprus Journal of Medical Sciences 2022;7(5):587-592.
20. Gülçin I, Bursal E, Sehitoğlu MH, Bilsel M, Gören AC, Polyphenol contents and antioxidant activity of lyophilized aqueous extract of propolis from Erzurum, Turkey, Food and Chemical Toxicology 2010;48(8-9):2227-2238.
21. Panche AN, Diwan AD, Chandra SR, Flavonoids: an overview, Journal of Nutritional Science 2016;5:e47.
22. Tauseef S, Rub R, Sasikumar S, Antimicrobial screening of Cichorium intybus seed extracts, Arabian Journal of Chemistry 2016:9(2):S1569-S1573.
23. Chadwick M, Trewin H, Gawthrop F, Wagstaff C, Sesquiterpenoids lactones: benefits to plants and people, International Journal of Molecular 2013;14(6):12780-12805.
24. Hoste H, Jackson F, Athanasiadou S, Thamsborg SM, Hoskin SO, The effects of tannin-rich plants on parasitic nematodes in ruminants, Trends in Parasitology 2006;22(6):253-261.
25. Foster JG, Cassida KA, Turner KE, In vitro analysis of the anthelmintic activity of forage chicory (Cichorium intybus L.) sesquiterpene lactones against a predominantly Haemonchus contortus egg population, Veterinary Parasitology 2011;180(3-4):298-306.
26. Williams AR, Peña-Espinoza MA, Boas U, Simonsen HT, Enemark HL, Thamsborg SM, Anthelmintic activity of chicory (Cichorium intybus): in vitro effects on swine nematodes and relationship to sesquiterpene lactone composition, Parasitology 2016;143(6):770-777.
27. Moloudi MR, Hassanzadeh K, Abdi M, Zandi F, Rahimi K, Izadpanah E, Hepatoprotective effect of the hydroalcoholic extract of Cichorium intybus in a rat model of obstructive cholestasis, Arab Journal of Gastroenterology 2021;22(1):34-39.
28. Naveed M, Hejazi V, Abbas M, et al, Chlorogenic acid (CGA): A pharmacological review and call for further research, Biomedicine & Pharmacotherapy 2018;97:67-74.
29. Al-Snai A, Mousa H, Wajdi JM, Medicinal plants possessed hepatoprotective activity, IOSR Journal of Pharmacy 2019;9(8):26-56.
30. Neelam, Khatkar A, Sharma KK, Phenylpropanoids and its derivatives: biological activities and its role in food, pharmaceutical and cosmetic industries, Critical Reviews in Food Science and Nutrition 2020;60(16):2655-2675.
31. Faraji S, Daneghian S, Alizadeh M, Effects of chicory (Cichorium intybus L.) on nonalcoholic fatty liver disease, Traditional Medicine Research 2020;5(6),476-86.
32. Roberfroid M. Prebiotics: the concept revisited, Journal of Nutrition 2007;137(3):830S-7S.
33. Zhou Y, Wang J, Zhang D, et al, Mechanism of drug-induced liver injury and hepatoprotective effects of natural drugs, Chinese medicine 2021;16(1):135.
34. Marzouk M, Sayed AA, Soliman AM, Hepatoprotective and antioxidant effects of Cichorium endivia L. leaves extract against acetaminophen toxicity on rats, Journal of Medical Science 2011;2(12):1273-1279.
35. Milovanovic Lj, Majkic T, Torovic Lj, Svircev E, Penic M, Beara I, In vitro study on hypoglycaemic activity of Serbian and some European Merlot wines, Hrana i ishrana 2023;64(1).
36. Hoste H, Jackson F, Athanasiadou S, Thamsborg SM, Hoskin SO, The effects of tannin-rich plants on parasitic nematodes in ruminants, Trends in Parasitology 2006;22(6):253-261.
37. Shad MA, Nawaz H, Rehman T, Ikram N, Determination of some biochemicals, phytochemicals and antioxidant properties of different parts of Cichorium intybus L.: A comparative study, Journal of Animal and Plant Sciences 2020;23(4):1060-1066.
38. Hazra B, Sarkar R, Bhattacharyya S, Roy P, Tumour inhibitory activity of chicory root extract against Ehrlich ascites carcinoma in mice, Fitoterapia 2002;73(7-8):730-733.
39. Lee KT, Kim JI, Park HJ, Yoo KO, Han YN, Miyamoto K, Differentiation-inducing effect of magnolialide, a 1 beta-hydroxyeudesmanolide isolated from Cichorium intybus, on human leukemia cells, Biological and Pharmaceutical Bulletin 2000;23(8):1005-1007.

Cichorium intybus L., Asteraceae: taksonomija, hemijski sastav i farmakološka aktivnost

Filip Balaz[1,2], Ana Tomas[1], Nevena Grujic[1], Emilia Gligoric[1], Branislava Teofilovic[1]

[1]Medicinski fakultet, Univerzitet u Novom Sadu, Novi Sad, Srbija
[2]Krka-Farma d.o.o, Beograd, Srbija

Kratak sadržaj

Cichorium intibus L. (cikorija) je višegodišnja zeljasta biljka iz porodice Asteraceae, široko poznata po tradicionalnoj i savremenoj primeni u medicini, poljoprivredi i ishrani. Ova studija potencira taksonomiju, hemijski sastav i farmakološke aktivnosti cikorije. Biljka je bogata bioaktivnim jedinjenjima, uključujući inulin, fenolne kiseline (npr. hlorogenske i kafeinske kiseline), seskviterpenske laktone i flavonoide (npr. kvercetin i luteolin). Ove fitokemikalije su ključne zbog svojih antioksidativnih, antiinflamatornih, hepatoprotektivnih, antimikrobnih, antihelmintičkih i antidijabetičkih svojstava. Inulin služi kao prebiotičko vlakno, promovišući zdravlje creva i metaboličku regulaciju, dok fenolne kiseline pokazuju snažne antioksidativne i antikancerogene aktivnosti. Seskviterpenski laktoni doprinose antiinflamatornim i antimikrobnim efektima, dok flavonoidi povećavaju terapeutski potencijal biljke modulacijom ključnih bioloških puteva. Farmakološka primena cikorije obuhvata zaštitu jetre, regulaciju metabolizma glukoze i imunološku modulaciju, naglašavajući njen potencijal u hroničnim bolestima. Uprkos širokom terapijskom profilu, neophodne su dalje kliničke studije kako bi se potvrdila efikasnost, uspostavile optimalne doze i istražila dugoročna bezbednost. Ovaj rad podržava integraciju cikorije u funkcionalnu hranu i farmaceutske formulacije, koristeći njene različite zdravstvene prednosti za rešavanje globalnih zdravstvenih izazova.

Ključne reči*: cikorija; inulin; fenolne komponente; seskviterpenski laktoni; farmakološka aktivnost.*