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Review Article

CICHORIUM INTYBUS LINN: A REVIEW OF PHARMACOLOGICAL PROFILE

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ABSTRACT

The use of natural products as medicinal agents presumably predates the earliest recorded history. *Cichorium Intybus L*. is a plant which is used in several traditional medicine systems to cure various diseases Chicory belongs to the family Asteraceae is a small aromatic biennial or perennial herb. This plant has been known to posses Anti-ulcer, Hepatoprotective, Antibacterial, Cardioprotective, Antioxidant and Free radical Scavenging, Anti-malarial, Anti-fungal, Gastroprotective, Antihelminthic, Analgesics, Tumour protective, Anti-allergic and other miscellaneous activities. The whole plant contains a number of medicinally important compounds showing therapeutic effects such as inulin, esculin, volatile compounds, bitter sesquiterpene lactones, coumarins, flavonoids and vitamins etc. The pharmacological studies reported in the present review confirm the therapeutic value of *Chichorium Intybus L*. Thus the use of this plant for human and animal disease therapy and reinforce the importance of the ethno-botanical approach as a potential source of bioactive substances.

Keywords: *Cichorium Intybus L*, Plant profile, Medicinal agents, Pharmacological activities.

INTRODUCTION

Cichorium intybus L, is an erect perennial herb 80±90 cm in height with a fleshy taproot up to 75 cm in length. The genus Cichorium consists of six species with major distribution areas in Europe and Asia. It is cultivated in countries such as the UK, Belgium, France, The Netherlands, Germany, South Africa, the USA and India. It is also known as common chicory, blue-sailor's succory. It is native to the temperate parts of the Old World and is found wild in India in the Punjab and Andhra Pradesh regions. Chicory also cultivated in Bihar, Gujarat, Himachal Pradesh and Tamil Nadu. Chicory has been successfully cultivated in India since 1918 at Coimbatore and subsequently Nilgiris in Tamil Nadu and at Broach, Amalsad and Jamnagar in Gujarat. Chicory forms flowering shoots and seeds after overwintering. Initially, chicory seed was imported into India, but nowadays it is successfully produced locally. Commercial seed production is undertaken in Jammu and Kashmir, temperate areas of Himachal Pradesh and some hilly regions of Uttar Pradesh. The agroclimatic conditions of these dry temperate areas are conducive to quality seed production. (Bais *et. al* 2001)

PLANT PROFILE

Chicory belongs to the family Asteraceae, Class Magnoliopsida and is a small aromatic biennial or perennial herb. The whole plant contains a number of medicinally important compounds such as inulin, esculin, volatile compounds, bitter sesquiterpene lactones, coumarins, flavonoids and vitamins.

Scientific Classification:

- Kingdom: Plantae
- Division: Magnoliophyta
- Class: Magnoliopsida
- Family: Asteraceae
- Genus: Cichorium
- Species: Cichorium *intybus* L

Phytochemical constituents:

The phytochemical or plant constituents are distributed throughout the whole chicory plant, but the main contents are present in the root. Analysis of fresh roots of chicory gave water 77%, gummy water 7.5%, cellulose, inulin and fibre 9% and ash 7.8%. The bitter substances are lactucin and lactucopicrin esculetin, esculin, cichoriin, umbelliferone, scopoletin and 6,7-dihydroxycoumarin from the racemes. The bitter principle is probably a glucoside of fructose and catechuic acid. The presence of stearin, mannites and tartaric acids in the juice of the roots has been reported. Betaine and choline are present in small concentrations. (Saxena *et. al* 2011)

The roots of chicory are brownish yellow outside and white inside, with a thin bark. The root is well developed; the central part is mature and contains a portion of xylem including numerous vessels. The leaves are broadly oblong, oblanceolate or lanceolate, crowded at the base, forming a rosette arranged spirally on the stem. The upper leaves are cordate and amplexicaul; the lower leaves are 7.5±15 cm long and pinnatied. The stems are angled or grooved, with spreading branches, bright blue flowers, short pappus and very long, spreading, negativetoddled ligules. The fruits are dry, indehiscent, 3 mm long, 2 mm broad and crowned with a ring of 0.5 mm long pappus which is usually white but sometimes half white and half straw coloured. Maturing fruits are brownish black as well as mottled, whereas those which are fully mature are pale. The seeds inside the fruits are 2.5 mm long and ovoid, with pointed apex, brownish tip and white plano-convex cotyledons. The average weight of 100 fruits is 207 mg. In the transverse section of mature fruits the pericarp consists of an outer single-layered, tangentially elongated epidermis with a thick cuticle on the outside. Numerous epicuticular rods of different sizes are deposited on the cuticle. (Bais *et. al* 2001)

Description of different parts of Chicory Plant:

Roots: The roots of chicory are brownish yellow outside and white inside, with a thin bark. It is well developed; the central part is mature and contains a portion of xylem including numerous vessels.

Leaves: The leaves are broadly oblong, oblanceolate or lanceolate, crowded at the base, forming a rosette arranged spirally on the stem. The upper leaves are cordate and amplexicaul; the lower leaves are long and pinnate.

Stems: The stems are angled or grooved, with spreading branches, bright blue owers, short pappus and very long, spreading,-toddled ligules.

Fruits: The fruits are dry, indehiscent, 3 mmlong, 2 mm broad and crowned with a ring of 0.5 mm long pappus which is usually white but sometimes half white and half straw coloured.

Geographical Distributions:

Northern and Central Europe, Siberia, Turkey, Afghanistan, North and Central China, South America, South Africa, Ethiopia, Madagascar, India, Australia, New Zealand. (Saxena *et. al* 2001)

PHARMACOLOGICAL PROPERTIES

Antiulcer and Antioxidant Activity

Cichorium intybus L. (Asteraceae) roots have been extensively used in Ayurveda medicine. It is variously used as a treatment

for gallstones, gastro-enteritis, sinus problems, diabetes and constipation. Antiulcer effect of HACI was evaluated in rats by the oral administration of ethanol 99.5% (dose 1 ml/200 gm b. w.) and pylorus ligation method. HACI was administered at the dose of (300mg/kg and 500mg/kg. p. o.) Antiulcer activity was assessed by determining and comparing ulcer index, total acidity, free acidity, gastric volume and pH, in test drug group with that of ulcer control group. Ranitidine was used as a standard (50mg/kg/p. o.). Antioxidant activity of HACI has been assayed by using ABTS radical cation decolorization assay. Maximum ulcer reduction was observed at a dose of 500mg/kg p. o. of HACI, in ethanol and pylorus ligation induced model, producing a protection index of 46.66% and 43.93% respectively, where as Ranitidine produced greater protection index of 59.99% and 68.29% respectively. A significant reduction in volume of gastric juice and acid output was also observed in ulcer induced animals treated with HACI when compared with ulcer control group. Simultaneously, pH of the gastric fluid was increased significantly. The result of study indicates that the antioxidant properties of HACI may contribute to gastro protective activity probably due to its free radical scavenging activity. These results suggest that HACI root extract possess antiulcer activity. (Saxena *et al*; 2011)

Phytochemical and Antibacterial Activity

Chicory (*Cichorium intybus* L.) belongs to the family Asteraceae and it is a small aromatic biennial or perennial herb. The whole plant contains a number of medicinally important compounds such as inulin, esculin, volatile compounds (monoterpenes and sesquiterpenes), coumarins, flavonoids and vitamins. In the present study, we evaluated the phytochemical analysis for the presence of various secondary metabolites and antibacterial activity of the root extracts of chicory against pathogenic bacteria like gram positive (*Bacillus subtilis, Staphylococcus aureus* and *Micrococcus luteus*) and gram negative (*Escherichia coli* and S*almonella typhi*) bacteria by *in vitro* agar well diffusion method. The hexane and ethyl acetate root extracts of chicory showed pronounced inhibition than chloroform, petroleum ether and water extracts. Root extracts showed more inhibitory action on *Bacillus subtilis, Staphylococcus aureus* and S*almonella typhi* than *Micrococcus luteus* and *Escherichia coli*. (Nandagopal *et al*; 2007)

Hepatoprotective Activity

Effect of chicory root extract (CRE) on the triglyceride metabolism in orotic acid (OA)-fed rats was investigated. Liver weights and hepatic triglyceride concentrations were markedly increased by OA-feeding rats. These results were attributed to the significant increase in the activity of hepatic phosphatidate phosphohydrolase (PAP), diacylglycerol acyltransferase (DGAT), and ratelimiting enzymes for triglyceride synthesis. Supplementation of CRE to OA did significantly reduced the hepatic triglyceride concentrations and DGAT activity without affecting PAP activity. Furthermore, OA treatment was significantly decreased plasma triglyceride (TG) and increased hepatic TG concentrations and reduced microsomal triglyceride transfer protein (MTP) activity without diminishing MTP mRNA expression in rats. However, hepatic TG concentration was significantly decreased and MTP activity was also reduced without diminishing MTP mRNA expression in rats fed simultaneous with OA and CRE diet. The hepatocytes in the OA-feeding rats contained numerous largely fat droplets, but CRE feeding prevented the OA-induced fat accumulation. Present study demonstrates that CRE reduces the liver TG accumulation by reduced DGAT and MTP activities without diminishing MTP mRNA expression by OA administration. (Young Cha *et. al* 2010)

Antioxidant and Free Radical Scavenging Properties

The methanolic crude extracts of traditionally used Indian medicinal plants were screened for their antioxidant and free radical scavenging properties using a-tocopherol and butylated hydroxy toluene (BHT) as standard antioxidants. Antioxidant activity was measured by ferric thiocyanate (FTC) assay and compared with the thiobarbituric acid (TBA) method. Free radical scavenging activity was evaluated using diphenyl picryl hydrazyl (DPPH) radicals. The overall antioxidant activity of Cichorium intybus, showed strong free radical scavenging activity with the DPPH method. Phytochemical analysis of plant extracts indicated the presence of major phytocompounds, including phenolics, alkaloids, glycosides, flavonoids, and tannins. The phenolic concentrations in the above plants ranged from 28.66 to 169.67 mg/g of dry plant extract. The tested plant extracts showed promising antioxidant and free radical scavenging activity, thus justifying their traditional use. (Aqil *et. al* 2006)

Cardioprotective effects

The cardioprotective effects of the aqueous extracts of the leaves of *Cichorium intybus* (CE) have been examined in the ageing myocardium of albino rats. Shade-dried powdered leaves of *C. intybus* were fed to the ageing animals for 30 days. The effects of CE on malondialdehyde level on taurine, glutathione and catalase activity of the heart have been studied. Ageing caused peroxidative damage, increase in taurine and glutathione levels in the heart. Catalase activity decreased in the ageing myocardium. CE was found to ameliorate the age induced injury and offered protection to the heart from oxidative damage, suggestive of ageing. (Nayeemunnisa et. al)

Antidiabetic activity

Anti-diabetic effects of *Cichorium intybus* in streptozotocin-induced diabetic rats The present study was designed to investigate the hypoglycemic and hypolipidemic properties of an ethanolic extract of *Cichorium intybus* (CIE) which is widely used in India as a traditional treatment for diabetes mellitus. Male Sprague–Dawley rats aged 9 weeks (160–200 g) were administered with streptozotocin (STZ, 50 mg/kg) intraperitoneally to induce experimental diabetes. The *Cichorium intybus*whole plant was exhaustively extracted with 80% ethanol, concentrated at 40 °C using a rotavapor and freeze dried to get powder. Hypoglycemic effects of CIE were observed in an oral glucose tolerance test (OGTT) in which, a dose of 125 mg of plant extract/kg body weight exhibited the most potent hypoglycemic effect. Moreover, daily administration of CIE (125 mg/kg) for 14 days to diabetic rats attenuated serum glucose by 20%, triglycerides by 91% and total cholesterol by 16%. However, there was no change in serum insulin levels, which ruled out the possibility that CIE induces insulin secretion from pancreatic β-cells. In addition, hepatic glucose-6-phosphatase activity (Glc-6-Pase) was markedly reduced by CIE when compared to the control group. The reduction in the hepatic Glc-6-Pase activity could decrease hepatic glucose production, which in turn results in lower concentration of blood glucose in CIE-treated diabetic rats. In conclusion, our results support the traditional belief that *Cichorium intybus* could ameliorate diabetic state. (Pushpraj *et. al* 2006)

Purification and properties of a second fructan exohydrolase from the roots of *Cichorium intybus*-1-FEH II (1-fructan exohydrolase, EC 3.2.1.80) was purified from forced chicory roots (*Cichorium intybus* L. var. *foliosum* cv. Flash) by a combination of ammonium sulfate precipitation, concanavalin A (Con A) affinity chromatography and anion and cation exchange chromatography. This protocol produced a 70-fold purification and a specific activity of 52 nkat mg^{-1} protein. The apparent size of the enzyme was 60 kDa as estimated by gel filtration and 64 kDa on SDS-PAGE. Optimal activity was found between pH 5.0 and 5.5. The temperature optimum was around 35°C. No product other than fructose could be detected with inulin as the substrate. The purified enzyme exhibited hyperbolic saturation kinetics with an apparent K_m of 58 m*M* for 1-kestose (Kes) and 64 m*M* for 1,1-nystose (Nys). The purified 1-FEH II hydrolyzed the *β*(2?1) linkages in inulin, Kes and Nys at rates at least 5 times faster than the *β*(2?6) linkages in levan oligosaccharides and levanbiose. Fructose did not affect the 1-FEH II activity but sucrose (Suc) was a strong inhibitor of this 1-FEH II (K_i=5.9 m*M*). The enzyme was partially inhibited by Na-EDTA and $CaCl_2$ (1 m*M*).

Antimalarial activity

Folklore reports described the use of aqueous root extracts of *Cichorium intybus* (L.) as a light-sensitive plant remedy for malaria. Preparative isolation and bioassay against HB3 clone of

strain *Honduras-1* of *Plasmodium falciparum* identified the previously known light-sensitive sesquiterpene lactones Lactucin and Lactucopicrin to be antimalarial compounds. (Kelley et. al 2004)

Polyphenol content and antiradical activity

Conventionally-and biodynamically-grown chicory (*Cichorium intybus* L.) was compared for its polyphenol content and antiradical activity. Two growing periods were analysed: in the first, the plants were subjected to severe water stress; in the second the stress was absent. The polyphenol content (Folin–Ciocalteu test) was higher in samples from the former than in the latter (about 650 and 420mg of gallic acid/100g fresh sample, respectively), and in any case did not differ between the two growing systems; antiradical activity for the second sampling was higher in the case of the biodynamic system. HPLC/DAD/MS analysis identified five hydroxycinnamic acids and eight flavonoids (quercetin, kaempferol, luteolin and apigenin glycosides) and indicated changes in hydroxycinnamic content in the four samplings which were greatest in the case of conventional farming. Biodynamic farming, like organic farming, allows the achievement of good results, with particular attention to environmental conditions. (Laura *et. al* 2009)

Immunomodulatory activity

Cichorium intybus were extracted with ethanol 70% and the mitogenic activity was examined both on human peripheral blood lymphocytes and thymocytes. Effect of these extracts on proliferative responsiveness of human lymphocytes to phytohemagglutinin (PHA) and on the mixed lymphocyte reaction (MLR) was also investigated. The results obtained indicated that none of the extracts had a direct mitogenic effect on human lymphocytes or thymocytes (stimulation index, SI<0.07). Among the plants studied, *C. intybus* and *C. officinalis* showed a complete inhibitory effect on the proliferation of lymphocytes in the presence of PHA (SI range 0.01–0.49). A dose dependent inhibitory effect was obtained in the case of *D. kotschyi*. Treatment of mixed lymphocytes with 0.1–10 μg/ml of *C. officinalis* (SI range 1.34–1.80) and *C. intybus* (SI 2.18 and 1.70, respectively) strongly increased the cell proliferation. In conclusion, this in vitro study revealed the capacity of all extracts to enhance the proliferation of lymphocytes after stimulation with the allogenic cells. (Zahara *et. al* 2000)

Evaluation of Phenolic content

Fresh aerial parts of different chicory varieties: green chicory two red chicory varieties and Witloof or Belgian endive were analyzed by HPLC/DAD/MS. The chromatographic fingerprint was diagnostic for each variety. A monocaffeoyl tartaric acid, chlorogenic acid, and chicoric acid were detected in all the varieties, while cyanidin 3-O-glucoside, delphinidin 3-O-(6‘‘ malonyl) glucoside, and cyanidin 3-O-(6‘‘ malonyl) glucoside were the main phenolic compounds in the red varieties. The flavonoidic compounds, quercetin 3-O-glucuronide and luteolin 7-O-glucuronide, were absent in the Witloof sample. The phenolic compounds from total leaves were the same as those obtained from only the colored parts; nevertheless, the total amount was remarkably lower with a decrease of up to 80% for Belgian endive. Chemical stability at high temperature was observed for the phenolic fraction from the green variety after decoction at 100 °C for 30 min. (Marzia *et. al* 2005)

Antioxidant, Antimicrobial and Phytochemical Analysis

This study was carried out to evaluate the antimicrobial and antioxidant effectiveness of methanolic extract and different fractions (*n*-butanol, ethyl acetate, chloroform and *n*-hexane) of *C. intybus* seeds. The antimicrobial activity was determined by the disc diffusion method and minimum inhibitory concentration (MIC) against a panel of microorganisms (four bacterial strains, *i. e. P. multocida, E. coli, B. subtilis* and *S. aureus* and three fungal strains, *i. e* A. *flavus, A. niger and R. solani)*. The results indicated that seeds extract and fractions of *C. intybus* showed moderate activity as antibacterial agent. While Antifungal activity of *C. intybus* seeds extract/fractions was very low against A. *flavus* and *A. niger* while mild against *R. solani*. The *C. intybus* seeds extract/fractions contained appreciable levels of total phenolic contents (50.8-285 GAE mg/100g of Dry plant matter) and total flavonoid contents (43.3-150 CE mg/100g of Dry plant matter). The *C. intybus* seed extract/fractions also exhibited good DPPH radical scavenging activity, with IC_{50} ranging from 21.28-72.14 μg/mL. Of the *C. intybus* seeds solvent extract/fractions tested, 100% methanolic extract and ethylacetate fraction exhibited the maximum antioxidant activity. The results of the present investigation demonstrated significant ($p< 0.01$) variations in the antioxidant and antimicrobial activities of *C. intybus* seeds solvent extract/fractions. (Mahmood *et. al* 2012)

Antifungal activity

In this work extracts from roots of the common vegetable *Cichorium intybus* L., highly appreciated for its bitter taste, were studied to investigate their possible biological activity on fungi from a variety of ecological environments: some are parasites on plants (phytopathogens) or of animals and humans (zoophilic and anthropophilic dermatophytes), others live on the soil and only seldom parasitize animals (geophilic dermatophytes). The extracts were ineffective on geophilic species and on tested phytopathogens, with the exception of *Pythium ultimum*, whereas they inhibited the growth of zoophilic and anthropophilic dermatophytes, in particular *Trichophyton tonsurans* var. *sulfureum*, whose treatment caused morphological anomalies, here observed by scanning electron microscopy. This behaviour is discussed on the basis of the presence in the chicory extract of the two main sesquiterpene lactones, 8-deoxylactucin and 11*β*,13-dihydrolactucin. (Mares *et. al* 2005)

Anti helminthic activity

Several studies have been conducted on grazing animals to determine the anthelmintic potential of secondary metabolites present in C. intybus. Grossly, it has been concluded that the animals grazing on chicory have a higher performance index and lower incidence of gastrointestinal nematode infestations. In the majority of the experiments, the condensed tannins and sesquiterpene lactones were responsible for anthelmintic activity. Anthelmintic activity of chicory has also been noticed in the case of lambs wherein the total number of abomasal helminths was found to be lesser in the lambs grazing on this plant. The condensed tannin and sesquiterpene-rich extracts of C. intybus were evaluated for their efficacy against the larvae of deer lungworm, Dictyocaulus viviparous and other gastrointestinal nematode larvae using a larval migration inhibition assay. A dose-dependent decrease in the larval motility was observed in both lungworm and gastrointestinal nematodes. The sesquiterpene lactone-rich extracts of C. intybus were also found to inhibit egg hatching of Haemonchus contortus. (Marley et. al 2003)

Gastroprotective activity

C. intybus has been used in Turkish folklore for its antiulcerogenic potency. The aqueous decoction of *C. intybus*roots was orally administered to Sprague-Dawley rats 15 minutes before the induction of ulcerogenesis by ethanol. More than 95% inhibition of ulcerogenesis was observed in the test group. (Gurbuj *et. al*. 2002)

Anti-Inflammatory activity

The inhibition of TNF-α mediated cyclooxygenase (COX) induction by chicory root extracts was investigated in the human colon carcinoma (HT 29) cell line. The ethyl acetate extract inhibited the production of prostaglandin E2 (PGE2) in a dose-dependent manner. TNF-α mediated induction of COX-2 expression was also suppressed by the chicory extract. (Cavin *et. al*. 2005)

Analgesic and Sedative activity

Lactucin (1) and its derivatives lactucopicrin (2) and 11 beta,13-dihydrolactucin (3), which are characteristic bitter sesquiterpene lactones of Lactuca virosa and Cichorium intybus, were evaluated for analgesic and sedative properties in mice. The compounds showed analgesic effects at doses of 15 and 30 mg/kg in the hot plate test similar to that of ibuprofen, used as a standard drug, at a dose of 30 mg/kg. The analgesic activities of the compounds at a dose of 30 mg/kg in the tail-flick test were comparable to that of ibuprofen

given at a dose of 60 mg/kg. Lactucopicrin appeared to be the most potent analgetic of the three tested compounds. Lactucin and lactucopicrin, but not 11beta,13-dihydrolactucin, also showed sedative properties in the spontaneous locomotor activity test. (Wesolowska et. al)

Tumor-Inhibitory activity

The crude ethanolic extract of *C. intybus* roots caused a significant inhibition of Ehrlich tumor carcinoma in mice. A 70% increase in the life span was observed with a 500 mg/kg/day intraperitoneal dose of the tested extract. The aqueous-alcoholic macerate of the leaves of *C. intybus* also exerted an antiproliferative effect on amelanotic melanoma C32 cell lines. Magnolialide, a 1*β*-hydroxyeudesmanolide isolated from the roots of *C. intybus*, inhibited several tumor cell lines and induced the differentiation of human leukemia HL-60 and U-937 cells to monocyte or macrophage-like cells. (Hazra *et. al*)

Anti allergic activity

The aqueous extract of *C. intybus* inhibited the mast cell-mediated immediate allergic reactions *in vitro* as well as *in vivo*. This extract restrained the systemic anaphylactic reaction in mice in a dose-dependent manner. It also significantly inhibited passive cutaneous anaphylactic reaction caused by anti-dinitrophenyl IgE in rats. Other markers of allergic reaction, namely, plasma histamine levels and histamine release from rat peritoneal mast cells, decreased significantly whereas the levels of C-AMP increased after the treatment with *C. intybus* extract. (Kim et. al 1999)

Toxicological Studies

Although *C. intybus* has a long history of human use, the high levels of secondary metabolites have shown potential toxicological effects. To evaluate the safety of the root extract of *C. intybus*, Ames test and subchronic toxicity assessment were conducted. The sesquiterpene-rich extract was evaluated for potential mutagenic properties (Ames test) using *Salmonella typhimurium* strains TA97a, TA98, TA100, and TA1535 and*Escherichia coli* strain WP2 *uvrA*. Though cytotoxicity was observed at high extract doses in some strains, mutagenicity was not noted. A 28-day (subchronic) oral toxicity study, conducted in CRL: CD (SD) IGS BR rats, concluded that there was no extract-related mortality or any other signs of toxicological significance. The toxicity evaluation of *C. intybus* extracts has also been done by *Vibrio fischeri* bioluminescence inhibition test (Microtox acute toxicity test). This bacterial test measures the decrease in light emission from the marine luminescent bacteria *V. fischeri* when exposed to organic extracts. The tested extracts showed less than 20% inhibition of bioluminescence and hence were concluded to be safe for human use. (Schmidt et. al 2007)

MISCLLENEOUS ACTIVITIES

The ethanol extract of the roots of C. intybus is reported to prevent the immunotoxic effects of ethanol in ICR mice. It was noted that body weight gains were markedly decreased in mice administered with ethanol. However, the body weight was not affected when ethanol was coadministered with the ethanol extract of C. intybus. Similarly, the weights of liver and spleen were not affected when ethanol extract was given along with ethanol. A considerable restoration in the other markers of immunity, namely, hemagglutination titer, plaque forming cells of spleen, secondary IgG antibody production, delayed-type hypersensitivity reaction (in response to subcutaneous administration of sheep red-blood cells to paw), phagocytic activity, number of circulating leucocytes, NK cell activity, cell proliferation, and production of interferon-γ, was registered. The immunoactive potential of an aqueous-alcoholic extract of the roots was established by a mitogen proliferation assay and mixed lymphocyte reaction (MLR). The extract showed an inhibitory effect on lymphocyte proliferation in the presence of phytohemagglutinin and a stimulatory effect on MLR.

Chicoric acid has shown vasorelaxant activity against nor-epinephrine-induced contractions in isolated rat aorta strips. A pronounced anticholinesterase activity of the dichloromethane extract of C. intybus roots was seen in the enzyme assay with Ellman's reagent. Two sesquiterpene lactones, namely, 8-deoxylactucin and lactucopicrin, also exhibited a dose-dependent inhibition of anticholinesterase. The methanolic extract displays wound healing effect and β-sitosterol was determined as the active compound responsible for the activity, possibly due to its significant anti-inflammatory and antioxidant effects, as well as hyaluronidase and collagenase inhibition.

CONCLUSION

Worldwide *Cichorium intybus* has a long tradition use. Historically, chicory was grown by the ancient Egyptians as a medicinal plant, coffee substitute, and vegetable crop and was occasionally used for animal forage. This plant contains high amounts of proteins, carbohydrates, and mineral elements. Inulin from chicory roots is considered as a functional food ingredient as it affects physiological and biochemical processes resulting in better health and reduction of the risk of many diseases.

At present chicory remains an extremely versatile plant, amenable to genetic manipulation, and there is interest shown in genetically engineered chicory to obtain higher yields and create new potentials. The documented indigenous knowledge relating to the various medicinal uses of chicory has been supported by phytochemical isolation and investigations into biological activity. Nonetheless, many of its constituents have not been explored for their pharmacological potential and further research is necessary to gain better understanding of the phytochemicals against various diseases. Toxicological data on *C. intybus* is currently limited; however, considering that the Asteraceae family is a known source of allergic problems, a contraindication for hypersensitivity should be included in the safety data. Recent studies suggest the use of *C. intybus* as a biomonitor for heavy metals; considering that chicory enters the food chain, this plant should be used with caution.

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