

## Review Article

# Phytochemistry and pharmacology of *Cichorium intybus*

**Tahreem Riaz<sup>1</sup>, Muhammad Akram<sup>1</sup>, Umme Laila<sup>1</sup>, Muhammad Talha Khalil<sup>1</sup>, Rida Zainab<sup>1</sup>, Momina Iftikhar<sup>1</sup>, Fethi Ahmet Ozdemir<sup>2</sup>, Gawel Sołowski<sup>2</sup>, Ebrahim Alinia-Ahandani<sup>3</sup>, Marcos Altable<sup>4</sup>, Chukwuebuka Egbuna<sup>5,6</sup>, Adonis Sfera<sup>7</sup>, Muhammad Adnan<sup>8\*</sup>, Pragnesh Parmar<sup>9</sup>**

<sup>1</sup>Department of Eastern Medicine, Government College University Faisalabad, Pakistan

<sup>2</sup>Department of Molecular Biology and Genetics, Faculty of Science and Art, Bingol University, Bingol, 1200, Türkiye

<sup>3</sup>Department of Biochemistry, Payame Noor University of Tehran, Tehran, Iran

<sup>4</sup>Department of Neurology, Neuroceuta, (Virgen de Africa Clinic), Spain

<sup>5</sup>Department of Biochemistry, Faculty of Natural Sciences, Chukwuemeka Odumegwu Ojukwu University, Uli, Anambra State, Nigeria

<sup>6</sup>Nutritional Biochemistry and Toxicology Unit, World Bank Africa Centre of Excellence, Centre for Public Health and Toxicological Research (ACE-PUTOR), University of Port-Harcourt, Port Harcourt, Rivers State, Nigeria

<sup>7</sup>University of California Riverside, Patton State Hospital, USA

<sup>8</sup>Alsehat Unani Medical College Faisalabad

<sup>9</sup>Additional Professor and HOD, Forensic Medicine and Toxicology, AIIMS, Bibinagar, Telangana, India

\*Corresponding author email: [adnanop99@gmail.com](mailto:adnanop99@gmail.com)



International Archives of Integrated Medicine, Vol. 11, Issue 2, February, 2024.

Available online at <http://iaimjournal.com/>

ISSN: 2394-0026 (P)

ISSN: 2394-0034 (O)

Received on: 1-2-2024

Accepted on: 11-2-2024

Source of support: Nil

Conflict of interest: None declared.

Article is under Creative Common Attribution 4.0 International

DOI: [10.5281/zenodo.10694047](https://doi.org/10.5281/zenodo.10694047)

**How to cite this article:** Tahreem Riaz, Muhammad Akram, Umme Laila, Muhammad Talha Khalil, Rida Zainab, Momina Iftikhar, Fethi Ahmet Ozdemir, Gawel Sołowski, Ebrahim Alinia-Ahandani, Marcos Altable, Chukwuebuka Egbuna, Adonis Sfera, Muhammad Adnan, Pragnesh Parmar. Phytochemistry and pharmacology of *Cichorium intybus*. Int. Arch. Integr. Med., 2024; 11(2): 33-46.

## Abstract

*Cichoriumintybus* L., often known as chicory, is a Mediterranean plant species that is a member of the Asteraceae family. It has been known to have therapeutic benefits for a very long time. *C. intybus* is unique among the six species of *Cichorium* that are grown in Europe and Asia because of its wide range of uses in conventional medicine. The plant has been used in many traditional medical systems, especially in India, where it has been used to treat a wide range of illnesses, from diabetes to wounds. Chicory contains a wide range of phytoconstituents, including cellulose, proteins, sugar, flavonoids, polyphenols, carotenoids, anthocyanins, tannins, coumarins, sesquiterpene lactones, fatty acids, cholins, benzo-isochromenes, alkaloids, vitamins, and minerals. The diverse ranges of therapeutic benefits associated with *C. intybus* are partly ascribed to this phytochemical composition. The pharmacological actions of chicory, which have been demonstrated to range from hepatoprotective to anti-inflammatory, demonstrate the plant's versatility and its potential to treat a variety of illnesses. This article offers a thorough investigation of *C. intybus* L.'s phytochemistry and pharmacological applications. This review attempts to be a useful resource for researchers, medical professionals, and practitioners interested in using *Cichoriumintybus*'s medicinal properties for improving human health by compiling the body of knowledge on the botanical and chemical aspects of chicory as well as its therapeutic applications.

## Key words

*Cichoriumintybus*, Phytochemistry, Bioactive compounds, Pharmacology, Health benefits.

## Introduction

Six species make up the genus *Cichorium*, which is part of the Asteraceae family and is mostly found in Europe and Asia [1]. These plants, which include the chicory *Cichoriumintybus* L., store inulin, a  $\beta$ -2,1 linked fructose polymer with a terminal glucose residue, in their stems, tubers, and taproots as a reserve carbohydrate [2]. One of the most well-known members of the genus is chicory, a tall, woody perennial herb that grows to a height of about one metre. It has huge basal leaves and a thick taproot that reaches up to 75 cm [1, 3]. With historical roots in ancient Egypt, cilantro has been used for a variety of purposes throughout history. It has been grown as a vegetable crop, a medicinal herb, an alternative to coffee, and even as sporadic animal feed. The discovery in the 1970s that the root plant *Cichoriumintybus* contains as much as 40% inulin—a carbohydrate that has little effect on blood sugar—established chicory as a viable option for people with diabetes. Because of this finding, *C. intybus* is now a major source for the synthesis of inulin on an industrial scale [4].

The Greek word "*Cichorium*" means "field," while the Latin word "*intybus*" means "cutting" (with reference to leaves) comes from both Greek and Latin sources. Gaining knowledge of its botanical and historical background might help one appreciate *Cichoriumintybus*'s many uses, from customary customs to contemporary industrial uses. The fact that the plant is known by several names in different places highlights how widely used it is. Chicory was originally farmed by the ancient Egyptians for medicinal, vegetable, and occasionally animal feed uses. It was also employed as a coffee replacement. The revelation in the 1970s that chicory's root contained up to 40% inulin made it a good choice for those with diabetes [5]. *C. intybus* is grown for a variety of uses and is divided into four major kinds: forage chicory that is derived from wild variations, Brussels or witloof chicory for etiolated buds, leaf chicory for culinary purposes, and industrial or root chicory for inulin extraction. This adaptability demonstrates the numerous use of chicory in global agriculture and cooking [6].

Despite its widespread historical use, *Cichoriumintybus*, a plant with medicinal value in Eurasia and parts of Africa, is not included in any official pharmacopoeia of a European Union member state or the European Pharmacopoeia [5]. However, because of its widespread distribution, different plant parts have been used in traditional remedies all throughout the world [7]. The root is the main source of significant phytochemicals, which adds to the plant's therapeutic qualities [1]. This paper explores traditional practices, scientific confirmation, and a thorough examination of *C. intybus*'s phytochemical composition, with a focus on the medical uses of the plant that are both commercially and culturally relevant.

### **Phytochemistry of *Cichoriumintybus***

A perennial herbaceous plant in the Asteraceae family is called *Cichoriumintybus*. The family is Asteraceae, sometimes referred to as the sunflower or aster family. It is a sizable and significant floral plant family with commercial importance. Based on its biological traits, *Cichoriumintybus* can be systematically categorised and identified due to its scientific categorization. The scientific classification is as follow [8]

Kingdom: Plantae-plants

Subkingdom: Tracheobionta

Class: Magnoliopsida

Subclass: Asteridae

Phylum: Angiosperms

Order: Asterales

Family: Asteraceae

Genus: *Cichorium*

Species: *intybus*

In the realm of botanical distribution, during the flowering stage, it grows to a height of up to 1.5 metres (5 feet) on a sturdy, hairy stem that has grooves [9]. The leaves are distinguished by their stalked, lanceolate form that does not have any lobes. With the smallest leaves on the top of the plant, their length ranges from 7.5 to 32 centimetres (3 to 12+1/2 inches), while their

widths vary from 2 to 8 centimetres (3/4 to 3+1/4 inches) [10]. The flower heads are rather large, ranging in width from 3 to 5 centimetres (1+1/4 to 2 inches), and are usually light blue or lavender in colour, though there have been isolated reports of white or pink blooms. The taller, erect inner bracts of the involucre bracts are separated from the shorter, spreading outer bracts by two rows. Chicory is known to bloom from March through October, and the tiny scales at the tip of the seeds are what identify them.

Across its natural habitat, chicory grows as a roadside wild plant across western Asia, North Africa, and Europe. Early European settlers brought the plant to North America, where it quickly took root. Chicory has spread considerably outside of its original region and is now found in many countries, including as China and Australia. Chicory is more likely to grow in places with higher levels of precipitation since it prefers areas with a lot of rainfall. This trait could affect its occurrence and dispersion in various geographic locations.

### **Chemical constituents of *Cichorium intybus***

*Cichorium intybus*'s chemical composition may vary depending on the plant portion, growing environment, and extraction techniques, among other things. Numerous studies have demonstrated that condensed tannins, one type of phytochemical that promotes animal health, are embodied in chicory. However, high dietary tannin concentrations have been linked to detrimental impacts on animal productivity [11]. A study involving the extraction of flavonoids and phenolic acids from several varieties of *Cichoriumintybus* var. *silvestre* was carried out by Carazzone, et al. (2013) [12]. Sixty-four compounds were found when the compounds were characterised using high-performance liquid chromatography-electrospray ionization/mass spectrometry. They contained three derivatives of tartaric acid, thirty-one flavonol, two flavone glycosides, and hydroxycinnamic acid derivatives including eight

mono- and dicaffeoylquinic acids. Ten anthocyanins and different isomers of caffeic acid derivatives were also included.

Massoud, et al. (2009) [13] have out a thorough analysis of *Cichorium Intybus*'s chemical composition in both its leaves and roots. Representative phytoconstituents were classified as macronutrients, micronutrients (vital minerals), and phenolic compounds in the study. The results provided important new information about the composition of chicory plants. The chicory plant's roots and leaves differ in several noteworthy ways, including moisture content, crude protein, crude ether extract, ash, total carbs, total soluble sugars, inulin, crude fiber, and dietary fiber (DF).

Nørbaek, et al. [14] (2002) determined that anthocyanins were the primary cause of the blue hue seen in the chicory flower perianth. The chemical constituents of chicory flowers was further characterised in later research [15, 16], which showed the presence of essential oils, saccharides, flavonoids, cichorine, and methoxycoumarin. In a previous study, these researchers [17] characterised in detail the components found in chicory flowers, leaves, and shoots. These components included inulin, fructose, choline, resin, chicoric acid, esculetin, esculin, cichoriin, umbelliferone, scopoletin, 6,7-dihydrocoumarin, and sesquiterpene lactones including their glycosides. Researchers have also isolated vitamins A, B6, and K from red chicory, which also includes minerals and carotenoids [18, 19]. Chicoric acid was found to be the main component obtained from methanolic extracts of chicory in a food chemistry study by [20, 21]. Octane, n-nonadecane, pentadecanone, and hexadecane were identified as the main volatile components of chicory in previous studies [15]. Terpenoids make up the minor components of the chicory plant, while aliphatic chemicals and their derivatives make up the majority of the plant [22]. The plant's rich and varied phytochemical profile is highlighted by this

thorough explanation of the components found in chicory blossoms, which adds to the plant's importance in both botanical and dietary contexts.

Chicory seeds are a nutrient-dense food that can be consumed by ruminants as well as monogastric eaters. Ying and Gui (2012) [23] report that chicory seeds of different kinds have a high crude protein content that is more than 19% of the dry weight. This protein concentration is 1.6–2.4 times higher than that of traditional cereals including wheat, rice, maize and barley. The authors also stress how chicory seeds meet the requirements for the perfect diet protein by being a great supply of important amino acids including methionine, lysine, leucine, isoleucine, and phenylalanine. Chicory seeds also have a high concentration of demulcent oils, which offer both unsaturated and saturated fatty acids [24]. Significantly, the profile of total fatty acids is mostly composed of essential linoleic acid, followed by monounsaturated oleic acid, stearic acid and palmitic acid [23]. When compared to lucerne seeds, chicory seeds exhibit higher concentrations of vital minerals, such as potassium, calcium, magnesium, selenium, and zinc [25]. The components of chicory seeds were found to include phosphorus, potassium, calcium, magnesium, sodium, iron, copper, zinc, and manganese in a mineral analysis [23]. Furthermore, scientists [26] extracted the sesquiterpene glycoside cichotyboside from *Cichorium intybus* seeds, and the results showed a strong hepatoprotective effect against rats' liver damage caused by carbon tetrachloride. Chicory seeds are a nutritious substitute or addition to animal and human diets due to their high nutritional content.

The chemical composition of fresh chicory roots has been thoroughly researched by numerous studies, providing insight into its nutritional and bioactive elements. According to reports, fresh chicory roots contain roughly inulin, a polysaccharide that resembles starch, by dry

weight, along with sucrose, cellulose, protein, ash, and miscellaneous substances. Dry chicory root extract has a much higher concentration of inulin, making up about 98% of its weight; the remaining 2% is made up of other components [27-30]. Chicory roots contain a high concentration of oligofructose and fructan of the inulin type, as confirmed by Soobo (2005) [31]. Chemically speaking, inulin is a polydisperse-(2,1)-fructan that can hydrolyze to produce glucose and fructose. Chicory has a high fructose concentration of up to 94%, which is attributed to its long-chain carbohydrate structure, which is made up of 22–60 fructose molecules and one terminal glucose molecule [32]. Chicory's noticeable bitterness is largely due to sesquiterpene lactones, such as lactucin, 8-deoxylactucin, lactucopicrin, and 11 $\beta$ -dihydro-derivatives [33].

Researchers have confirmed that sesquiterpene lactones play a role in imparting bitterness by isolating them from chicory roots, and among them is a (+)-germacrene [34]. In addition, chicory root extract contains volatile oils, fatty acids, alkaloids, triterpenes, flavonoids, latex, tannins, and saponins. It is produced by filtering and centrifuging insoluble fractions from milled dry roots in water [35]. Moreover, three recently obtained benzo-isochromenes (Cichorins A, B, and C) have been found in chicory roots, which are noteworthy chemicals [36, 37]. According to these researchers' findings [36, 37], the roots also include tannins, fatty acids (mainly palmitic and linoleic acids), pectin,  $\alpha$ -lactucol (taraxasterol), cichoriin (esculetin-7-glucoside), sugars (especially fructose and mannose), fixed oils, choline, and other components. Chicory roots are significant in both nutritional and therapeutic contexts, and this thorough analysis highlights their complex and varied chemical profile.

## Pharmacology of *Cichoriumintybus*

### Anti-inflammatory activity

Chicory, or *Cichoriumintybus*, is a plant that is noted for its anti-inflammatory properties, which

can be linked to a wide range of bioactive chemicals. Sesquiterpene lactones, a family of phytochemicals that are widely distributed throughout the plant, are mainly responsible for the anti-inflammatory properties of chicory. Among these lactones, substances with strong anti-inflammatory qualities include lactucin, lactone, and various derivatives. Chicory's anti-inflammatory properties are mediated through the regulation of important inflammatory pathways. Sesquiterpene lactones obstruct the synthesis of pro-inflammatory cytokines that are essential to the inflammatory response, like interleukins and tumour necrosis factor- $\alpha$  (TNF- $\alpha$ ). Furthermore, it has been demonstrated that components of chicory decrease the activity of enzymes, such as lipoxygenase (LOX) and cyclooxygenase-2 (COX-2) that are involved in the manufacture of inflammatory mediators [38]. Chicory has anti-inflammatory properties that also affect different immune cells at the cellular level. The inhibition of inflammatory processes is partly due to the manipulation of leukocyte function, namely that of neutrophils and macrophages. The reduction of oxidative stress is connected to chicory's anti-inflammatory properties. Moreover, chicory suppresses leukocyte adhesion and migration, which further reduces the inflammatory response, by down regulating the expression of adhesion molecules on endothelial cells. Chicory is a potential treatment option for inflammatory diseases because of these complex systems that work together to reduce inflammation.

### Anti-oxidant activity

*Cichoriumintybus*, is a plant that is high in flavonoids and phenolic acids, two types of polyphenols that have been shown to have significant antioxidant action [39]. Chicory's antioxidant capacity is essential for scavenging damaging free radicals and reactive oxygen species (ROS), which helps shield cells and tissues from damage brought on by oxidative stress. Strong antioxidants have been found in the polyphenolic chemicals found in chicory,

including quercetin glycosides, chicoric acid, and derivatives of caffeic acid. By scavenging free radicals, these substances shield cellular constituents like lipids, proteins, and DNA from oxidative damage. Chicory's antioxidant properties also include the capacity to increase the activity of antioxidant enzymes found in the body, which strengthens the body's defences against oxidative stress. Redox-sensitive signalling pathways are modulated and oxidative activities are inhibited as part of the mechanism of action. Chicory's polyphenols have the ability to neutralise free radicals and give electrons, breaking the cycle of oxidative damage and lipid peroxidation. Furthermore, it has been documented that chicory increases the expression and function of antioxidant enzymes, such as glutathione peroxidase (GPx), catalase (CAT), and superoxide dismutase (SOD). Studies have looked into the antioxidant capacity of chicory using a range of *in vivo* and *in vitro* methods. Chicory extracts have demonstrated the capacity to scavenge a variety of free radicals, including hydroxyl and superoxide anion radicals. Moreover, chicory's antioxidant qualities have been linked to its ability to lessen ailments linked to oxidative stress, such as cancer, neurological disorders, and cardiovascular diseases.

### **Gastroprotective activity**

Significant gastroprotective action has been shown for *Cichoriumintybus*, suggesting that it may be able to shield the gastric mucosa and treat disorders associated with gastric injury. Empirical evidence supports the use of *Cichoriumintybus*, also known as chicory, in Turkish folklore due to its antiulcerogenic properties. An aqueous infusion of *C. intybus* roots was given orally to Sprague-Dawley rats in a research 15 minutes before ethanol was used to induce ulcerogenesis. The test group showed almost 95% suppression of ulcerogenesis, indicating a significant efficacy [40]. The study's observation of antiulcerogenic capability highlights *C. intybus*'s gastroprotective characteristics. The aqueous decoction was

essential in reducing the harmful effects of ethanol-induced ulcer development because it was probably enhanced by bioactive chemicals found in chicory roots. This antiulcerogenic effect may be due to mechanisms that modulate inflammatory responses, improve mucus production, and attenuate oxidative stress—all of which are known to be linked to the development of ulcers. These results support the traditional Turkish folkloric usage of *C. intybus* for treating ulcers and demonstrate the plant's potential as a medicinal agent for the treatment and prevention of stomach ulcers.

### **Hepatoprotective activity**

*Cichoriumintybus*, or chicory, has a well-established hepatoprotective effect, which supports its traditional usage in folk medicine. One of the ingredients in Liv-52, a popular traditional Indian tonic with hepatoprotective properties, is chicory. Liv-52 treatment was associated with a considerable decrease in serum levels of liver enzymes, specifically alanine aminotransferase (ALT) and aspartate aminotransferase (AST), in a randomised, double-blind clinical trial including cirrhotic patients. It also resulted in a significant decline in ascites and Child-Pugh scores [41].

A different polyherbal formulation called Jigrine, which includes chicory leaves among its ingredients, showed hepatoprotective efficacy in a research conducted on male Wistar albino rats that had hepatopathy caused by galactosamine. Jigrinepretreatment raised blood and tissue glutathione levels while markedly lowering urea, ALT, and AST levels. A significant reduction in inflammatory cells was seen upon histopathological inspection, suggesting protection against galactosamine toxicity [42].

The hepatoprotective potential of several chicory extracts, such as the alcoholic and aqueous extracts of the roots and root callus, as well as the aqueous-methanolic extract of the seeds, has been studied. The hepatic enzyme levels were

effectively reduced by these extracts, and a histological analysis indicated no evidence of liver damage or fat formation. Chicory's phenolic constituents, such as cichotyboside and esculetin, have also shown hepatoprotective properties. Chicory extracts were found to reduce serum levels of hepatic enzymes and the death rate in mice whose liver damage was caused by acetaminophen and carbon tetrachloride. Rats treated intraperitoneally with crude extracts and fractions of chicory showed comparable hepatoprotective effects against liver toxicities produced by carbon tetrachloride and paracetamol [43].

Chicory's effectiveness against hepatic steatosis was investigated in both in vitro and in vivo models. In HepG2 cells, the chicory seed extract was effective in lowering intracellular fat accumulation, and in diabetic rats, it reduced both fat accumulation and fibrosis. Chicory is thought to have hepatoprotective properties because of its capacity to prevent damage caused by free radicals. A portion of the chicory leaf ethanolic extract showed a dose-dependent reduction in free radical-induced DNA damage [44].

### **Analgesic activity**

Using experimental models in mice, the analgesic effect of *Cichorium intybus* has been studied. It has been specifically linked to lactucin, lactucopicrin, and 11 $\beta$ , 13-dihydrolactucin. The analgesic effects of these substances were considerable in both tail-flick and hot plate tests. All three of the substances had significant analgesic effects in the hot plate test. Of the compounds examined, lactucopicrin proved to be the most effective analgesic. Mice's reaction time to a hot surface is measured in this test, and the analgesic effects that are seen suggest that these substances may have a role in reducing thermal pain. Similarly, in the tail-flick test, 30 mg/kg of lactucin, lactucopicrin, and 11 $\beta$ , 13-dihydrolactucin had antinociceptive (pain-relieving) effects that were similar to 60 mg/kg

of ibuprofen. The tail-flick test measures how quickly animals react to a harsh stimuli (heat), and similar results to those of a well-known painkiller, such as ibuprofen, imply that these substances are effective at reducing pain [45]. Additionally, it was shown that lactucin and lactucopicrin have sedative effects, as shown by a reduction in the spontaneous locomotor activity of mice. The overall analgesic effects could be enhanced by this sedation effect, which could affect the tested animals' perception and reaction to pain.

### **Anti-diabetic activity**

Numerous studies examining chicory's (*Cichorium intybus*) effects on lipid profiles, glucose metabolism, and associated parameters have confirmed the plant's potential antidiabetic action. The entire chicory plant's ethanol extracts shown notable antidiabetic effects in one research. Male Sprague-Dawley rats with streptozotocin-induced diabetes were given 125 mg/kg body weight of the ethanol extract as treatment. In the oral glucose tolerance test, the extract showed a significant decrease in serum glucose levels. Serum triglyceride and cholesterol levels in treated rats also significantly decreased. When compared to diabetic rats that were not treated, the extract also helped to lower the hepatic glucose-6-phosphatase activity in the former group [46].

Studies on the antidiabetic properties of chicory's aqueous seed extract have also been conducted. Chicory extract inhibited weight loss and resisted excessive increases in fasting blood sugar in rats with early-stage and late-stage diabetes caused by streptozotocin-niacinamide and streptozotocin alone, respectively. Blood markers such as total cholesterol, glycosylated haemoglobin, triacylglycerol, and alanine aminotransferase were all brought back to normal after receiving chicory extract treatment. Treatment with chicory increased insulin levels in early-stage diabetic rats, suggesting an insulin-sensitizing effect [47].

When *C. intybus* leaf powder was fed to diabetic Wistar rats, the rats' blood glucose levels significantly decreased and eventually approached normal levels. Chicory supplementation also resulted in a reduction in brain lipopolysaccharide, an increase in glutathione content, a drop in malondialdehyde levels (a sign of oxidative stress), and a restoration of anticholinesterase action [48]. Numerous substances found in chicory, such as chicoric acid, caffeic acid, and chlorogenic acid, have been suggested as possible antidiabetic drugs. It was shown that these substances have the ability to sensitise and secrete insulin, as well as boost the absorption of glucose by muscle cells and stimulate the release of insulin from islets of Langerhans and insulin-secreting cell lines [49].

#### **Anti-tumor activity**

Chicory has shown strong tumor-inhibitory action in a number of studies, suggesting that it may be a good candidate for cancer treatments. In one study, the effects of a crude chicory root ethanolic extract on Ehrlich tumour carcinoma in mice were examined. When given intraperitoneally at a dose of 500 mg/kg/day, the extract significantly inhibited the growth of the tumour, which in turn extended the life span of the treated mice by an astounding 70% [50]. Apart from the root extracts, the aqueous-alcoholic macerate obtained from chicory leaves has demonstrated potential in preventing the growth of tumours. In particular, the macerate showed antiproliferative effects on amelanotic melanoma C32 cell lines, indicating possible uses in cancer treatment. These results imply that chemicals found in chicory leaves may be able to inhibit the proliferation of melanoma cells [51]. Moreover, a  $1\beta$ -hydroxyeudesmanolide found in chicory roots called magnolialide has been shown to have inhibitory effects on a range of tumour cell lines. Magnolialide not only inhibited but also caused human leukaemia cells to differentiate into monocyte or macrophage-like cells. Due to its potential to contribute to a

less aggressive cancer phenotype, this differentiation-inducing trait is important in cancer therapy [52].

#### **Anti-malarial activity**

For its antimalarial qualities, *Cichorium intybus* has been utilised traditionally. This is especially true in some parts of Afghanistan, where the infusion of fresh roots has been used as a treatment for malarial fevers. It has been determined that the bitter chemicals found in chicory, such as lactucin, lactucopicrin, and guaianolidesesquiterpenes, may have antimalarial properties. These bitter chemicals were detected in chicory root extracts that were aqueous in nature. Lactucin and lactucopicrin, at dosages of 10 and 50  $\mu\text{g/mL}$ , respectively, showed full suppression of the HB3 clone of the Honduras-1 strain of *Plasmodium falciparum* in a research evaluating their antimalarial efficacy [53, 54]. These results imply that chicory's antimalarial properties are facilitated by its bitter constituents, specifically lactucin and lactucopicrin. Although the scientific results support the historical use of chicory in treating malarial fevers, more investigation is necessary to determine the precise mechanisms of action, evaluate the safety and effectiveness in various populations, and possibly create compounds derived from chicory that could be used as antimalarial drugs.

#### **Anti-microbial activity**

*Cichorium intybus* demonstrates noteworthy antibacterial efficacy against a diverse array of pathogenic pathogens. The antibacterial activities of the organic acid-rich extract obtained from fresh red chicory, specifically *C. intybus* var. *sylvestre*, were evaluated against periodontopathic bacteria, such as *Actinomyces naeslundii*, *Prevotella intermedia*, and *Streptococcus mutans*. This active extract showed the ability to reduce bacterial adhesion to cells and the production of biofilms. It contained quinic acid, oxalic acid, succinic acid, and shikimic acid. Furthermore, with differing



degrees of effectiveness, these organic acids caused biofilm breakdown and dead cell separation from the cultured substratum [55].

Aqueous and organic chicory seed extracts have demonstrated antibacterial efficacy against a variety of pathogenic pathogens. This comprises *Candida albicans*, *Escherichia coli*, *Pseudomonas aeruginosa*, and *Staphylococcus aureus*. Chicory root extracts also demonstrated strong antibacterial activity against *E. Coli*, *Bacillus subtilis*, *S. aureus*, and *Salmonella typhi* [56-58]. *C. intybus* leaf extract exhibited a modest level of antibacterial activity, namely against *Salmonella typhi* that is resistant to many drugs. Chicory root extracts rich in guaianolides demonstrated antifungal effects against anthropophilic fungi such as *Trichophyton tonsurans*, *T. rubrum*, and *T. violaceum*. Moreover, *Pseudomonas cichorii* was well inhibited by cichoralenin, a sesquiterpenoid phytoalexin that was isolated from chicory [59, 60, 61].

These results highlight the varied antibacterial potential present in *Cichorium intybus*'s many constituent parts. There is potential in investigating compounds produced from chicory as natural antibacterial agents; however, additional study is required to clarify the precise mechanisms of action and evaluate the safety and effectiveness of these compounds for possible medicinal uses.

### **Analgesic activity**

In mice, the chemicals lactucin, lactucopicrin, and 11 $\beta$ , 13-dihydrolactucin, found in *Cichorium intybus*, or chicory, have shown analgesic effects through tail-flick and hot plate tests. All three of the compounds demonstrated analgesic effects in the hot plate test; lactucopicrin shown the greatest efficacy. In the tail-flick test, the antinociceptive effects of these compounds at a dose of 30 mg/kg were similar to those of ibuprofen, which was delivered at a dose of 60 mg/kg. It was observed that lactucin and

lactucopicrin have some sleepy properties in addition to their analgesic effects. A reduction in the mice's spontaneous locomotor activity served as proof of this sedative effect. These results imply that the chemicals obtained from chicory, in particular lactucin and lactucopicrin, have sedative and analgesic effects, suggesting a possible use for them in the treatment of pain and associated ailments.

### **Conclusion**

In conclusion, this review offers a thorough summary of the various bioactive substances and medicinal qualities present in this plant species. Chicory, or *Cichorium intybus*, is a plant that has been widely examined for its phytochemical composition. This research has revealed a wide range of secondary metabolites, including organic acids, polyphenols, and sesquiterpene lactones. These substances add to the diverse pharmacological activity that chicory displays; these activities include antioxidant, anti-inflammatory, and analgesic qualities. The review's examination of *C. intybus*' phytochemistry highlights the plant's potential as a source of organic chemicals with major health advantages. The pharmacological insights offered demonstrate its potential uses in a variety of therapeutic domains, such as hepatoprotective effects, antibacterial therapies, anti-inflammatory and analgesic interventions, and possible involvement in the management of diseases including cancer and diabetes. Furthermore, chicory's historical application in conventional medicine is consistent with the results of recent studies, underscoring the herb's long-standing importance in herbal therapies. Overall, *Cichorium intybus* is positioned as a valuable botanical resource that merits further investigation for its therapeutic potential and possible applications in contemporary medicine, according to the synthesis of phytochemical and pharmacological knowledge offered in this research.

## References

1. Bais HP, Ravishankar GA. *Cichoriumintybus* L.—cultivation, processing, utility, value addition and biotechnology, with an emphasis on current status and future prospects. Journal of the Science of Food and Agriculture, 2001; 81(5): 467–484.
2. vanArkel J, Vergauwen R, Sévenier R, et al. Sink filling, inulin metabolizing enzymes and carbohydrate status in field grown chicory (*Cichoriumintybus* L.) Journal of Plant Physiology, 2012; 169(15): 1520–1529.
3. Tehreem Riaz, Muhammad Akram, Momina Iftikhar, Fethi Ahmet Ozdemir, Gawel Solosky, Aymen Owais Ghauri, Adonis Sfera, Pragnesh Parmar. A critical discussion of the outcome literature of cognitive behavioural therapy for social anxiety disorder. Int. Arch. Integr. Med., 2024; 11(1): 9-15. DOI: 10.5281/zenodo.10556726
4. Judžentienė A, Būdienė J. Volatile constituents from aerial parts and roots of *Cichoriumintybus* L. (chicory) grown in Lithuania. Chemija., 2008; 19: 25–28.
5. Muhammad Amjad Chishti, Muhammad Akram, Fethi Ahmet Ozdemir, Aymen Owais Ghauri, Adonis Sfera, Pragnesh Parmar. *Cuscuta reflexa* Traditional miracle plant: A Review on ethnomedicinal and therapeutic Potential. Int. Arch. Integr. Med., 2024; 11(1): 1-8. DOI: 10.5281/zenodo.10556608
6. Cadalen T, Morchen M, Blassiau C. Development of SSR markers and construction of a consensus genetic map for chicory *Cichoriumintybus* L. Molecular Breeding, 2010; 25(4): 699-722.
7. Süntar I, Akkola EK, Kelesb H, Yesiladac E, Sarkerd SD, Baykala T. Comparative evaluation of traditional prescriptions from *Cichoriumintybus* L. for wound healing: stepwise isolation of an active component by in vivo bioassay and its mode of activity. Journal of Ethnopharmacology, 2012; 143(1): 299–309.
8. Saeed M, Abd El-Hack ME, Alagawany M, Arain MA, Arif M, Mirza MA, et al. Chicory (*Cichoriumintybus*) herb: Chemical composition, pharmacology, nutritional and healthical applications. International Journal of Pharmacology, 2017; 13: 351-360.
9. Masato Hada, El Hadji Seydou Mbaye, Muhammad Akram, Umme Laila, Momina Iftikhar, Sundus Saleem, Rida Zainab, FethiAhmet Ozdemir, WalaaFikry Elbossaty, Pragnesh Parmar. Implication effect of Probiotics and chemotherapy drugs in prohibition and remediation of lung carcinoma induced by COVID-19. IAIM, 2023; 10(12): 45-55.
10. Masato Hada, Abid Rashid, Abdulazeez M. Abaka, Muhammad Akram, Umme Laila, Rida Zainab, Momina Iftikhar, Sundus Saleem, Muhammad Talha Khalil, El Hadji Seydou Mbaye, Pragnesh Parmar, Walaa Fikry Elbossaty. Chemotherapeutic Prevention and Treatment of COVID-19 Myocardial Injury with Thalidomide and Celecoxib. IAIM, 2023; 10(12): 29-44.
11. Makkar H. P. S. Effects and fate of tannins in ruminant animals, adaptation to tannins, and strategies to overcome detrimental effects of feeding tannin-rich feeds. Small Ruminant Research, 2003; 49(3): 241–256.
12. Carazzone C., Mascherpa D., Gazzani G., Papetti A. Identification of phenolic constituents in red chicory salads (*Cichoriumintybus*) by high-performance liquid chromatography with diode array detection and electrospray ionisation tandem mass spectrometry. Food Chemistry, 2013; 138(2-3): 1062–1071.

13. Massoud M. I., Amin W. A., Elgindy A. A. Chemical and technological studies on Chicory (*CichoriumIntybus L*) and its applications in some functional food. Journal of Advanced Agricultural Research, 2009; 14(3): 735–756.
14. Parmar P. Study of students' perceptions towards case based learning in Forensic Medicine. Indian Journal of Forensic Medicine and Toxicology, 2018; 12(1): 154-157.
15. Judžentiene A., Budiene J. Volatile constituents from aerial parts and roots of *Cichoriumintybus L.* (chicory) grown in Lithuania. Chemija., 2008; 19(2): 25–28.
16. Abbas Z. K., Saggi S., Sakeran M. I., Zidan N., Rehman H., Ansari A. A. Phytochemical, antioxidant and mineral composition of hydroalcoholic extract of chicory (*Cichoriumintybus L.*) leaves. Saudi Journal of Biological Sciences, 2014; 22(3): 322–326.
17. Parmar P. Study of students' perceptions regarding open book test in Forensic Medicine. J Indian Acad Forensic Med, 2017; 39(4): 404-406.
18. Ćustić M., Poljak M., Toth N. Effects of nitrogen nutrition upon the quality and yield of head chicory (*Cichoriumintybus L.* var. *foliosum*). Acta Horticulturae, 2000; 533: 401–410.
19. Mulabagal V., Wang H., Ngouajio M., Nair M. G. Characterization and quantification of health beneficial anthocyanins in leaf chicory (*Cichoriumintybus*) varieties. European Food Research and Technology, 2009; 230(1): 47–53.
20. Parmar P, Rathod G. Knowledge and awareness regarding poison information centre among medical students. Journal of Forensic Toxicology and Pharmacology, 2017; 6:1.
21. Drazen J. M. Inappropriate advertising of dietary supplements. The New England Journal of Medicine, 2003; 348(9): 777–778.
22. Street R. A., Sidana J., Prinsloo G. *Cichoriumintybus*: Traditional uses, phytochemistry, pharmacology, and toxicology. Evidence-Based Complementary and Alternative Medicine, 2013; 2013. doi: 10.1155/2013/579319.579319
23. Parmar P. Study of students' perceptions on evidence based curriculum of Forensic Medicine. J Indian Acad Forensic Med., 2017; 39(1): 11-15.
24. Marcone M. F., Jahaniaval F., Aliee H., Kakuda Y. Chemical characterization of *Achyranthesbidentata* seed. Food Chemistry, 2003; 81(1): 7–12.
25. Plaza L., De Ancos B., Cano M. P. Nutritional and health-related compounds in sprouts and seeds of soybean (*Glycine max*), wheat (*Triticumaestivum.L*) and alfalfa (*Medicago sativa*) treated by a new drying method. European Food Research and Technology, 2003; 216(2): 138–144.
26. Ahmed B., Khan S., Masood M. H., Siddique A. H. Anti-hepatotoxic activity of cichotyboside, a sesquiterpene glycoside from the seeds of *Cichoriumintybus*. Journal of Asian Natural Products Research, 2008; 10(3-4): 223–231.
27. Kim M., Shin H. K. The water-soluble extract of chicory reduces glucose uptake from the perfused jejunum in rats. Journal of Nutrition, 1996; 126: 2236–2242.
28. Parmar PB, Rathod GB, Bansal P, Maru AM, Pandya B, Bansal AK. Pattern of suspicious deaths of married females brought for medico-legal autopsy at teaching institute of India. J Family Med Prim Care, 2023; 12: 2110-3.
29. Gandhi H, Maru A, Shah N, Mansuriya RK, Rathod G, Parmar P. Correlation of

- Robinson's Cytological Grading with Elston and Ellis' Nottingham Modification of Bloom Richardson Score of Histopathology for Breast Carcinoma. *Maedica – A Journal of Clinical Medicine*, 2023; 18(1): 55-60.
30. Wilson R. G., Smith J. A., Yonts C. D. Chicory root yield and carbohydrate composition is influenced by cultivar selection, planting, and harvest date. *Crop Science*, 2004; 44(3): 748–752.
31. Anupam Kumar Bansal, Pragnesh Parmar, Gunvanti Rathod. Ethical principles in hospital settings – Perceptions of intern doctors of tertiary care hospital. *Journal of Forensic Medicine and Toxicology*, 2020; 37(2): 77-79.
32. Phelps C. F. The physical properties of inulin solutions. *Biochemical Journal*, 1965; 95: 41–47.
33. Peters A. M., Van Amerongen A. Relationship between levels of sesquiterpene lactones in chicory and sensory evaluation. *Journal of the American Society for Horticultural Science*, 1998; 123(2): 326–329.
34. Bhoot RR, Parmar PB. Dowry and domestic violence against women – Knowledge and awareness among medical students. *Indian Journal of Forensic Medicine and Toxicology*, 2018; 12(3): 79-81.
35. Kraker J.W., Franssen M. C. R., De Groot A., König W. A., Bouwmeester H. J. (+)-Germacrene A biosynthesis - The committed step in the biosynthesis of bitter sesquiterpene lactones in chicory. *Plant Physiology*, 1998; 117(4): 1381–1392.
36. Pragnesh Parmar. Students' perceptions regarding Objective Structured Practical Examination (OSPE) in Forensic Medicine. *J Punjab Acad Forensic Med Toxicol.*, 2018; 18(2): 27-29. DOI: 1.10.5958/0974-083X.2018.00027.4
37. Hussain H., Hussain J., Saleem M., et al. Cichorin A: A new benzo-isochromene from *Cichoriumintybus*. *Journal of Asian Natural Products Research*, 2011; 13(6): 566–569.
38. Bansal AK, Parmar P, Bansal P, Patel R, Barai PH, Thomas E. Ethical climate and its effect in teaching hospital: A vision from 3<sup>rd</sup> eye. *J Indian Acad Forensic Med*, 2019; 41(1): 45-49.
39. Cavin C, Delannoy M, Malnoe A, et al. Inhibition of the expression and activity of cyclooxygenase-2 by chicory extract. *Biochemical and Biophysical Research Communications*, 2005; 327(3): 742–749.
40. Heimler D, Isolani L, Vignolini P, Romani A. Polyphenol content and antiradical activity of *Cichoriumintybus* L. from biodynamic and conventional farming. *Food Chemistry*, 2009; 114(3): 765–770.
41. Gürbüz I, Üstün O, Yeşilada E, Sezik E, Akyürek N. *In vivo* gastroprotective effects of five Turkish folk remedies against ethanol-induced lesions. *Journal of Ethnopharmacology*, 2002; 83(3): 241–244.
42. FallahHuseini H, Alavian SM, Heshmat R, Heydari MR, Abolmaali K. The efficacy of Liv-52 on liver cirrhotic patients: a randomized, double-blind, placebo-controlled first approach. *Phytomedicine*, 2005; 12(9): 619–624.
43. Najmi AK, Pillai KK, Pal SN, Aqil M. Free radical scavenging and hepatoprotective activity of jigrine against galactosamine induced hepatopathy in rats. *Journal of Ethnopharmacology*, 2005; 97(3): 521–525.
44. Pragnesh Parmar, Swapnil Patond, Gunvanti Rathod, Sudhir Ninave.

- Awareness among intern doctors regarding privacy and confidentiality in medical practice. Indian Journal of Forensic Medicine and Toxicology, 2020; 14(3): 539-544.
45. Sultana S, Perwaiz S, Iqbal M, Athar M. Crude extracts of hepatoprotective plants, *solanumnigrum* and *cichoriunzintybus* inhibit free radical-mediated DNA damage. Journal of Ethnopharmacology, 1995; 45(3): 189–192.
46. Wesołowska A, Nikiforuk A, Michalska K, Kisiel W, Chojnacka-Wójcik E. Analgesic and sedative activities of lactucin and some lactucin-like guaianolides in mice. Journal of Ethnopharmacology, 2006; 107(2): 254–258.
47. Pushparaj PN, Low HK, Manikandan J, Tan BKH, Tan CH. Anti-diabetic effects of *Cichoriumintybus* in streptozotocin-induced diabetic rats. Journal of Ethnopharmacology, 2007; 111(2): 430–434.
48. Ghamarian A, Abdollahi M, Su X, Amiri A, Ahadi A, Nowrouzi A. Effect of chicory seed extract on glucose tolerance test (GTT) and metabolic profile in early and late stage diabetic rats. DARU Journal of Pharmaceutical Sciences, 2012; 20: 56–65.
49. Pragnesh Parmar, Swapnil Patond, Gunvanti Rathod, Sudhir Ninave. Awareness among intern doctors about medical records and duty of doctors in tertiary care hospital, Valsad. Indian Journal of Forensic Medicine and Toxicology, 2020; 14(3): 545-548.
50. Tusch D, Lajoix A-D, Hosal E, et al. Chicoric acid, a new compound able to enhance insulin release and glucose uptake. Biochemical and Biophysical Research Communications, 2008; 377(1): 131–135.
51. Gunvanti Rathod, Pragnesh Parmar. Development of an e learning module and evaluation of this method of teaching to supplement traditional education in pathology. South-East Asian Journal of Medical Education, 2020; 14(1): 72-75.
52. Conforti F, Ioele G, Statti GA, Marrelli M, Ragno G, Menichini F. Antiproliferative activity against human tumor cell lines and toxicity test on Mediterranean dietary plants. Food and Chemical Toxicology, 2008; 46(10): 3325–3332.
53. Lee KT, Kim JI, Park HJ, Yoo KO, Han YN, Miyamoto KI. Differentiation-inducing effect of magnolialide, a 1 $\beta$ -hydroxyeudesmanolide isolated from *Cichoriumintybus*, on human leukemia cells. Biological and Pharmaceutical Bulletin, 2000; 23(8): 1005–1007.
54. Bischoff TA, Kelley CJ, Karchesy Y, Laurantos M, Nguyen-Dinh P, Arefi AG. Antimalarial activity of Lactucin and Lactucopicrin: sesquiterpene lactones isolated from *Cichoriumintybus* L. Journal of Ethnopharmacology, 2004; 95(2-3): 455–457.
55. Leclercq E. Determination of lactucin in roots of chicory (*Cichoriumintybus* L.) by high-performance liquid chromatography. Journal of Chromatography A., 1984; 283: 441–444.
56. Gazzani G, Daglia M, Papetti A, Gregotti C. *In vitro* and *ex vivo* anti- and prooxidant components of *Cichoriumintybus*. Journal of Pharmaceutical and Biomedical Analysis, 2000; 23(1): 127–133.
57. Pragnesh Parmar, Swapnil Patond, Gunvanti Rathod, Sudhir Ninave. Google site as a tool for teaching undergraduate students in Forensic Medicine. Indian Journal of Forensic

- Medicine and Toxicology, 2020; 14(4): 479-483.
58. Nandagopal S, Kumari RBD. Phytochemical and antibacterial studies of chicory (*Cichoriumintybus* L.)—a multipurpose medicinal plant. *Advances in Biological Research*, 2007; 1(1-2): 17–21.
59. Rani P, Khullar N. Antimicrobial evaluation of some medicinal plants for their anti-enteric potential against multi-drug resistant *Salmonella typhi*. *Phytotherapy Research*, 2004; 18(8): 670–673.
60. Mares D, Romagnoli C, Tosi B, Andreotti E, Chillemi G, Poli F. Chicory extracts from *Cichoriumintybus* L. as potential antifungals. *Mycopathologia*, 2005; 160(1): 85–91.
61. Monde K, Oya T, Shirata A, Takasugi M. A guaianolidephytoalexin, cichoralexin, from *Cichoriumintybus*. *Phytochemistry*, 1990; 29(11): 3449–3451.