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Review Article

Chemical compositions and health-promoting effects of *Cichorium intybus* L. (chicory): a narrative review

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Abstract: In the present day, the investigation of herbal plants is essential to maintain a healthy and disease-free lifestyle by adhering to traditional medicinal systems and developing novel plant-based pharmaceuticals for a wide range of therapeutic applications. Nature provides a variety of therapeutic ingredients in the form of the versatile medicinal plant known as 'chicory' (*Cichorium intybus*). It has a wide geographical distribution (mostly in Asia, South Africa, and Europe) and a long history of use in folkloric treatments. Folk healers utilize this herb to treat various diseases, including diabetes and liver issues. Chicory (*C. intybus* L.) is a popular food plant in many parts of the world, and its unique phytochemical content has made it a staple in traditional medicine. It is a viable source of biologically relevant elements (potassium (K), iron (Fe), calcium (Ca)), vitamins (vitamin A, B_1, B_2, C), and bioactive compounds (inulin, sesquiterpene lactones, coumarin derivatives, cichoric acid, phenolic acids), with several biological effects including hepatoprotective, cardiovascular, antioxidant, anticancer, reproductive, anti-diabetic, anti-inflammatory, analgesic, antimicrobial, and other pharmacological effects. This review was created to highlight the chemical ingredients and medical significance of *C. intybus* based on recent literature.

Keywords: *Cichorium intybus* L.; chemical composition; benefits; biological effects

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1 Introduction

The common chicory plant's name (*Cichorium intybus* L.) is most likely a combination of Greek and Latin terms. Cichorium means "field" in Latin, while intybus has a counterpart in both languages. The Greek counterpart means "to cut" and refers to the morphology of leaves. The stem's structure is described by the Latin tubus, which means "(a) tube"[1]. The genus name represents its habitat, but the species name defines the plant itself[2]. The name Cichorium was coined by Latinizing the Greek word kichorion, which was frequently seen in works by ancient doctors. It is an archeophyte of Mediterranean-Irano-Turkish provenance. The plant has a lengthy history of practically widespread application, but its medical use is particularly intriguing, dating back to prehistoric times. In ancient Rome, Greece, and Egypt, it was used to improve metabolism and digestion in addition it was employed as a vegetable and a pasture plant[2]. Chicory (*C. intybus* L.), a dicotelydonous herb, can help regulate normal intestinal microflora and immune response, maintain body weight, absorb minerals, and improve bone health[3-5]. More importantly, chicory is a deeply rooted, drought-resistant plant. It contains a high concentration of minerals and uronic acid[6], as well as high fiber digestibility, and is likely capable of preserving the animal diet's high energy and nutritive value[7].

Several studies have demonstrated the potential effects of various medical plants. Treatment with herbal medicines may have some advantages over treatment with single purified chemicals; herbal medicines are mixtures of more therapeutic or preventive components, and thus may have more activity than single products alone. Pure chemicals can also be created from medical plants; the various byproducts or secondary metabolites found in medical plants have made them a valuable source for the development of novel drugs. In addition to specialized medicinal components, the antioxidant activity of medical plants contributes to their beneficial effects. In this review, attempts were made to investigate one of the valuable herbal remedies (*C. intybus* L.) and present its effects by evaluating recently released records, as well as illustrating the significant importance of legacy inherited from ancient times.

2 Botanical characteristics

C. intybus L. is a plant in the Asteraceae (previously

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Compositae) family that grows annually, biennially, or perennially (Table 1). It is cold hardy and typically grows to be between 20 and 150 cm tall. It grows a long, robust, spindly, thick, brown tapio root. The stem and vein are normally green; however, they can occasionally develop a red ring. *C. intybus* can produce numerous tall, empty, ribbed stems, each of which can be lifted or raised. It is rigid, with few leaves. Short, thick hairs cover the bottom of the stem, while the majority of the branches are found at the top. The buds are branching and rigid, with no juice. The leaves of *C. intybus* are green and grouped in a 10–25 cmlong rosette[8].

Table 1 Botanical classification of *C. intybus*[9]

Classification	Chicory herb
Kingdom	Plantae (plants)
Sub kingdom	Tracheoblonta (vascular plants)
Super division	Spermatophyta (flowering plants)
Division	Asterales
Order	Asterids
Suborder	Asterids
Family	Asteraceae (Eudicots family)
Sub family	Asteradeae
Tribe	Cichorieae
Genus	*Cichorium*
Species	Indica *C. intybus*
Botanical name	*C. intybus*
English name	Chicory

The leaf hair may be present on the bottom side of the leaf, primarily on the nerve, throughout the entire leaf surface, or absent altogether. The bottom leaves are caudal, with a large top section, and the side segments are triangular, with the apex towards the leaf's base. The stem's leaves are green with grey tones, oblong or lanceolate, and have an arrow or heart-shaped base. The margins are serrated, with teeth becoming smaller towards the top of the leaf. The upper leaves are entire along the edges and ciliated on the surface. *C. intybus* L.'s inflorescence comprises numerous, multi-flower anthodiums 2–4 cm in diameter, placed on short, thick peduncles alone or in groups of various individuals. The core tube flowers are darker than the marginal flowers, which are light blue. The flowers open only on sunny days. They are especially rich in nectar and pollen (Fig. 1). The chicory plant produces a light brown shell that is 2–3 mm long, triangular or pentagonal, and covered with small pappus hairs. The stalk is topped by a circle of scales in the upper portion. *C. intybus* grows wild in Europe's temperate climate zone, Southwest Asia, the Ural Mountains, and North Africa. It has also spread over Australia, New Zealand, and the Americas. In temperate climate zones, it is common both as a wild plant and as a cultivated variety. It lives in meadows, wastelands, fallows, grasslands, and trackways in both lowland and lower mountain areas[11-14].

3 Chemical composition

All morphological aspects of chicory (roots, herbs, flowers, and leaves) contain a wide range of chemical substances (Fig. 2). Cichoric acid was discovered to be the primary component of the methanolic extract from *C. intybus*. Aliphatic chemicals and their derivatives account for the majority of the plant's composition, with terpenoids being significantly less plentiful.

Roots of chicory contain, amongst others, sap, sesquiterpene lactones, such as e.g., germacranolides (lactucin, lactucopicrin and 8-deoxylactucin) as well as guajanolides (cycriozides B and C, sonchuzide C), which gives a bitter taste. Additionally, taraxane-type triterpenes are present here, such as taraxasterol, and phenolic acids (e.g., chlorogenic, isochlorogenic, neochlorogenic, caffeic, and cichoric acids). The root contains 0.01%–0.02% of the bitter intybin glycoside (whereby the herb contains between 0.1%–2.0% of this chemical), 9%–15% reducing sugars, and between 40%–60% of inulin (as the plant energy store); however, no starch is present in chicory roots. Also, worth mentioning are:

Figure 1 *C. intybus* L. plant[10].

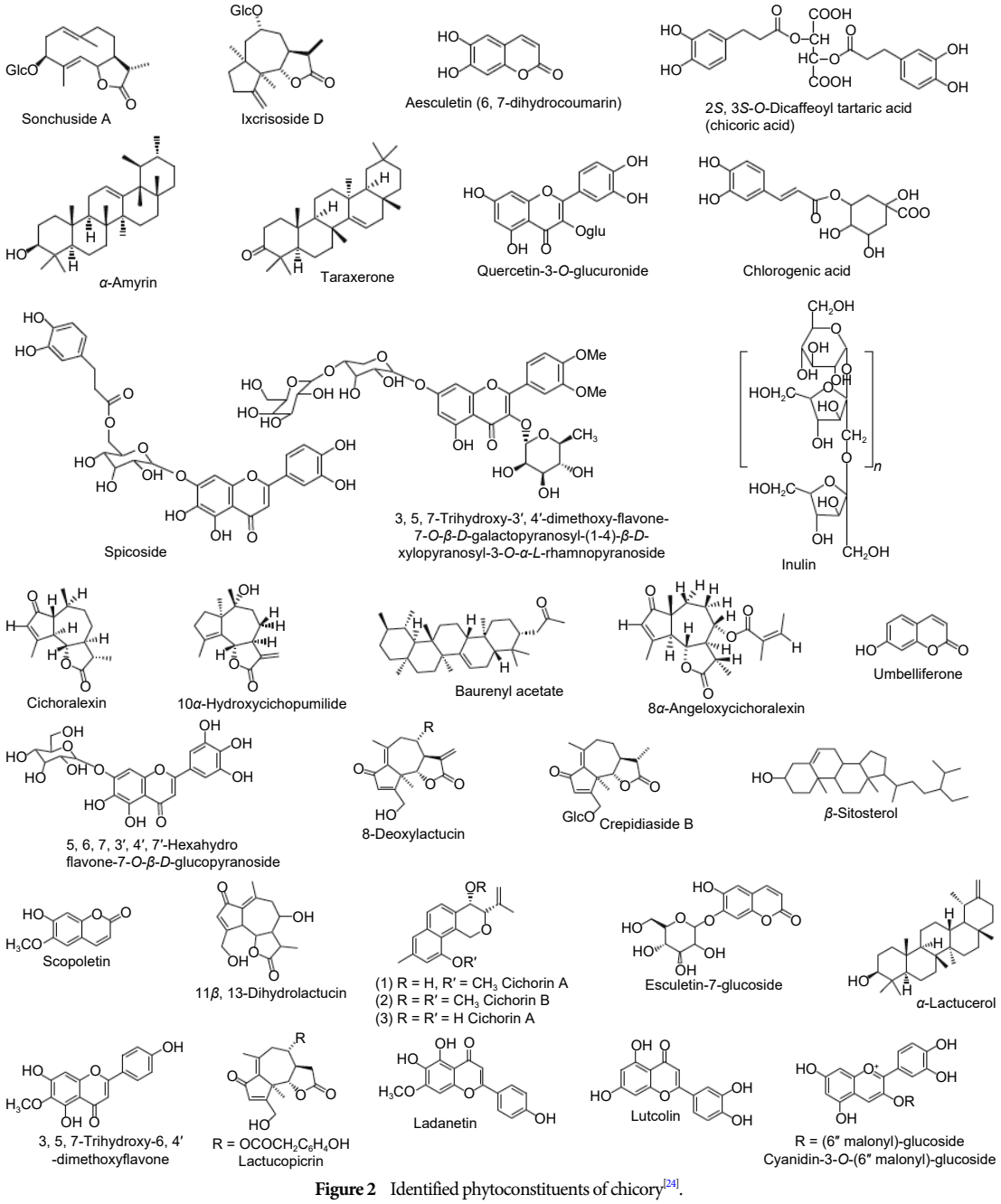

Figure 2 Identified phytoconstituents of chicory[24].

intybinene, a common component of the coffee substitutes, pectins, vitamins B and C[15, 16]. Chicory leaves contain inulin, A, B_1, B_2, and C vitamins, Ca, K, Mg, Na, Fe, Cu, Mn, Zn, and phenolic compounds, amongst others[16].

Flowers contain various sugars, coumarin derivatives (e.g., umbelliferone, esculin, cicorin (esculetin 7-*O*-glucoside, scopoletin), silicic acid, taraxosterol, valeric acid, flavonoids (hyperoside), etheric oils and anthocyanins, the latter of which bring about the perianth's blue color[17]. Also, present in the plant are: gum, choline, phytosterols, mucus, tannins, copper, latex, lipids, proteins, phosphate (P) and K vitamins, amino acids, *β*-sitosterol, malic acid, oxalic acid, shikimic acid, quinic acid, succinic acid, tannins, saponins, flavonoids, terpenoids, cardiac glycosides, anthocyanins[12, 15, 16, 18-20].

The aerial parts and roots are also a source of essential oils[21, 22]. These compounds are present in various amounts, which depend on both the part of the plant and the origin of the chicory. Aerial parts contain carvacrol (50.1%); thymol (13.3%); cinnamic aldehyde (12.4%); camphor (4.4%); carvone (4.1%); linalool (3.9%); *α*-terpineol (2.1%); octane (8%–25.6%); octen-3-ol-1 (0.3%); 2-pentylfuran (up to 2.6%); (2*E*, 4*E*)-heptadienal (up to 2.6%); 1,8-cineole (up to 1.0%); phenylacetaldehyde (1%–4.5%); *n*-nonanal (2.1%–6.5%); camphor (1.4%); (2*E*, 6*Z*)-nonadienal[21, 22]. Roots contain kaempferol; octane (34.3%–69.8%), octen-3-ol-1; 2-pentylfuran; *n*-nonanal (up to 1.2%); *n*-tridecane (0.3%–0.4%); (2*E*, 4*E*)-decadienal (2.2%–3.4%); (2*E*, 4*Z*)-decadienal (0.8%–0.9%); (2*E*, 4*E*)-heptadienal (up to 1.0%); *β*-elemene (0.3%–0.6%); (*E*)-caryophyllene (up to 0.4%); *β*-ylangene (0.3%–0.7%); (*E*)-*β*-farnesene (0.4%–2.2%); geranyl acetone (up to 0.6%); allo-aromadendrene (up to 3.9%); dehydro-aromadendrene (0.6%); *β*-ionone (0.5%); pentadecane (1.8%); *trans*-*β*-guaiene (0.5%–0.7%); (2*E*)-undecenol acetate (1.3%–1.9%); sesquicineole (up to 0.8%); (2*E*)-tridecanol (0.5%–2.6%); pentenyl salicilate (4.8%–22.7%); *n*-hexadecane (1.7%–18.1%); tetradecanal

(1.1%–2.7%); 2-pentadecanone (0.4%–1.3%); *n*-nonadecane (0.3%–3.9%); *n*-eicosane (2.1%–5.1%); *n*-heicosane (0.4%–0.6%); (2*E*)-nonen-1-al (0.9%); *n*-decanal (0.8%–1.7%); (2*E*, 4*E*)-nonadienal (up to 0.4%); *n*-decanol (up to 0.9%); (2*E*, 4*Z*)-decadienal (0.5%–1.3%); (2*E*, 4*E*)-decadienal (1.5%–1.9%); geranyl acetone (0.7%–3.2%); *β*-ionone (1.9%–3.0%); (2*E*)-tridecanol (6.3%); pentenyl salicylate (0.9%); *n*-hexadecane (0.9%–5.9%); tetradecanal (1.0%–2.8%); tetradecanol (0.8%); 2-pentadecanone (4.2%–14.9%); (*E*)-2-hexylcinnamaldehyde (0.4%); octadecane (0.5%); *n*-nonadecane (5.1%–46.9%); (5*E*, 9*E*)-farnesyl acetone (0.6%–2.3%); *n*-eicosane (0.9%–2.9%); *n*-octadecanol (0.3%–1.0%); *n*-heicosane (2.5%–8.0%)[22, 23].

4 Health-promoting properties

The most prevalent types of material used for therapeutic purposes are fresh and dried (Fig. 3)[25]. It is the most important therapeutic herb in the Asteraceae family[26]. *C. intybus* extracts have been shown to have a variety of biological and pharmacological properties, including anti-hyperuricemia, anti-inflammatory, antidiabetic, antinematodal, antioxidant, antiproliferative, hepatoprotective, antibacterial, and antiprotozoal effects[1, 14, 18, 27, 28] The plant has laxative, detoxifying, energizing, blood-cleansing, and antioxidant qualities. Also, found is a diuretic effect, which is ascribed to phenolic acids. *C. intybus* seeds have been utilized effectively in Unani and Ayurvedic medicine[26]. High quantities of inulin promote the development and preservation of appropriate gut flora, giving the plant the name "probiotic"[15, 29, 30]. Table 2 summarizes the bioactivity of *C. intybus* L.

4.1 Anti-inflammatory

Alcoholic preparations of *C. intybus* root demonstrated anti-inflammatory properties in the treatment of pyorrhea and gingival inflammation[32]. Chicory inhibited both prostaglandin E2 and the cyclooxygenase enzyme. Chicory root ethyl acetate extract inhibits tumor necrosis factor alpha (TNF-α)-mediated cyclooxygenase production in human colon cancer cells. It reduced the synthesis of prostaglandin E2 in a dose-dependent manner[33]. Chicory also reduced ethanol-induced immunotoxicity while demonstrating anti-inflammatory effects[34, 35]. Chicory roots also showed strong dose-dependent anti-inflammatory efficacy in a carrageenan-induced paw edema model. It reduced serum TNF-α, iterleukin (IL)-6, and IL-1 levels, resulting in enhanced antioxidant activity in paw tissue. This suggested that chicory roots' anti-inflammatory and antioxidant effects may be mediated by cytokine suppression[36]. The herbal blend of *Origanum majorana* and *C. intybus* extract was reported to reduce food intake and body weight in obese rats, as well as improve lipid profile, liver function, and thyroid activity[37].

4.2 Anti-diabetic activity

Using radiolabeled glucose uptake and lipid accumulation tests, the impact of *C. intybus* methanolic extract on glucose transport and adipocyte development in 3T3-L1 cells was investigated. A dose-dependent response was observed in the considerable increase in glucose absorption by chicory methanolic extract. Additionally, it prevented preadipocytes from differentiating[38]. Because of their antioxidant activity, the chicory roots' polyphenol-rich fraction had a great potential for hypoglycemia[39]. Also. inulin and chicory root extract (CRE) supplementation reduced the amount of glucose absorbed in the jejunum[40, 41]. These findings also indicated that chicory formulations (such as tea) might help both diabetics and healthy individuals with post-prandial hyperglycemia by reducing intestinal glucose absorption. The anti-diabetic properties of *C. intybus* ethanolic extract were studied in male Sprague-Dawley rats administered streptozotocin (STZ). An oral glucose tolerance test was affected by a dose of 125 mg/kg BW; the same quantity taken orally for 14 days decreased serum glucose by 20% and cholesterol by 16%. Throughout the experiment, there was no change in insulin secretion[42]. Chicoric

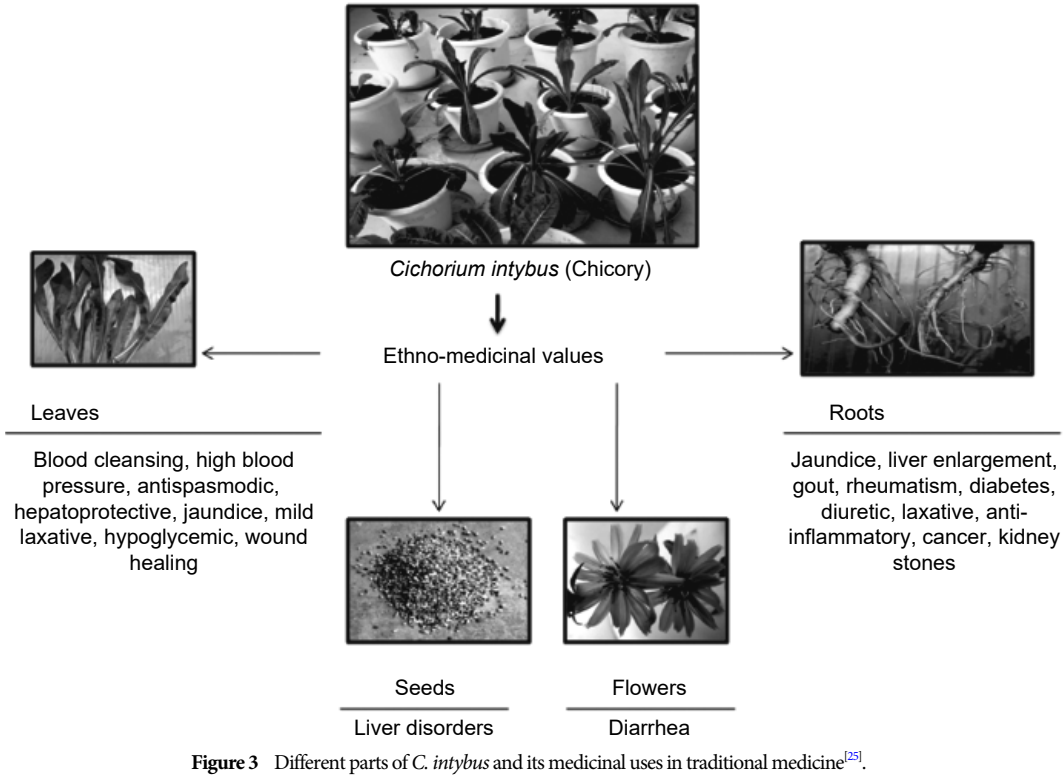

Figure 3 Different parts of *C. intybus* and its medicinal uses in traditional medicine[25].

Table 2 Summarized bioactivity of *C. intybus* L.[31]

Bioactivity/Health condition	Plant part	Extract type	Compound/s
Anti-hepatotoxic activity	Chicory plant	Ethyl-acetate extracts	
	Leaf	Water extract	Cichoric acid
	Leaf	Ethanolic extract	Flavonoids
	Seed	Alcoholic extract	Phytoconstituents from extracts such as flavonoids, saponins and their glycosides
Anti-diabetic	Plant (root, leaves, and stems)	Ethanolic extract	Potentially inulin
	Seed	Aqueous extract	Phytochemicals such as anthocyanins, tannins, coumarins, chicoric acid, chlorogenic acid (CGA), and caffeic acid
	Root	Ethyl acetate extract	Potentially inulin, sesquiterpene lactones, coumarins, flavonoids
	Root and leaf	Methanolic extract	Root Sesquiterpenoid lactones from chicory root: cichoralexin, 10α-hydroxycichopumilide and 8α-angeloyloxycichoralexin; terpenoids and phenolics
Antimicrobial	Leaf		Phenolic compounds–gallic acid, protocatechic acid, chicoric acid, and CGA
	Leaf and root	Ethanolic and methanolic extracts of γ-irradiated chicory	Phenolic compounds and flavonoids
	Seed	Methanolic extract and ethylacetate fraction	Alkaloids, flavonoids, saponins, tannins, steroids, anthraquinone
	Seed	Aqueous and organic (ethanol and ethyl acetate) extracts	Water soluble compounds (inulin, flavonoids, etc)
	Flower	Ethyl acetate extract	
	Flower	Methanolic extract	Phenolic compounds
	Root	Ethanolic extract	Caffeoylquinic acid
Antioxidant	Leaf	The ethanolic and methanolic extracts of γ-irradiated chicory	Phenolic compounds and flavonoids
	Seed	The methanolic extract and ethyl acetate fraction	Alkaloids, flavonoids, saponins, tannins, steroids, anthraquinone
Anti-inflammatory	Root	Polar solvent extract	Sesquiterpene lactones
Anti-cancer activity	Root	Methanolic extract	Lactucin, β-sitosterol, quinic acid, succinic acid, and polyphenols like flavonoids

acid, the caffeoyl ester purified from chicory, stimulated glucose transport and insulin secretion, according to contradictory results reported by Tousch *et al.*[43]. This suggested that chicoric acid could be used clinically as a type 2 diabetes medication that acts on both insulin sensitivity and insulin secretion.

Aqueous extract of chicory seed had both short-term (approximately 2 h; glucose tolerance test) and long-term effects on diabetes. Chicory may be effective as a natural dietary supplement for slowing diabetes progression[44]. This discovery was reinforced by Kaskoos[45], who found that administering *C. intybus* seed extract (500 mg/kg BW, 21 days) produced a prolonged anti-hyperglycemic effect in STZ-induced diabetic rats. Caffeoylquinic acid-rich chicory seed extract reduced diet-induced metabolic abnormalities in type 2 diabetes[46]. An intra-peritoneal injection of *C. intybus* extract into STZ-induced diabetic rats resulted in a significant decrease in blood glucose, lipid profile, and malondialdehyde levels, as well as an increase in reduced glutathione (GSH), superoxide dismutase, GSH-*S*-transferase, and catalase activities when compared to rats treated with STZ alone. These findings suggested that the *C. intybus* extract possessed antioxidant properties and prevented diabetes complications by modulating oxidative stress[47]. Chicory had the potential to treat hyperglycemia, hyperlipidemia, insulin resistance, non-alcoholic fatty liver disease (NAFLD), and non-alcoholic steatohepatitis all at once, possibly by modulating the peroxisome proliferator-activated receptor-alpha/sterol receptor element-binding protein-1 ratio[48]. A randomized, double-blind, placebo-controlled trial was conducted on 47 adult healthy volunteers, who were separated into two groups: a test group that received CRE orally and a placebo group that drank barley tea containing 10% coffee (300 mL daily for 4 weeks). The CRE produced excellent results, including antihyperglycemic and antidyslipidemic effects, as well as better bowel movement. Furthermore, when baseline and post-intervention values were compared, the CRE group showed a significant increase in adiponectin levels[49].

4.3 Antimicrobial activity

Microorganisms develop resistance to many antimicrobial treatments, allowing them to survive for lengthy periods and cause numerous infectious diseases and other disorders in people[50]. As a result, plant-based medications or herbal plants may be a viable alternative to synthetic antibacterial treatments for protecting against harmful microbes. Plants are a rich source of antimicrobial compounds that are employed to reduce bacteria with antibiotic resistance patterns; thus, employing plant-based medications can provide critical steps toward eradicating the threat posed by antibiotic-resistant microorganisms[51]. The prospective outcomes obtained from herbal plants encourage the increased use and investigation of herbal-based medications for the treatment of various bacterial infections or disorders. As a result, chicory (*C. intybus*) could be utilized as an herbal remedy to treat bacterial infections caused by a variety of Gram-negative and Gram-positive bacteria. The alcoholic extract of this herb has shown promising antibacterial activity against a variety of bacterial infections.

According to Rani and Khullar[52], the methanolic leaf extract showed a modest level of antibacterial action against bacteria that cause intestinal infections. Additionally, the aerial portion and root of plants were found to contain aqueous and alcoholic-based

(ethanolic and ethyl acetate) extracts that were effective antibacterial agents against a variety of bacteria, including Gram-positive (*Bacillus subtilis*, *Staphylococcus aureus*, and *Sarcina lutea*) and Gram-negative (*Pseudomonas aeruginosa* and *Pseudomonas fluorescens*) bacteria[53]. Furthermore, chicory water and ethyl acetate fractions showed antifungal efficacy against *Fusarium solani* and *Aspergillus niger*[54]. While ethanolic and ethyl acetate extracts of chicory seeds showed promise for antibacterial action against *P. aeruginosa* and *S. aureus*, the aqueous extracts of the seeds did not exhibit any antibacterial activity against the two bacteria[55]. Chicory has been proposed as a natural antibacterial agent for dairy products due to *C. intybus*'s antimicrobial activity against *Bacillus cereus*[56]. Scientists are searching for natural or plant-based medicines that can specifically target various virulence features of bacteria. This strategy has the potential to be a viable substitute for antibiotic-based therapy. This strategy further demonstrates its advancement as it does not disturb the host's microbiota. It would have enormous benefits in fighting the infection process without causing cells to acquire antibiotic-resistant patterns[32, 57]. The low molecular mass extract of chicory (*C. intybus* var. *silvestre*) has been shown to exhibit an anti-virulence effect against a few oral pathogens, including *Actinomyces naeslundii*, *Streptococcus mutans*, and *Prevotella intermedia*. Additionally, certain components (oxalic, succinic, shikimic, and quinic acids) contribute to this anti-virulence effect, which helps to prevent infections that cause gingivitis and tooth decay[32].

4.4 Anti-hepatotoxic activity

The liver is identified as the most significant organ involved in the body's defense mechanism against bacteria and other exogenous/foreign macromolecules. The liver's enzymatic system has the strongest capacity to change or metabolize foreign molecules, resulting in detoxification and activation of endogenous substances (fatty acids and steroids) and exogenous compounds (drugs and insecticides). Furthermore, the liver contains well-developed organelles that participate in the manufacture of a variety of substances including albumin, cholesterol, and fibrinogen. Hepatotoxicity is regarded as a critical health issue around the world, and the generation of free radicals or reactive oxygen species (ROS) is a key cause of liver disease progression. Carbon tetrachloride (CCl_4) free radicals inhibit the activity of antioxidant enzymes such as GSH of phase II detoxification enzymes and GSH-dependent antioxidant enzymes, resulting in the onset of oxidative stress, a major cause of acute and chronic liver damage[58, 59] . As a result, the role of antioxidants has become critical, as they have the potential to provide hepatoprotective activity by eliminating ROS and free radicals.

C. intybus has been portrayed as a significant hepatoprotective plant in the Unani medicine system, and it is particularly beneficial in liver-related diseases such as jaundice and hepatitis[60]. Elgengaihi *et al.*[61] investigated the hepato-protective properties of different chicory extracts against carbon tetrachloride-intoxicated albino rats. Also, the aqueous-methanolic extract from *C. intybus* seeds was tested for hepatoprotective activity against carbon tetrachloride and acetaminophen-induced liver damage in mice, and it also reduced death rates and serum levels of glutamyl pyruvate transaminase, alkaline phosphatase, and glutamylboxaloacetate transaminase[62]. Furthermore, the root callus extract of *C. intybus* root extract was found to be a better means of protecting against hepatocellular damage than the natural root extract[63].

Recent studies demonstrate that treatment of rats with Chicory extract restored body weight and reduced relative liver weight, total cholesterol levels, triglycerides, glucose, and hepatic enzymes in the model of acute liver injury. *C. intybus* is a known plant with hepatoprotective properties[64, 65]. For example, chicory syrup treatment decreased lipid peroxidation and improved liver histology in weanling rats exposed to deltamethrin[66]. The treatment of rats with obstructive cholestasis with 70% ethanolic extract of chicory reduced bilirubin and liver enzyme (alanine aminotransferase (ALT) aspartate aminotransferase (AST), and alkanine phosphatase (ALP)) levels[67]. Chicory extract administered to rats with thioacetamide-induced liver cirrhosis was able to normalize serum liver enzyme activity, albumin, and bilirubin levels[68]. This treatment reduced oxidative stress levels and IL-6 production by regulating AMP-activated protein kinase signaling. 6-Gingerol, a main constituent of ginger, attenuated liver injury induced by a well-known hepatocarcinogen, diethylnitrosamine[69].

Hepatoprotective compounds can be classified based on their mechanisms of action: antioxidants, compounds capable of regenerating hepatocytic membranes, and stimulators of regeneration of hepatic parenchyma[70]. The mechanisms of chicory's hepatoprotective properties can be mainly attributed to its antioxidant activity. The hepatoprotective effects of chicory extracts have been attributed to the presence of phenolic compounds, specifically, chicoric acid, and its antioxidant and anti-inflammatory properties[71, 72]. The hepatoprotective effects of another polyphenolic compound, kaempferol, are also ascribed to its antioxidant and anti-inflammatory properties (Fig. 4)[22, 73, 74].

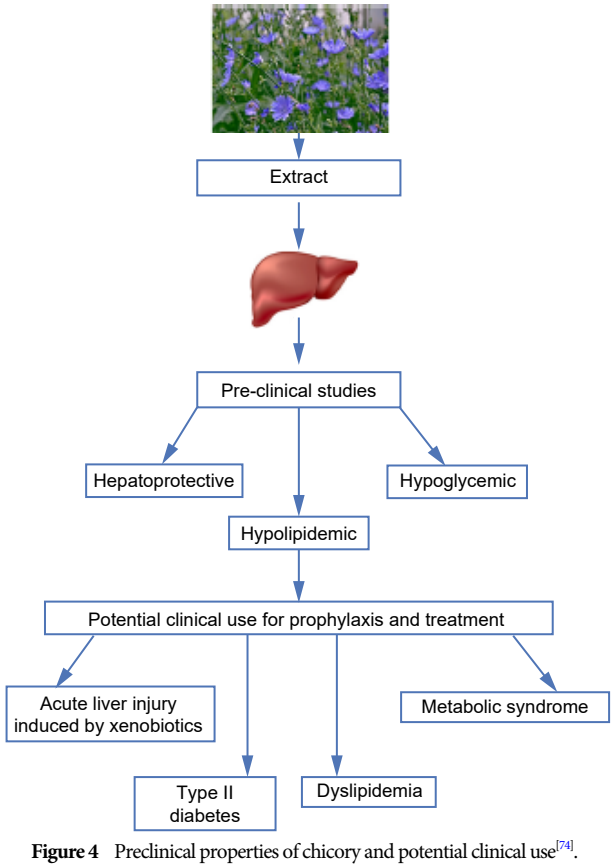

Figure 4 Preclinical properties of chicory and potential clinical use[74].

4.5 Antioxidant activity

Numerous investigations have demonstrated the antioxidant

activity of the chicory plant. Liu *et al.*[75] connected the antioxidant and antibacterial properties of CRE to its bioactive compounds known as caffeoylquinic acids. Rub *et al.*[39] studied the antioxidant activity of the polyphenol-rich fraction of chicory roots and discovered a substantial hypoglycemic potential. Dalar and Konczak[76] investigated the antioxidative activity of the roots, stems, leaves, flowers, and entire plant of *C. intybus* L. According to their findings, the leaves contained the most total phenols (22.6 mg GAE/g DW) and had the maximum antioxidant capacity. The leaf's ferric reducing antioxidant capacity (FRAP) value was 251.6 μmol Fe^{2+}/g DW. The oxygen radical absorbance capacity (ORAC) value of chicory plant sections decreases in the following order: flower ≥ leaf > root > stem. They also discovered numerous important phenolic compounds in an ethanol-based lyophilized extract of *C. intybus* L. leaf, including apigenin, hydroxybenzoic acid-*O*-hexoside, caftaric acid, isorhamnetin, 4-*O*-caffeoylquinic acid, 5-*O*-caffeoylquinic acid, apigenin glucoside, luteolin hexoside, quercetin/hesperitin glucoside, cichoric acid, and quercetin rutinoside (rutin). Heimler *et al.*[77] found that 19.30–48.60 mg sample FW/mg 1,1-diphenyl-2-picrylhydrazyl radical (DPPH) had antiradical activity the antiradical dose necessary to produce 50% inhibition (IC_{50}) in chicory leaves.

According to Khalaf *et al.*[78], irradiation treatment was superior for enhancing the antimicrobial, antioxidant, and phytochemical activities. The most recommended doses for chicory roots and leaves, respectively, were 4 and 12 kGy to maintain phytochemical content, boost antioxidant activity, and enhance antimicrobial activity. Additionally, they stated that leaves had an (80.95 ± 0.39)% DPPH radical scavenging activity. Chicory flowers, as measured by FRAP (240.8 μmol Fe^{2+}/g DW), appear to have higher antioxidant capabilities than their roots or stems. In addition, flowers had the highest ORAC (1,307.7 μmol trolox equivalent (TE)/g DW) when compared to the stem, leaf, and root. Also, Jurgoński *et al.*[79] announced that the antioxidant activity of the chicory leaf extract (210.1 nmol/g FW) was shown to be higher than that of the seed extract (505.1 nmol/g FW). Similar to Chinese medicinal herbs, chicory leaves, and flowers have significant oxygen radical scavenging and overall reducing capacities[76]. In cultivated and wild chicory cultivars, the contents of lutein (8.0–30.1 μg/g FW), *β*-cryptoxanthin (0.13–0.41 μg/g FW), and *β*-carotene (3.3–14.1 μg/g FW) varied, according to the results of Montefusco *et al.*[80], who looked into the hydrophilic and lipophilic antioxidant activities.

Chicory cultivars' antioxidant activity varied from 352 μmol TE/100 g FW to 1,056 μmol TE/100 g FW, contingent on varietal and environmental parameters on soil, growing circumstances, and climate. The total phenolic content of both wild and farmed chicory was found to range from 30.1 mg GAE/100 g FW to 101.7 mg GAE/100 g FW. In chicory leaves, the total antioxidant activity was associated with the flavonoid content, which ranged from 11.1 mg catechin equivalents (CE)/100 g FW to 66.2 mg CE/100 g FW They also concluded that, among the many types of chicory, the hydrophilic antioxidant activity was greater than the lipophilic antioxidant activity. When Jurgoński *et al.*[79] and Fathi *et al.*[81] compared the effects of rutin and chicory seed extract, which is high in caffeoylquinic acid, on rats' diets, they discovered that the latter increased blood antioxidant status and decreased serum atherogenicity, whereas the former did the opposite.

4.6 Digestive support

The most prevalent benefit of chicory is improved digestion. Friendly bacteria, also known as symbiotic bacteria, such as lactobacillus and bifidobacteria, live in our intestines and help with digestion. These bacteria suppress infections such as candida and aid in immunological function[82]. Chicory also includes inulin, a highly effective probiotic and soluble fiber. All plants contain inulin, but chicory has the largest concentration. Inulin can lower the body's acidity, which can assist in preventing digestive issues such as acid reflux and indigestion. According to studies, chicory root enhances the flow of bile, which aids in the breakdown of fat and consequently digestion[83]. Furthermore, CREs helps to decrease digestive discomfort caused by Intestinal stomach issues.

4.7 Anxiety and stress

Chicory is a natural sedative for the nervous system that helps relieve anxiety and relax the mind. This reduces the stress and potentially harmful effects on the body. Chicory extract has been demonstrated in studies to serve as a sedative and anti-inflammatory for the neurological system. This can lower inflammation in persons with nervous system diseases, decreasing pain[84]. CRE can also be used as a sleep aid due to its sedative properties, and it is a far superior natural option to sleeping drugs. Relieving stress and anxiety can assist in minimizing the risk of heart disease, hormone imbalance, insomnia, and premature aging[85].

4.8 Anti-cancer activity

Chicory roots and leaves demonstrated promising anticancer activity against human hepatocellular carcinoma (HepG2) and breast cancer (MCF-7) cell lines. The ethanolic extract of chicory had the opposite impact as the ethanolic extract of dandelion, which dramatically promoted cellular proliferation of MCF-7 and further induced the expression of estrogen-related genes[86]. Chicory's anticancer properties can be linked to its phytochemical richness, which includes terpenoids, *β*-sitosterol, taraxasterol, luteolins, *α*-amyrin, and inulin compounds in the extract of roots and leaves. Terpenoids have been found to preferentially kill hepatocellular carcinoma cells using a multidirectional mechanism while sparing normal cells[87]. Furthermore, terpenoids provide a new approach to overcoming breast cancer therapy failure[88]. Taraxasterol and *β*-sitosterol can decrease tumor progression at several phases, such as creation, promotion, invasion, and metastasis[89]. Other proposed options for chicory's anti-cancer potential include luteolin and lactucin, both of which are plentiful in the plant. Luteolin has suppressed MCF-7 cell proliferation by blocking the insulin-like growth factor (IGF)-1-mediated PI3K-Akt pathway dependent on estrogen receptor α (ERα) expression[90] and produced G1 arrest in HepG2 cells[91]. Furthermore, luteolin reduced doxorubicin-induced cytotoxicity in MCF-7[92]. Furthermore, lactucin has been shown to increase the expression of apoptosis-related proteins such as B-cell lymphoma 2 (BCL-2) and CASP8 and FADD-like apoptosis regulator (CFLAR) in Caki-1 human kidney carcinoma cells via ROS generation[93]. Chicory extract is similarly rich in chicoric acid[94, 95]. Chicoric acid may promote autophagy in gastric cancer via enhancing endoplasmic reticulum (ER) stress, which is regulated by AMPK[96]. Chicoric acid, when coupled with doxorubicin, exhibits a cytoprotective effect against doxorubicin-induced damage and suppresses apoptosis via antioxidant activity[97].

4.9 Effect on energy homeostasis

Using 3T3-L1 adipocytes, the impact of chicory (*C. intybus*)

salad leaves on protein tyrosine phosphatase 1B (PTP1B) inhibition was investigated, along with their function in regulating the major indicators involved in insulin cell signaling and adipogenesis. Research on purification revealed the synergistic effects of CGA and other derivatives of caffeic acid in the methanolic extract of *C. intybus* (CME). By modifying the expression of insulin signaling and adipogenesis markers, the incubation of CME and CGA with 3T3-L1 adipocytes dramatically increased the 2-deoxy-d-3[*H*]-glucose uptake and prevented adipogenesis. Additionally, in mild STZ-induced diabetic rats fed a high-fat diet, the impact of CME on insulin sensitivity was studied. The plasma metabolic profile and insulin sensitivity were restored after a two-week CME supplementation. Thus, the findings indicate that both *in vitro* and *in vivo*, the caffeoyl derivatives of chicory salad leaves exhibit a promising pharmacological effect on energy homeostasis via PTP1B inhibition[98].

4.10 Cardiovascular effect

Eight *C.intybus* variations were studied pharmacologically on an isolated toad's heart, and the results indicated that while their potencies varied, all eight types had an activity similar to quinidine. The location of the action was identified on a representative sample where it generated an effect following atropinization and ganglion blocking[99]. In isolated rat aorta strips, the vasorelaxant effects of chicoric acid from *C. intybus* and caffeic acid were investigated. Rat aorta contraction caused by norepinephrine (NE) demonstrated gradual relaxation activity in response to chicoric acid, a diester consisting of (*S*, *S*)-tartaric acid and caffeic acid, with or without endothelium. While t hese drugs decreased NE-induced vasocontraction in the presence of nicardipine, they did not affect contraction caused by a high potassium concentration (60 mmol/L K^+). According to Sakura *et al.*[100], the findings demonstrated that NE-induced vasocontraction is inhibited by a reduction in calcium influx from the extracellular area. Rats exposed to cisplatin-induced toxicity had their electrolyte balance tested to determine the detoxifying potential of *C. intybus*. Pretreatment demonstrated a partial counteraction on the electrolyte imbalances and Na^+-K^+-ATPase activity at a dose of 500 mg/kg BW of *C. intybus* ethanolic extract[101].

The plant phenolics found in caffeine-free chicory coffee are abundant and include caffeic acid, which prevents platelet aggregation in vitro, and phenylpyruvate tautomerase, which catalyzes the proinflammatory cytokine macrophage migration inhibitory factor (MIF). 27 healthy participants who drank 300 cc of chicory coffee daily for a week were used to evaluate the cardiovascular advantages of the beverage. Depending on the inducer utilized for the aggregation test, the food intervention had differing effects on platelet aggregation. Following a week of chicory coffee drinking, there was a significant drop in serum MIF levels as well as whole blood and plasma viscosity. Furthermore, notable advancements in red blood cell deformability were observed. There were no modifications found in the levels of red blood cells, fibrinogen, or hematocrit. Although it is doubtful that any one of the compounds in chicory coffee can account for the complete range of these effects, caffeic acid and other phenolics are anticipated to play a significant part[102].

4.11 Toxicity and side effects

C. intybus was regarded as a safe medicine due to its extensive use. There are no known health risks or side effects associated with the correct administration of prescribed therapeutic doses. There is a minor risk of sensitization from skin contact with the medication[74]. A 28-day subchronic oral toxicity trial in rats found no extract-related mortality or other toxicological indications[103]. The toxicity of *C. intybus* extracts was assessed using the *Vibrio fischeri* bioluminescence inhibition test. This bacterial test detects the decrease in light emission from the marine luminescent bacteria *V. fischeri* when exposed to toxins. *C. intybus* was considered safe for human usage because the studied extracts inhibited bioluminescence by less than 20%[104]. A placebo-controlled, double-blind experiment was conducted to assess the safety and tolerability of a bioactive extract (dose escalation trial) of chicory root in patients with osteoarthritis. The medication was well tolerated; only one patient receiving the highest dose of chicory stopped because of the side effects[105].

4.12 Safety and health claims

The FDA has classified chicory extract and inulin as Generally Regarded as Safe (GRAS) and added them to the Everything Added to Food in the United States (EAFUS) list. Schmidt *et al.*[103] demonstrated the safety of a CRE during the Ames test and a 4-week subchronic toxicity investigation in male and female Sprague-Dawley rats. CRE containing sesquiterpene lactones was shown to be non-toxic and non-mutagenic when supplied orally at doses of 70, 350, or 1,000 mg/kg. Toxicological profiling (subacute and chronic toxicity) of aqueous chicory seed extract has been confirmed to have no adverse effects, and a dose of 200 mg/kg BW resulted in a significant reduction in serum glucose (52.7%) and triglyceride levels (65.3%), as well as a decrease in the oxidative burden in high-fat-diet-induced diabetic rats[106].

The claim of chicory products' short-term and/or long-term effects on diabetes has been proven by the glucose tolerance test and hemoglobin A1c (HbA1c) measurement[107]. Furthermore, some clinical studies on human subjects have demonstrated the potential role of bioactive CRE in the management of osteoarthritis[105], a positive effect of chicory inulin or oligofructose to reduce the postprandial blood glucose response[108], as well as oligofructose-enriched chicory inulin positive effects on the improvement of the glucose and calcium homeostasis, liver function tests, blood pressure and reduction in hematologic risk factors of diabetes in female patients with type 2 diabetes mellitus (T2DM)[109].

European Food Safety Authority (EFSA) confirmed health claim that non-digestible carbohydrates from chicory (fructo-oligosaccharides (FOS, oligofructose) obtained from chicory inulin), which should replace sugars in foods or beverages reduce post-prandial glycemic responses[110]. EFSA and Commission Regulation (EU) 2015/2314 confirmed that the effect on bowel function demonstrated by the intake of native chicory inulin is a beneficial physiological effect with a dosage of 12 g/day for this claim[111].

4.13 Current and potential applications

Chicory has various known applications, including baking and grinding chicons or roots for coffee substitutes and supplements, using leaves as a vegetable, and cultivating chicory as a forage plant for poultry and animal feed[9]. Chicory, being a rich source of dietary fibers like inulin and FOS, as well as many functional food elements, can help you stay healthy and avoid disease. According to Drabińska *et al.*[112], inulin is commonly used in food as a low-

calorie sweetener, fat substitute, and texture modifier to boost dietary fiber content and enhance product technology and sensory value. Many studies have looked into the bioactivity of inulin, including its tumor-inhibitory, anti-diabetic, anti-hepatotoxic, and antioxidant properties. Chicory powdered roots find another application in successfully replacing wheat flour (10%) and fat (25%) in cracker production after 659 debittering by soaking the roots in water or citric acid solution[113]. Chicory fibers were also incorporated in restructured sausages in order to replace fat, with conclusion that addition of chicory fiber significantly reduced the moisture, fat, hardness, and pH values of sausages[114]. Bossard *et al.*[115] obtained flour from dehydrated chicory root in order to prepare food dough for baking. Wang and Cui[116] also mentioned the utilization of chicory for tea production, such as tea for keeping fit. Also, implementation of CREs (1%, 2% and 3%) in yogurt due to health promoting effect of chicory inulin as well as its ability to form creamy emulsions with aqueous liquid were investigated[117]. Dried CRE (2%–6%) was implemented into yogurt-ice cream formulation with the intention to decrease production costs by replacing dairy ingredients with other low-cost alternatives, such as inulin and buttermilk. By increasing the amount of dried CRE in yoghurt-ice cream formulation increased the textural and flavor properties and overall acceptability score while melting rate was decreased[118]. Future studies should be focused more closely to the utilization of chicory in food products on an industrial basis, given its considerable benefits and potential.

4.14 Future prospects

Chicory's use in phytotherapy is expanding, but current hurdles must be addressed before further investigation of this herb's unknown therapeutic potential. Because *C. intybus* is amenable to genetic manipulation, future emphasis will be in gaining plants' new therapeutic potential. The majority of phytoconstituents have not been examined for their medicinal potential, thus further research is needed to acquire a more comprehensive understanding of bioactive chemicals against various illnesses.

5 Conclusion

In conclusion, *C. intybus* L. is a common plant with a high potential. It undoubtedly deserves more widespread usage in medical prophylaxis and phytotherapy (Fig. 5). Individual portions, such as leaves or flowers, both fresh and dried, can be a helpful addition to a daily diet. *C. intybus* extracts' multifunctional activities suggest they could be a promising natural health-promoting source.

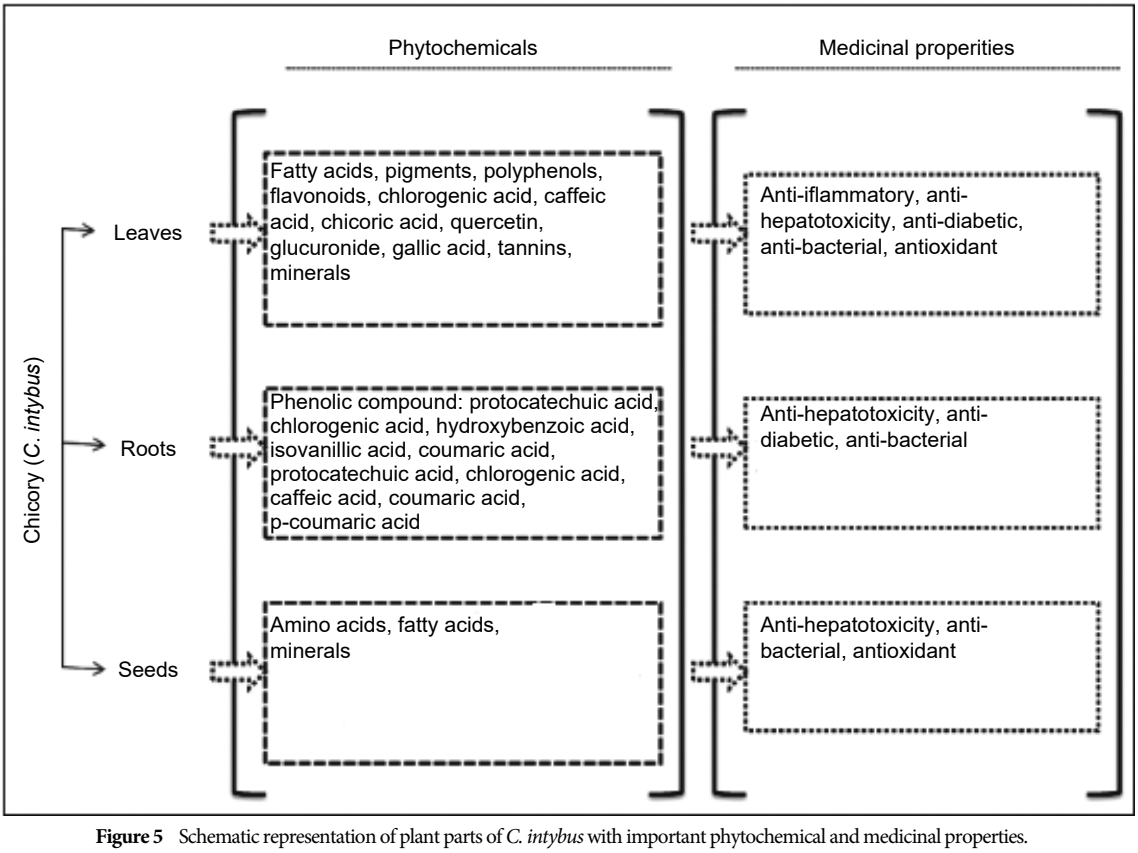

Figure 5 Schematic representation of plant parts of *C. intybus* with important phytochemical and medicinal properties.

Conflicts of interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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