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KASNI (CICHORIUM INTYBUS L.) A PROPITIOUS TRADITIONAL MEDICINAL HERB

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ABSTRACT: The Kasni, Cichorium intybus of family Asteraceae Class Magnoliopsida, which is also known as Chicory, is well known traditional herb included in many systems of medicine like Ayurveda, Unani and Siddha system of medicine. The genus Cichorium has six species with majorly distributed in Europe and Asia. It is cultivated in countries such as the UK, Belgium, France, Netherlands, Germany, South Africa, USA, and India. Kasni is a small aromatic biennial erect perennial herb around 1 m. in height with a fleshy taproot up to 75 cm in length and mainly it contains alkaloids, inulin, sesquiterpene lactones, coumarins, vitamins, chlorophyll pigments, unsaturated sterols, flavonoids, saponins, tannins, carbohydrates, glycosides, fats, gums, and minerals. Fresh chicory typically contains 68% inulin, 14% sucrose, 5% cellulose, 6% protein, 4% ash, and 3% other compounds, while dried chicory contains approximately 98% inulin and 2% other compounds. Kasni is used as antidiabetic, liver tonic, cardiotonic, diuretic, stomachic, cholagogue, depurative, and emmenagogue, etc. The present article reviews the historical, phytochemical, pharmacological, therapeutic and toxicological aspects of Kasni well supported by the available literature based on animal and clinical studies.

INTRODUCTION: Kasni commonly known as chicory (*Cichorium intybus* L.), belongs to family Asteraceae (Compositae) and widely distributed in Asia and Europe ¹. All parts of this plant have great medicinal importance due to the presence of some medicinally essential compounds such as alkaloids, inulin, sesquiterpene lactones, coumarins, Vitamins, chlorophyll pigments, unsaturated sterols, flavonoids, saponins and tannins ^{2,3,4,5}.



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It has been reported that fresh chicory typically contains 68% inulin, 14% sucrose, 5% cellulose, 6% protein, 4% ash, and 3% other compounds, while dried chicory contains approximately 98% inulin and 2% other compounds ⁶.

Due to this, the medicinal herb has been used in Ayurveda, Unani and Siddha system of medicine for the disease of the hepatobiliary system and renal system. C. intybus has been traditionally used for the treatment of fever, diarrhea, jaundice and gallstones 7, 8. The studies on rats have shown that *C*. intybus possesses antihepatotoxic antidiabetic activities ⁹. It has also been reported that C. intybus have antibacterial antiinflammatory antihyperglycaemic and antiulcerogenic activities 11.

Additionally, it is a useful biomonitor of heavy metals such as Pb, Zn, Cu, and Cd ¹². Forage chicory was used to produce a large quantity of high-quality feed in the warm season under favorable conditions. It has been reported that grazing chicory results in a reduction of some internal parasites in livestock ¹³ and, therefore, has the potential to reduce the use of antihelminthics. Due to its prevalent distribution, different parts of the plant have been used in traditional medicines globally ¹⁴.

Botanical Summary:

Chicory belongs to the

Kingdom: Plantae,

Division : Magnoliophyta,

Class : Magnoilopsida,

Family : Asteraceae,

Genus : Cichorium,

Species : Cichorium intybus L.

(Saxena et al. 2014)

Genus chicorium consists of six species ¹. It is an erect fairly woody perennial herb around 1m height with a fleshy taproot of up to 75 cm: length & large basal leaves ^{1, 15}.

Parts:

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 ¹.

Stems: The stems are angled or grooved, with spreading branches, bright blue flowers, short pappus and very long, spreading,-toddled ligules ¹.

Roots: The roots of chicory are brownish yellow outside and white inside, with thin bark. It is well developed; the central part is mature and contains a portion of xylem including numerous vessels ¹.

Fruits: 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 colored ¹.

Seeds: The seed inside the fruits are 2.5 mm long & ovoid, with a pointed apex, brownish tip and while plano-convex cotyledons ¹.

Cultivation: The plant can be grown on almost all types of soil and occurs throughout North West India up to 6000 feet Punjab, Kashmir, Andhra Pradesh, Karnataka, and Maharashtra. Other countries which produce Kasni are Baluchistan, Belgium, Europe, France, Germany, Netherlands. Switzerland. South Africa. Waziristan, West Asia and the United Kingdom ¹, ¹⁶. Kasni is also cultivated in Siberia, Turkey, North & Central China, Australia, New-Zealand and Madagascar ¹⁷. Today, it is cultivated in Europe and North America for many commercial uses 1.

Historical Perspective: Historically Chicory was grown by the ancient Egyptians as a medicinal plant 18, coffee substitute, vegetable crop, and occasionally for animal forage 19, 20, 21, 22. Greeks and Romans also began to grow chicory as a vegetable crop 4000 years ago 21, 22. It has a long history of therapeutic use both in areas where it is indigenous and in areas where it has been introduced. The various common or local names describing this plant may be ascribed to the widespread use by different folkloric groups. Chicorium intybus is called as Hindubar, Indyba in Arabic, Zral in Baluchistan, Chicory in California, Bunk, Chicory in English, Kichora, Kikori in greek, Kasani in gujrathi, Kasni in Hindi, Kasani in Persian, Gul, Hand in Punjabi, Kasni, Tsikorie, Kashini virai in Tamil, Kasini Bintulu in Telugu, Kasani in Urdu ²³.

Different preparations of this plant are employed to treat various symptoms and ailments. The juice is said to be a folk remedy for cancer of the uterus and tumors ²⁴. In South Africa, although it is considered a widespread weed, leaves, stems, and roots are made into a tea for jaundice and chicory syrup is used as a tonic and purifying medicine for infants ¹⁵. In Turkey, an ointment is made from the leaves for wound healing ²⁵. Decoction refers to a preparation that is made by adding cold water to the plant material which is then boiled and allowed to simmer for 5-10 min after which it is strained. Chicory decoctions are traditionally made from individual plant parts and from the plant as a whole

²⁶. In India, seeds are used for liver disorders, whole plant for diabetes and preparation of roots for jaundice, liver enlargement, gout and rheumatism ^{27, 28}. According to the European monograph, the traditional use of chicory roots includes the relief of symptoms related to mild digestive disorders (such as a feeling of abdominal fullness, flatulence, and slow digestion) and temporary loss of appetite ²⁹. Prior to the wars in Afghanistan, folkloric reports described the use of aqueous root extracts as a light-sensitive plant remedy for malaria. This indigenous knowledge has since been confirmed and the antimalarial compounds of *C. intybus* roots have been identified as the light-sensitive sesquiterpene lactones lactucin and lactucopicrin ³⁰.

The flowers of the chicory plant (*Cichorii flows*) are used as a herbal treatment of everyday ailments such as a tonic and appetite stimulant and as a treatment of gallstones, gastro-enteritis, sinus problems, cuts, and bruises ²⁴. In Italy, the whorls are made into a decoction and used as a depurative ³¹. Chicory seeds are one of the main ingredients of Jigrine, a herbal hepatoprotective commercial product, used for the treatment of various diseases of the liver ²⁷. Other plant parts are also used for liver disorders, namely, aerial parts in Bosnia and Herzegovina ³² and roots in Serbia and India ^{28, 33}.

Phytochemical Analysis: 4.7% of Oil was found on analysis of Kasni seeds, the fatty acid composition: Saturated 21.7%, Unsaturated 78.3%. ³⁴ Preliminary phytochemical screening of *Cichorium intybus* L. seeds revealed the presence of carbohydrates, glycosides, flavonoids, saponins, fats, and gums ³⁵.

The analysis of the fresh roots of *C. intybus* gave the following values: Moisture- 77. Fat: 0.6gm, Cellulose, Inulin and fiber-9.0gm, Gummy matter-7.5gm, Glucose- 1.1gm, Bitter extractives- 4.0gm, Ash- 0.8%. The roots contain the sesquiterpenes lactones like sonchusides A and C, and, cytokinin, crepidiase B, cichoriolide A, cichoriosides B and C, ribosylzeatin a nucleotidsugar, lactucopicrin, uridine-5'-diphosphoglucose and chlorogenic, neochlorogenic, 8-deoxylactucin, isochlorogenic, lactucin. caffeic and chicoric acids. carbohydrates present in the roots include a series of glucofructosans between sucrose and inulin

besides glucose, fructose, pentose, dextrose, taraxarcine and levulose. During storage, the inulin is converted into inulide and finally into fructose due to the presence of an enzyme inulocoagulase ³⁴. The roots of Cichorium intybus produce latex, inulin 58%, a bitter compound composed of lactucopictin, intybin, lactucin, taraxasteral, tannins, fructose, pectin, fixed oils, and alkaloids ³⁶. The bitter substances are lactucin and lactucopicrin esculetin, esculin, cichoriin, umbelliferone. scopoletin, 6.7and hydroxycoumarin 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 along with betaine and choline, which are present in small concentrations ¹⁷. The aerial part of Kasni contains inulin, fructose, resin, Cichorium and esculetin ³⁶.

The phytochemical screening of leaves of C. intybus showed the presence of tannins, saponins, flavonoids, and DPPH inhibition. Tannins, the high molecular weight polyphenolic compounds found naturally in many plants and have been found to a protective role in plants microorganisms, unfavorable climatic conditions and damage by animals. On the other hand, they can form multiple hydrogen bonds with carboxylic groups of dietary proteins and proteolytic enzymes in the gastrointestinal tract which leads to reduced digestibility of proteins and finally the retardation of animal growth ³⁷. Saponins are the glycosidic compounds found in most of the plants, possess a bitter taste and foaming properties and are found to be responsible for anticarcinogenic and antifungal activity 38. Leaves of chicory are good sources of phenols, vitamins A and C as well as potassium, calcium, and phosphorus ³⁹.

The leaves of chicory contain coumarins, esculetin, cichoriin and sesquiterpene lactones, and recently a new coumarin glucoside ester Cichoriin-6'-*p*-hydroxyphenyl acetate, was isolated from chicory leaves along with cichoriin, similarly new sesquiterpene lactone like cichoridiol, Cichosterol (seco-sterol), Lactucin, Lactucopicrin, 11,13-dihydrolactupicrin were also reported in roots and leaves of *Cichorium intybus* ^{40,41}.

The flowers of chicory contain saccharides, methoxycoumarin cichorine, flavonoids, essential oils²⁴, and anthocyanins contributing to the blue color of the perianth ⁴². Two new anthocyanins have been isolated from flowers of Cichorium intybus and identified as delphinidin 3, 5-di-O-(6-O-malonyl beta glucoside) and delphinidin 3-O (6-O-malonyl-beta-D-glucoside)-5-O - beta - Dglucoside. Octane, n-nonadecane, pentadecane, hexadecane, and a tentatively identified compound have been found as principal volatile components ²⁴. Along with inulin and sesquiterpene lactones, chicory also contains vitamins and minerals which make it mild bitter tonic and laxative 43. Chicory is reported to contain more than 10% of total polyphenols, the most dominant being dicaffeoylquinic acids (71% of total polyphenols) with marked antioxidant and anti-hyperlipidemic activity 44, 45

The plant also contains Chicoric acid which was found to stimulate insulin release from INS-1 E insulin-secreting cell lines and rats islet Langerhans as well as glucose uptake Compounds namely Lactucin, Sonchuside A, Cichoriolide. Chlorogenic acid. 3.5-Dicaffeolyquinic acid, 4,5Dicaffeolyquinic acid, Crepidiaside A, Cichoralexin, Malic acid, Caffeic acid, 3-Caffeoylquinic acid, 5-Caffeoylquinic acid, 4-Caffeoylquinic acid, Dicaffeoyltartaric acid, (chicoric acid), Cyanidin, Glucoside etc. isolated and identified from the chicory ^{30, 47, 48, 49, 42, 50, 51, 46,}

Large mass fractions of inulin characterized the root and peel extracts while phenolics, determined as caffeoylquinic acids, made up 0.5 and 1.7 g per 100 g of fresh mass, respectively. The leaf and seed extracts had decidedly lower mass fractions of inulin and higher mass fractions of phenolics, recognized as caffeoylquinic acids, chicoric acid and quercetin glucuronide ⁴⁴.

Pharmacological Studies: Chicory (*Cichorium intybus*) has a long history of its use, and various studies have revealed its medicinal value viz. hypoglycemic, hypolipidemic, hepatoprotective, antimicrobial, anthelmintic, antimalarial, anti-inflammatory, analgesic antioxidant, tumorinhibitory, antiallergic and other important activities. It is an excellent mild bitter tonic for the

liver and digestive tract and cleansing the urinary tract. Chicory is also taken as a mild laxative ⁴³.

Hypoglycemic and Hypolipidemic Effects: Based on the traditional use of *C. intybus* in diabetes mellitus, the hypoglycemic and hypolipidemic properties of the ethanol extract of the whole plant were investigated. Diabetes was induced by intraperitoneal administration of streptozotocin in male Sprague-Dawley rats. The ethanol extract, at a dose of 125 mg/Kg body weight, significantly attenuated the serum glucose levels in the oral glucose tolerance test. A marked decrease in the serum triglycerides and cholesterol was also observed in the extract-treated rats. Hepatic glucose-6-phosphatase activity was found to be reduced in extract-treated diabetic rats as compared to untreated diabetic rats

The antidiabetic effect of the aqueous seed extract of C. intybus has also been investigated. Earlystage and late-stage diabetes were differently Wistar albino induced in male rats streptozotocin-niacinamide and streptozotocin alone, respectively. The treatment with chicory extract prevented weight loss in both early-stage and late-stage diabetic rats. Chicory-treated diabetic animals resisted an excessive increase in fasting blood sugar (assessed by glucose tolerance test). Grossly, normalization of blood parameters, namely alanine aminotransferase, triacylglycerol, total cholesterol, and glycosylated hemoglobin, was seen in these animals. In early-stage diabetic rats, chicory treatment led to the increase in insulin levels pointing toward the insulin-sensitizing action of chicory ⁵⁵.

Feeding the diabetic Wistar rats with C. intybus leaf powder led to a decrease in blood glucose levels to the near normal value. C. intybus administration also decreased the malondialdehyde (formed by thiobarbituric acid) levels and increased glutathione content. Anticholinesterase activity was restored to near normal, brain lipopolysaccharide decreased, and catalase activity increased ⁵⁶. Caffeic acid and chlorogenic acid have been described as potential antidiabetic agents by increasing glucose uptake in muscle cells. Both compounds were also able to stimulate insulin secretion from an insulin-secreting cell line and islets of Langerhans. Another compound, chicoric acid, is also revealed as a new potential antidiabetic agent exhibiting both insulin-sensitizing and insulin-secreting properties ⁵⁰.

Chicory extract was found to influence the lipid metabolism and the redox balance of pancreatic tissue of rats in experimental dislipidemia ⁵⁷. Application of chicory inulin in reducing the risk of non-insulin dependent diabetes was also discussed ⁵⁸. It was noticed that feeding on chicory roots decreased the levels of plasma glucose, cholesterol, HDL-cholesterol and also reduced liver cholesterol, triglyceride and total lipids of streptozotocin-diabetic rats ⁵⁹.

In a biological experiment, an alcoholic extract of chicory leaf produced a significant decrease in serum triglycerides and total cholesterol, while an increase in high-density lipoprotein (HDL) was detected when compared to the normal control (NC) and high-fat (HF) diet groups 60. Chicory (inulin) increased HDL-C after its treatment as a hypoglycaemic agent and is concluded hypolipidemic in diabetic rats ⁶¹. Improvement in lipid profiles by lowering plasma total cholesterol and triglyceride concentrations and elevating HDLc concentration was found due to the presence of inulin 62. Further higher serum concentration of HDL-c and lower serum concentration of LDL-c in rats consumed diets containing 1%, 5% chicory extract or 5% inulin for 4 weeks were also recorded ⁶³. Inulin has been found to decrease the serum triglycerides in rats due to decrease synthesis of triglyceride in the liver. The improved lipid metabolism may be due to an alteration in the absorption and synthesis of cholesterol which might result from the changes in cecal fermentation and by an increase in fecal excretion of lipids, cholesterol and bile acids ⁶³.

In a study, the effect of *Cichorium intybus* L. on fatty liver induced by oxytetracycline in albino rats, oxytetracycline induced hyperglycemia which may be attributed to its inhibitory action on the absorbing function of the intestine and the retarded glucose utilization in the tissues ⁶⁴, treating rats with chicory turned glucose level back to reasonable value. The improvement in glycemic status may be due to inulin (an active substance of chicory) which modulate the hormonal level of insulin and glucagons, thereby regulating

carbohydrate and lipid metabolism by lowering serum glucose level ⁶⁵. The experimental results revealed that the hyperlipidemic effect of oxytetracycline was ameliorated with the treatment of rats with chicory. The effect of chicory on lipid profile may be due to the main active compounds of chicory root extract, inulin, which is a polymer of fructose with B (1-2) glycosidic linkage ⁶⁶.

Inulin can cause alteration of hormone secretion which affects lipid metabolism. The dietary fibers of Kasni would inhibit cholesterol accumulation in blood and enhance the resistance of vascular walls ⁶⁷. The cholesterol-lowering effect of dietary fibers may be related to its viscosity–raising properties, which could reduce fat and cholesterol absorption or bile acid reabsorption from the gastrointestinal tract. HDLc transports cholesterol from tissues to the liver for excretion into bile ⁶⁸.

Hepatoprotective Effect: The folkloric use of *C*. intybus as a hepatoprotectant has been well documented. It is one of the herbal components of Liv-52. a widely used traditional hepatoprotective tonic. In a randomized, doubleblind clinical trial conducted on cirrhotic patients, Liv-52 medication reduced the serum levels of hepatic enzymes, namely, alanine aminotransferase and aspartate aminotransferase; also reduced the Child-Pugh scores and ascites significantly ⁶⁹. Another polyherbal formulation, Jigrine, contains the leaves of C. intybus as one of its 14 constituents. Jigrine was evaluated for hepatoprotective activity against galactosamineinduced hepatopathy in rats. The pretreatment of male Wistar-albino rats with Jigrine significantly reduced the levels of aspartate transaminase, alanine transaminase, and urea and increased the levels of blood and tissue glutathione. Histopathological examination of the liver revealed that jigrine pretreatment prevented galactosamine toxicity and caused a marked decrease in inflamed cells ⁷⁰. The aqueous-methanolic extract of the seeds of C. intybus has been investigated for the hepatoprotective activity against acetaminophen and carbon tetrachloride-induced liver damage in mice, and it was found to decrease both the death rate and the serum levels of alkaline phosphatase, glutamyl oxaloacetate transaminase, and glutamyl pyruvate transaminase 71.

In analogous studies, the antihepatotoxic activity of the alcoholic extract of the seeds and aqueous extracts of the roots and root callus of *C. intybus* was estimated, and oral administration of these extracts in albino rats led to a marked decrease in the levels of hepatic enzymes; histopathological examination of the liver also showed no fat accumulation or necrosis after the treatment ^{27,72}. Similar studies have established the hepatoprotective effect of esculetin, a phenolic compound, and cichotyboside, a guaianolide sesquiterpene glycoside reported from *C. intybus* ^{73,74}

Aqueous extract of chicory was when mixed with stirred yogurt and estimated for alanine and aspartate aminotransferase (ALT and AST) and activities before after alloxan-induced oxidative stress and diabetes in rats, then it was found that ALT and AST activities of treated rats were nearest to the level of untreated rats fed basal diet (Negative control) ⁷⁵. It is known that chicory contains isoflavones, polyphenols and other antioxidants that can reduce the elevation of serum ALT and AST. Antioxidants in chicory extract have not only hepatoprotective activity but also improve liver function ⁷⁶.

Hydroalcoholic extract of *Cichorium intybus* significantly suppressed mainly the increase in plasma activities of AST, ALT and ALP concentration and confirmed the hepatoprotective activity ⁷⁷. Cichorium root extract therapy leads to normalization of some morphofunctional liver features (decreases glycogen content and cell of necrosis and increases the number of cells with pronounced protein synthesis activity) in rats with CCl₄-induced hepatitis ⁷⁸. Chicory has an antihepatotoxic effect and significantly lower serum levels of ASAT and ALAT enzymes even in CCL4 intoxicated rats ^{72, 79, 27}.

Antimicrobial Effect: The antibacterial activity of the organic acid-rich extract of fresh red chicory (C. intybus var. Sylvestre) was tested against periodontopathic bacteria including Streptococcus mutans, Actinomyces naeslundii and Prevotella intermedia. The compounds identified from the active extract include oxalic acid, succinic acid, quinic acid, and shikimic acid. All of the organic acids were found to decrease biofilm formation and

adhesion of bacteria to the cells, with different levels of efficacy. These compounds also induced biofilm disruption and detachment of dead cells for the cultured substratum ⁷⁶.

In other reports on the antimicrobial activity of C. intybus, the crude aqueous and organic seed extracts were found to be active against four pathogenic microorganisms, namely, Staphyloaureus, Pseudomonas coccus aeruginosa, Escherichia coli, and Candida albicans and root extracts had pronounced effects on Bacillus subtilis, S. aureus, Salmonella typhi, Micrococcus luteus and E. coli 80,3. The leaf extract of C. intybus also showed moderate activity against multidrugresistant S. typhi 81. Guaianolides-rich root extracts of C. intybus have shown antifungal properties anthropophilic fungi Trichophyton tonsurans, T. rubrum, and T. violaceum 82.

Among the various root extracts of *C. intybus* against *E. coli*, *S. aureus*, *B. subtilis* and *P. multocida* strains, where all the tested extracts showed antibacterial activity, the ethyl acetate extract is the most active antibacterial ⁸³. Overall *C. intybus* seeds showed mild antibacterial and poor antifungal activity.

During the study of antimicrobial activity of Cichorium intybus, it was experimentally proved that the whole plant contains some medicinally important compounds such as inulin, esculin, volatile compounds (monoterpenes and sesquiterpenes), coumarins, flavonoids, and vitamins. Root extracts showed more inhibitory action on Bacillus subtilis, Staphylococcus aureus and Salmonella typhi than Micrococcus luteus and Escherichia coli ³.

Anthelmintic Effect: Many 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 has 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 ⁸⁴. 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 ⁸⁵. The condensed tannin and sesquiterpenerich 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 ². The sesquiterpene lactone-rich extracts of *C. intybus* was also found to inhibit egg hatching of Haemonchus contortus ⁸⁶.

Antimalarial Effect: The infusion of fresh roots of *C. intybus* has a history of use as a remedy for malarial fever in some parts of Afghanistan. The bitter compounds in the plant, namely, lactucin, lactucopicrin, and the guaianolide sesquiterpenes, isolated from aqueous root extracts of chicory were concluded to be the antimalarial components of the plant. Lactucin and lactucopicrin completely inhibited the HB3 clone of strain Honduras-1 of *Plasmodium falciparum* at concentrations of 10 and 50 µg/mL, respectively ^{30, 47}.

Gastroprotective Effect: *Cichorium 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 ⁸⁷.

Anti-Inflammatory Effect: 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 E_2 (PGE₂) in a dose-dependent manner. TNF- α mediated induction of COX-2 expression was also suppressed by the chicory extract 10 .

Analgesic Effect: Lactucin, lactucopicrin, and 11β, 13-dihydro-lactucin found in *C. intybus* exhibited analgesic action in mice in the hot plate and tail-flick tests. In the hot plate test, all three compounds exerted an analgesic effect, with lactucopicrin being the most potent compound. In the tail-flick test, the antinociceptive effects of all the tested compounds (30 mg/kg dose) were comparable to

that of ibuprofen (60 mg/kg dose). Lactucin and lactucopicrin were also established to have some sedative action (which may contribute to the analgesic effect in part) as evident from the decreased spontaneous locomotor activity in mice 88

Antioxidant Effect: The flavonoids and phenolic acids present in leaves of C. intybus are known to possess antioxidant activities due to the presence of hydroxyl groups in their structures and their contribution to defense system against the oxidative damage due to endogenous free radicals are extremely important ⁹. Phenolics or polyphenols secondary plant metabolites that ubiquitously present in plants and their products. Many of them have been shown to contain high levels of antioxidant activities 89. Due to their redox properties, these compounds contribute to the overall antioxidant activities of plants. Usually, the mechanisms of their antioxidant activity are neutralizing lipid free radicals and preventing decomposition of hydroperoxides into free radicals

Chicory supplemented diet is reported to have free radical scavenging and antioxidant properties by restoring glutathione, GSP, SOD and catalase levels. These findings may be due to the presence of antioxidant compounds such as anthocyanins, flavonoids, polyphenols and vitamin C that could contribute to protection against free radicals generation and carcinogenic effects of nitrosamines ^{91, 39}.

The antioxidant properties of *Cichorium intybus* were evaluated *in-vitro* as antioxidant activity and *in-vivo* as protective activity against rat liver cell microsome lipid peroxidation ⁷⁶. The obtained results proved that chicory contained both biological antioxidant and prooxidant compounds. An antioxidant, antimicrobial & phytochemical analysis of *Cichorium intybus* seeds extract and various organic fractions, it was concluded that methanolic extract & ethyl acetate fraction of seeds exhibited good antioxidant activity ⁹².

Tumor-Inhibitory Effect: 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 ⁹³. The aqueous-alcoholic macerate of the C. intybus also leaves of exerted antiproliferative effect on amelanotic melanoma C32 cell lines 94. Magnolialide, 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 macrophagelike cells ⁹⁵.

Antiallergic Effect: 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 response 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 cAMP increased after the treatment with *C. intybus* extract ⁹⁶.

Cardioprotective Effects: The cardioprotective effects of the aqueous extracts of the leaves of Cichorium intybus have been examined in the ageing myocardium of albino rats. Shade-dried powdered leaves of C. intybus were fed to the senescent animals for 30 days. The effects of chicory extract on malondialdehyde level on taurine, glutathione and catalase activity of the heart have been studied. Aging caused peroxidative damage, increase in taurine and glutathione levels in the heart. Catalase activity decreased in the ageing myocardium. Kasni was found to ameliorate the age-induced injury and offered protection to the heart from oxidative damage, suggestive of age ⁹⁷. It was also found that chicory is one of the medicinal plants used for the treatment of cardiovascular diseases in the Unani system of medicine ⁹⁸.

Antifungal Effect: Extracts from roots of the common vegetable *Cichorium intybus* L., highly appreciated for its bitter taste 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 tested phytopathogens, except *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 behavior is discussed by the presence in the chicory extract of the two main sesquiterpene lactones, 8-deoxylactucin and 11β ,13-dihydro-lactucin ⁸².

Prebiotics Effect: Chicory is rich in fibrous polysaccharide inulin; it is a soluble dietary fiber and resistant to the digestive enzyme. It reaches to large intestine or colon essentially intact, where it is fermented by resident bacteria. Lactobacilli and bifidobacteria agent digest inulin and feed themselves on it. Hence prebiotics act as fertilizers for these symbiotic bacteria. Inulin serves the role of dietary fiber; safety of inulin has been evaluated and accepted by FDA of United States ⁹⁹.

Appetizer effect: It is reported that chicory contains many essential lipids, vitamins and a variety of sugar and thus useful as a tonic for digestive tract ^{28, 66, 100}. The root and the leaves of chicory are an appetizer, cholagogue, depurative, digestive, diuretic, hypoglycaemic, laxative and Chicory extract contains inulin fructooligosaccharides. Inulin behaves like a soluble fiber to increase the viscosity of the stomach content and slow down the rate of gastric emptying of water, nutrients and lipids. A study of Urias-Silvas et al. concluded that inulin-type fructans extracted from chicory regulate appetite and lipid/glucose metabolism. It has also promising effects on the body weight and fat mass development ¹⁰¹.

Other Important Pharmacological Effects: 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 co-administered with the ethanol extract of *C. intybus*. Similarly, the weights of the 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, natural killer cell activity, cell proliferation, and production of interferon-γ, was registered ¹⁰². The immunoreactive 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 ¹⁰³.

Chicoric acid has shown vasorelaxant activity against nor-epinephrine-induced contractions in isolated rat aorta strips ¹⁰⁴. A pronounced anticholinesterase activity of the dichloromethane extract of C. intybus roots was seen in the enzyme assay with Ellman's reagent. Two sesquiterpene 8-deoxylactucin lactones, namely, lactucopicrin, also exhibited a dose-dependent inhibition of anticholinesterase ¹⁰⁵. The methanolic extract displays wound healing effect, and βsitosterol 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 ¹⁴.

Medicinal Uses According to Unani System of **Medicine:** Cichorium intybus removes the visceral, hepatic and vascular obstruction. It is a good but not very strong astringent. Application of paint prepared from its juice with white lead and vinegar elicits a remarkable cooling effect on the organs. It is used as plaster in case of gout. It is useful in chronic conjunctivitis. The latex of the wild variety removes opacity of the cornea. It is plastered on the chest with barley flour in cases of palpitation. It strengthens the heart; Purging cassia is dissolved in its juice and used as a gargle in pharyngitis. It relieves nausea and counteracts the ill effects of excessive yellow bile, it strengthens the heart, and it is one of the best drugs for the stomach having a hot temperament.

The wild endive is better than the cultivated variety for stomach diseases, endive is said to be suitable for all kinds of temperaments of the liver, the drug is particularly suitable for hot-tempered livers, and however, it is not harmful to cold tempered organs, unlike some cold vegetables. Oral intake of endive, especially of its wild variety along with vinegar, causes constipation. Endive is useful in quarton fevers and also in fevers attributed to cold exposure. Plaster of the roots of endive as well as its roasted flour is beneficial against the bites of scorpion, insects, wasps, snakes *etc.* ¹⁰⁶

Toxicological Studies: While Kasni has a long history of human use, the high levels of secondary metabolites have shown 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 observed. 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 ¹⁰⁷. The toxicological significance 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 than showed less 20% inhibition bioluminescence and hence were concluded to be safe for human use 94.

CONCLUSION: Kasni (*Cichorium intybus*) has a long record of its traditional use globally. Historically, Kasni was grown by the ancient Egyptians as a medicinal plant, coffee substitute, and vegetable crop and was occasionally used for animal forage. This multipurpose plant contains high amounts of proteins, carbohydrates, and mineral elements ¹⁸. Inulin from chicory roots is considered a functional food ingredient as it affects physiological and biochemical processes resulting in better health and decreasing the risk of many diseases ¹⁰⁹. Till date, chicory remains an extremely versatile plant, open to genetic management, and there is interest shown in genetically engineered chicory to obtain higher yields and create new

potentials ¹. 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 a better understanding of the phytochemicals against various diseases ¹⁸; herb-drug interactions *in-vivo* and clinically with major phytochemicals of Kasni and specific ingredient responsible and to determine the precise molecular mechanism of action of Kasni (C. intybus) 111. Studies about the toxic effect of C. intybus are 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 29 . New studies recommend the use of C. intybus as a biomonitor for heavy metals 11, 109; since Kasni enters the food chain, this plant should be used with caution.

The magnitude of the Kasni is now no more limited to preclinical level but stretched to clinical level as reflected in a study on beta-thalassemia patients where chicory reduced serum ferritin and confirmation of the relationship between the level of liver enzymes and onset of type 2 diabetic patients 110. Therefore, it's alleged that Kasni is a propitious traditional medicinal herb which could be of a great benefit to mankind if investigated properly.

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