Review Article

Cichorium intybus: A concise report on its ethnomedicinal, botanical, and phytopharmacological aspects

Abstract

Cichorium intybus L. (chicory) is a Mediterranean plant species belonging to the *Asteraceae* family. Chicory is gaining interests because of its culinary features, nutritional values and medicinal characteristics. *C. intybus* has been implemented in folk medicine from North Africa to South Asia for several 100 years. In Indian medicine, it has been used to treat fever, diarrhea, spleen enlargement, jaundice, liver enlargement, gout, and rheumatism. In China, it is valued for its tonic effects upon the liver and digestive tract. In Germany, chicory has been used as a folk medicine for everyday ailments. Thus, *C. intybus* is a plant of great economic potential due to high concentrations of fructooligosacharide, known as inulin, in its roots, used as a replacement ingredient for sugar and fat. The other various phytoconstituents reported in chicory are sucrose, cellulose, proteins, caffeic acid derivatives, flavonoids, polyphenols, carotenoids, anthocyanins, tannins, coumarins, sesquiterpene lactones, fatty acids, pectin, cholins, benzo-isochromenes, alkaloids, vitamins, amino acids, and minerals. The therapeutic investigations reveal that *C. intybus* is useful for maintaining normal health and has nematicidal, antihepatotoxic, antidiabetic, cardioprotective, antiallergic, antihyperlipidemic, anti-inflammatory, antineoplastic, calcium homeostater, bulking agent, immunostimulatory, prebiotic, protective against pancreatitis, antimicrobial, and antioxidant effects. This review encompasses botany, ethnomedicinal uses, phytoconstituents, pharmacological uses, and toxicity studies of *C. intybus* L.

Key words:
Chicory, Cichorium, herbal medicine, pharmacological uses, phytochemicals, review

Introduction

Cichorium intybus L. (chicory) is a Mediterranean plant species belonging to the *Asteraceae* family. *Cichorieae* tribe includes approximately hundred genera and many hundreds species of which some genera are used as salad vegetables.[1] This crop is widely cultivated in a number of temperate regions around the world including South Africa but has its origins in Europe, Central Russia, Western Asia, and also found in Egypt and North America.[2] Although leaf chicory is often called "endive," true endive (*Cichorium endivia*) is a different species in the genus.

In traditional Indian medicine, chicory has been used to treat fever, diarrhea, spleen enlargement, jaundice, liver enlargement, gout, and rheumatism.[3,4] This plant is also used to treat AIDS, cancer, diabetes, dysmenorrhea, impotence, insomnia, splenitis, tachycardia, gallstones, gastroenteritis, sinus problems, and cuts and bruises. It is also used as a tonic. In China, it is valued for its tonic effects upon the liver and digestive tract. In Germany,

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chicory (especially the flower) has been used as a folk medicine for everyday ailments. The roasted roots are used as the traditional coffee substitute with no caffeine and less well known as grazed forage for ruminants.[5]

C. intybus is a plant of great economic potential due to high concentrations of fructooligosaccharide (FOS), known as inulin, in its roots, used as a replacement ingredient for sugar and fat. Inulin is a polysaccharide consisting of a chain of fructose units with a terminal glucose unit. Vegetables such as asparagus, onion, garlic, dahlia, and chicory are the predominant source for commercial inulin.[6] Inulin is particularly suitable for fat replacement in low-fat or fat-free products, such as chocolate, confectionery, cheese, and ice cream dressing, as it has a fat creamy form, gelling capacity and good body, texture, and mouthfeel. Raftiline and raftilose are used as dietary fiber, having the additional advantages of being able to replace fat and sugar in foods.[7]

The present review has been written as chicory is gaining increasing interests because of the culinary features, nutritional values and medicinal characteristics. Hence, the need was felt to prepare a manuscript based upon its botany, cultivation, collection, storage, and pharmacological uses.

Botany

Scientific name and classification

It can be classified as kingdom: Plantae-plants; Subkingdom: Tracheobionta – vascular plants; Superdivision: *Spermatophyta* – seed plants; Division: Magnoliophyta – flowering plants; Class: *Magnoliopsida* – dicotyledons; Subclass: *Asteridae*; Phylum: Angiosperms; Order: *Asterales*; Family: *Asteraceae*; Tribe: *Cichorieae*; Genus: *Cichorium*; Species: *Intybus* [Figure 1].[8]

Common names and varieties

Commonly it is known as chicory, blue sailors, succory, coffee weed, cornflower, wild chicory, wild succory, garden endive, garden chicory, endive, blue daisy, blue dandelion, blue weed, bunk, hendibeh, horseweed, ragged sailors, wild bachelor's buttons, and wild endive.[9] Common names for varieties of var. *foliosum* include endive, radicchio, Belgian endive, French endive, red endive, sugarloaf, and witloof (or witlof).

There are mainly three subspecies of *C. intybus* namely *C. intybus* L. var. *foliosum* (Hegi) Bisch., *C. intybus* L. var. *silvestre* Bisch, and *C. intybus* L. var. *sativus* Bishoff.

C. intybus L. var. *foliosum* (Hegi) Bisch. known as botanical variety salad chicory include three types of this plant: Belgian endive (also called witloof), sugar chicory (sugarloaf), and radicchio chicory (Italian/red chicory).[10] There are eleven types and cultivars of *C. intybus* L. var. *foliosum* (Hegi) (red chicory), i.e., "Palla Rossa 3," "Orchidea Rossa," "Indigo," "Fidelio," "Rosso di Verona," green – leaf: "Grumolo bionda,"

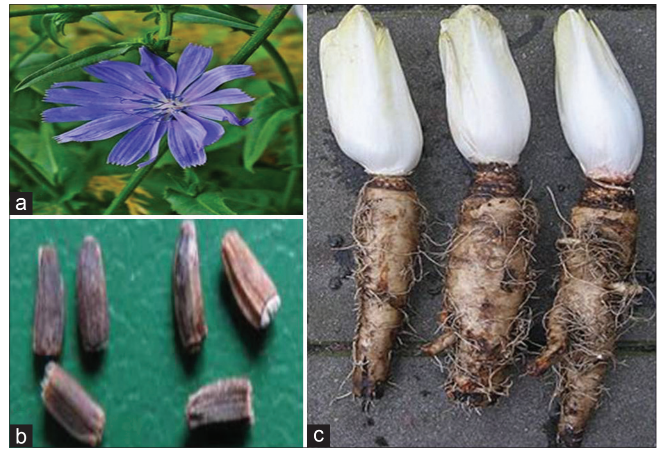

Figure 1: (a) Chicory flower; (b) seeds of Puna chicory; (c) blanched leaves and roots of Belgian endive (source: www.wikipedia.com)

"Capotta di mantovana" and "Pan di Zucchero" (sugarloaf type), then 3 containing anthocyanins coloration of leaves: "Rosso di Chioggia," "Rosso di Treviso 2," and "Variegato di Castelfranco."[11]

C. intybus L. var. *silvestre* Bisch known as wild red variety have been used in New Zealand to produce following varieties: (i) Puna (grasslands Puna) - It is resistant to bolting, resistance to grazing pressure and is an excellent companion to clover. (ii) Forage Feast - It is lower in tannins than Puna and more palatable. (iii) Choice - It has lower rates of lactucin and lactone for the dairy industry, compounds believed to taint the milk. (iv) Oasis - It has increased lactone rates for the forage industry and for higher resistance to fungal diseases such as *Sclerotinia*. (v) Puna II - It has greater persistence and longevity. (vi) Grouse - It is considered to be a better companion to brassicas; also have higher rates of bolting and higher crowns susceptible to over browsing.[12] (vii) Six point - This variety is produced in the USA and is similar to Puna. (viii) Inia Le Certa and La Ninia - These varieties are very useful for food plots where conditions are too hot and dry to grow perennials. (ix) Chico - A short-term cultivar, better suited as an annual with very low spring and summer production levels. (x) Forager - This variety is very similar to Chico and (xi) WINA-100. (xii) Plot enhancer.[13]

The third variety is *C. intybus* L. var. *sativus* Bishoff commonly known as Belgian endive.

Distribution

Natural Habitat: Europe, North America, and Australia.

Botanical description

It is an erect, bushy perennial herb having rhizome which is light yellow from outside and white from within containing bitter milky juice; stems are 0.3–0.9 m. in length, angled are grooved; branched are tough, rigid, and spreading. Radical and lower leaves are 7.5–15 cm. in length while upper leaves are alternate, small, entire, and their bases clasp the stem. Heads are ligulate 2.5–3.8 cm. in diameter, terminal and solitary or axillary's and clustered, sessile or on short, thick stalks. Flowers are white to light blue and lavender, toothed at the ends. There are two rows of involucral bracts; the inner are longer and erect in comparison to the outer bracts which are shorter and spreading. Flowering occurs from July to October. Achene's are smooth, angled, crowned with the ring of pappus scales. Parts generally used are roots, seeds, and herb during blooming period.[14]

Propagation, cultivation, collection, and storage

It is a vegetable known as endive (American) or witloof (Australian). Chicory is grown for a number of reasons in different countries. In Brazil, it is cultivated for the production of leaves, while in India, South Africa, and Belgium roasted chicory is mixed with coffee seeds for the preparation of coffee powder. Recently, Belgium has been active in processing the root for the production of inulin (fructose polymer) and its hydrolysis products such as oligofructose and fructose.[15-18] It has been cultivated as both summer forage and as "coffee substitute" for centuries and was introduced into Australia in the 19th century.[12] *C. intybus* is now a domesticated plant cultivated for food, fodder, and medicine. Phytochemicals are distributed in whole plant.[19] *C. intybus* var. *sativum* Hegi (Belgian endives) is a leafy vegetable with a limited production Area.[20]

In temperate environments, where there is adequate summer rainfall, chicory grows actively from early spring to late autumn. In winter, growth is checked by frosts, but it continues to grow slowly if the soil temperature is more than 9°C. In a given season, not all the plants will be reproductive and those that are vegetative in 1 year are more likely to be reproductive in the following year. Chicory plants require both vernalization and long days to flower. In order to be florally induced, chicory must undergo exposure to low temperature (3 weeks at 4°C) that can be applied to germinating seeds or to the entire plant.[21]

Seed should be sown at a depth of 10 mm, with a seeding rate of 4–5 kg/ha (seed size 830,000/kg). A residual insecticide is essential as it is susceptible to red-legged earth mites. To maintain production and quality, the key is to maximize leaf growth (highly palatable) and minimize stem growth (reduced palatability). A ratio of 70% leaf to 30% stem is regarded as optimal in terms of production and feed quality. The main diseases of chicory are *Sclerotinia* (*Sclerotinia sclerotiorum*) and charcoal rot caused by *Fusarium* spp. where the lower stem and tap-root darken in color until they appear black. Thus, sowing of chicory should be avoided following crops susceptible to *Sclerotinia*, like the pulse crops and canola. If it is sown too early the plant shows bolting. To obtain roots of a large size, the ground must be rich, light, and well manured. The leaves are used in salads, for which they must be cut and used from young plants, which have been generally blanched, as the unblanched leaves are bitter. For blanching, the soil is dugged up around October and after cutting off the leaves, the roots are exposed to the air for a fortnight or 3 weeks; then they are planted in deep boxes or pots of sand or light soil, leaving 8 inches between the soil and the top of the box. A cover of some sort is put on the box to exclude the light and the box is kept into a warm place where frost is excluded. Deprived of light, the young oncoming leaves become blanched and greatly elongated, and in this state are cut and sent to the market. If light is totally debarred, the produce will be of a beautiful creamy white color, soft, and nearly destitute of the bitter flavor present when the plants are grown in the open air.

Soil–climate adaptation

Chicory requires rainfall more than 500 mm. It has good tolerance capacity to aluminum, moderate to drought and frost and low tolerance against waterlogging and salt. It requires deep, well-drained fertile soil with good nitrogen content and pH should be around 4.3 for a good yield.

Cultivation of red chicory, also known as radicchio (*C. intybus* L. var. *silvestre* Bisch.), may be of greater commercial importance.[22] The expansion of its cultivation is determined by the marketing success of freshly cut salad.[23] Radicchio is a red, broad leaf, heading form of chicory. Its leaf colors range from pink to maroon with white midribs. All the red types of radicchio now being cultivated derive from red-leaved individuals belonging to *C. intybus* L. var. *foliosum* (Hegi) Bischoff, while the types with spotted or variegated leaves originated from spontaneous or controlled crosses between these individuals and members of the species *C. intybus* L. var. *latifolium* Hegi, commonly known as broad-leaved endive.[10] Some cultivars form loose heads while others have folded leaves and resemble small cabbages. The red coloration increases during the colder months.[24] Production problems including the early stalk development (bolting) greatly reduce the marketable produce. Bolting of radicchio depend on vernalization and photoperiod. Many studies reported about the effect of environmental conditions on bolting and flowering of chicory, but all information were derived from *in vitro* cultivation of root tissue.[25] However, little information is available on the response of radicchio to temperature and photoperiod in natural field conditions. Low temperature between sowing and germination (below 8°C), long days (above 13 h), and the age of seedlings at transplanting (above 35 days) are known to be a primary environmental factor associated with flower stalk initiation in radicchio. Summer heat can also cause bolting. The crops could not tolerate high ambient temperatures and promote stalk elongation when the temperature exceeded 32°C.[13]

Ethnomedicinal uses

C. intybus has been implemented in folk medicine from North Africa to South Asia for several 100 years. Aqua distillate of aerial parts of *C. intybus* (Aragh-e-Kasni) is used to purify blood and liver disease in different parts of Iran. In the Persian folk medicine, the seeds and leaves of the plant have been considered to be hepatoprotective and blood purifier. The seeds of the plant are used in hepatobiliary disorders in Ayurvedic medicine.[26] Whole plant, especially root, contains volatile oils, which produce high toxicity to internal parasites. Chicory is used as a tonic in the treatment of gallstones, gastroenteritis, sinus problems, cuts, and bruises. Inulin, the dietary fiber found in chicory is a helpful ingredient in treating diabetes and constipation. Chicory is also often recommended for jaundice and spleen problems. The juice made of leaves and a tea made from the blooming plant help the release of gallstones, elimination of internal mucus, and production of bile. They are also useful for gastrointestinal problems: digestive difficulties, gastritis, and lack of appetite. The plant root is used as antihepatotoxic, antiulcerogenic, anti-inflammatory, appetizer, digestive, stomachic, liver tonic, cholagogue, cardiotonic, depurative, diuretic, emmenagogue, febrifuge, alexeteric, and also as tonic. It is useful in vitiated conditions of Kapha and Pitta, cephalalgia, hepatomegaly, inflammations, anorexia, dyspepsia, flatulence, colic, gout, burning sensation, allergic conditions of skin, jaundice, splenomegaly, hyperdipsia, skin diseases, leprosy, strangury, amenorrhea, chronic and bilious fevers, ophthalmia, pharyngitis, vomiting, arthralgia, lumbago, asthma, and general debility.[27,28]

The fresh root is bitter, with a milky juice which is somewhat aperient and is slightly sedative. A decoction of 1 oz. of the root to a pint of boiling water, taken freely, has been found effective in jaundice, liver enlargements, gout and rheumatic complaints, and a decoction of the plant freshly gathered has been recommended for gravel. Syrup of succory acts without irritation, so it is an excellent laxative for children. An infusion of the herb is useful for skin eruptions in connection with gout. The old herbalists described the use of leaves as a good poultice for swellings, inflammations, and inflamed eyes, and that "when boiled in broth for those that have hot, weak, and feeble stomachs do strengthen the same." The leaves have been used to dye blue.

Phytochemistry

Fresh chicory root typically contains, by dry weight, 68% inulin, 14% sucrose, 5% cellulose, 6% protein, 4% ash, and 3% other compounds. Dried chicory root extract contains, by weight, approximately 98% inulin and 2% other compounds.[29] Fresh chicory root may contain between 13 and 23% inulin, by total weight which is a polysaccharide similar to starch.[30] Inulin is mainly found in the plant family *Asteraceae* as a storage carbohydrate (e.g., Jerusalem artichoke, dahlia, yacon, etc.). It is used as a sweetener in the food industry with a sweetening power 1/10 that of sucrose and is sometimes added to yogurts as a prebiotic. Inulin can be converted to fructose and glucose through hydrolysis. Inulin is also gaining popularity as a source of soluble dietary fiber and functional food.[31,32] It is used to replace fat or sugar and reduce the calories of food. Thus suitable for consumption by diabetics[33] and is also used in inulin clearance test to measure glomerular filtration rate.[34] Chicory root extract is a dietary supplement or food additive produced by mixing dried, ground chicory root with water, and removing the insoluble fraction by filtration and centrifugation. Other methods may be used to remove pigments and sugars. It is used as a source of soluble fiber.

Chicory has high fructose content (about 94%). It is a reserve carbohydrate, which consists of a long chain made up of 22–60 fructose molecules with a terminal glucose molecule. Inulin is a blend of fructan chains found widely distributed in nature as plant storage carbohydrate. It may be classified as a FOS and is present in more than 36,000 plant species, mainly plants of the *Asteraceae* and Graminae families.[35,36] Chemically, inulin is polydisperse -(2,1) fructan.[37] The fructose units in this mixture of linear fructose polymers and oligomers are linked to each other by -(2,1) bonds. A glucose molecule typically resides at the end of each fructose chain and is linked by an -(1,2) bond, as in sucrose. Fructans have been extracted from chicory roots.[38] The seeds contain abundantly demulcent oil, while the petals furnish a glucoside which is colorless unless treated with alkalies, when it becomes of a golden yellow.

It is well-known from the literature that the main active compounds of chicory are: inulin, FOS, coffee acid derivatives, flavonoids, and polyphenols. Oligofructose significantly alters liver lipid metabolism, resulting over time in a significant reduction in plasma triacylglycerols, phospholipids, and cholesterol levels.[39] Red chicory also features considerable antioxidant properties, and it contains carotenoids, Vitamins: A, B_6, K, as well as macro- and micro-elements, such as phosphorus, potassium, zinc, copper, or iron.[3,40]

The root extracts have volatile oils, fatty acids, alkaloids, triterpenes, flavonoids, latex, tannins, and saponins.[34] Other compounds which have been isolated and identified from chicory, include flavone derivatives, saccharides, anthocyanins, sesquiterpenes, and vitamins.[41,42]

Chicory is well-known to contain several sesquiterpene lactones, especially in the roots.[42,43] Two guaianolides having different chemical structures, including 8-deoxylactucin and 11 β, 13-dihydrolactucin, from the root extracts of *C. intybus* var. "Rosso di Chioggia."[44,45] An antimicrobial sesquiterpenoid, 8α-angeloyloxycichoralexin exhibits antifungal activities. Two kinds of guaianolides cichoralexin and 10α hydroxycichopumilide have been isolated and identified. This bitterness is due to the presence of large quantities of sesquiterpene lactones, such as lactucin, 8-desoxylactuctin, lactucopicrin, and 11ß-dihydro-derivates.[46]

The root also contains fatty acids (mostly palmitic and linoleic), cichoriin (esculetin-7-glucoside), α-lactucerol (taraxasterol), tannins, sugars (fructose, mannose, etc.), pectin, fixed oils, choline, and others. Cichorins A, B, and C, three new benzo-isochromenes have been isolated from *C. intybus*.[47,48]

The roasted root contains a steam-distillable fraction (aroma), composed of pyrazines, benzothiazoles, aldehydes, aromatic hydrocarbons, furans, phenols, organic acids, and others. Other constituents of the roasted root include 2-acetylpyrrole, furfural, phenyl acetaldehyde, phenyl acetic acid, and vanillin. Small amounts of two insole alkaloid (β carbolines), harman and norharman, have also been isolated from the roasted root. The herb (leaves, flowers, shoots, etc.) contains inulin, fructose, choline, resin, chicoric acid (dicaffeoyl tartaric acid), esculetin, esculin (esculetin-6-glucoside), cichoriin, umbelliferone, scopoletin and 6,7-dihydrocoumarin, and further sesquiterpene lactones and their glycosides.[49] Presence of sesquiterpene lactones has been confirmed by the isolation of a (+)-germacrene, which is a synthase from chicory roots.[50]

C. intybus L. contained alpha-amyrin, taraxerone, baurenyl acetate and beta-sitosterol.[51] Inulooligosaccharides production from chicory extract was carried out using endoinulinase obtained from a new isolate, xanthomonas oryzae number 5.[52] The roots of C. intybus contain 2, 3, 4, 9-tetrahydro-1H-pyrido-(3,4-b) indole-3-carboxylic acid [Figure 2].[53]

Chicory seeds contain amino acids arginine, histidine, isoleucine, leucine, lysine, methionine, cysteine, phenylalanine, tyrosine, threonine, valine, serine, glutamic acid, glycine, alanine, aspartic acid, and proline. Various minerals present in seeds are phosphorus, potassium, calcium, magnesium, sodium (mg g-1), iron (mg g-1), copper (μg g-1), zinc (μg g-1), manganese (μg g-1), molybdenum (μg g-1), selenium (μg g-1), strontium (mg g-1), and cadmium (μg g-1).[54]

The presence of flavones and flavonols in *C. intybus* has also been reported.[55]

The phenolic content in the aerial parts of different varieties of chicory and presence of 2S, 3S-O-di-caffeoyl tartaric acid (chicoric acid), cyanidin-3-O-(6” malonyl)-glucoside, quercetin-3-O-glucuronide, and chlorogenic acid has been reported.[56] A transformed root culture of *C. intybus* L. (*Asteraceae*) was found to produce sesquiterpene lactones of guaiane and germacrane type. Lactucopicrin, 8-desoxylactucin, and three sesquiterpene lactone glycosides: Crepidiaside B, sonchuside A, and ixerisoside D were isolated from the roots.[57]

Pharmacological Activities

General health

Chicory contains inulin,[58,59] which may help humans with weight loss and weight control through the promotion of satiety,[60] constipation, improving bowel function, and general health. In rats, it may increase calcium absorption and bone mineral density. Moreover, cichory has a potent hepatoprotective, antioxidant, hypoglycemic, diuretic, antitesticular toxicity, and immunomodulatory effects.[61-63]

Nematicidal

Chicory is well-known for its toxicity to internal parasites. Ether-soluble phenolics from the chicory rhizome possess nematicidal activity and that the addition of dry powder from chicory rhizome to foods elongates food preservation time.[64] Studies indicate that ingestion of chicory by farm animals resulted in reduction of worm burdens which has prompted its widespread use as a forage supplement.[65-67]

Antihepatotoxic

Chicory roots and seeds have demonstrated antihepatotoxic potential in animal studies.[19,26,68-70] Naseem *et al*. studied the hepatocurative effects (posttreatment study) of aqueous and alcoholic extracts of seeds against carbon tetrachloride (CCl_4) induced hepatotoxicity in the albino rats of Sprague-Dawley strain and found that alcoholic extract exhibited more significant hepatocurative effect.[71,72] Many evidence showed that leaves alcoholic extract, natural root, and root callus extracts possessed potent hepatoprotective activity in rats against CCl_4 induced hepatic damage.[19,73] In line with that the cichotyboside, a sesquiterpene glycoside from seeds of *C. intybus* was also verified to have antihepatotoxic activity comparable to the standard drug silymarin.[70,74]

Hassan investigated the modulating effect of chicory supplemented diet against nitrosamnine-induced oxidative stress and hepatotoxicity in male rats and concluded that chicory can ameliorate any oxidative stress and hepatic injury induced by nitrosamine compounds.[69]

Atta *et al*., 2010, also investigated the effect of chicory extract on CCl_4 induced hepatotoxicity in Sprague-Dawley rats whilst acute toxicity was assessed in Swiss mice over a 5 days period.[75] Rodents were orally administered CCl_4 (2.5 ml/kg, 50% CCl_4 in corn oil), and treated rodents with 250 or 500 mg/kg chicory extract. This suggested that doses up to 5 g/kg showed no symptoms of morbidity or mortality and so an LD_{50} of *C. intybus* is >5g/kg.

Antidiabetic

Chicory root contains dietary inulin-type fructans, which modulate the production of peptides, such as incretins, by

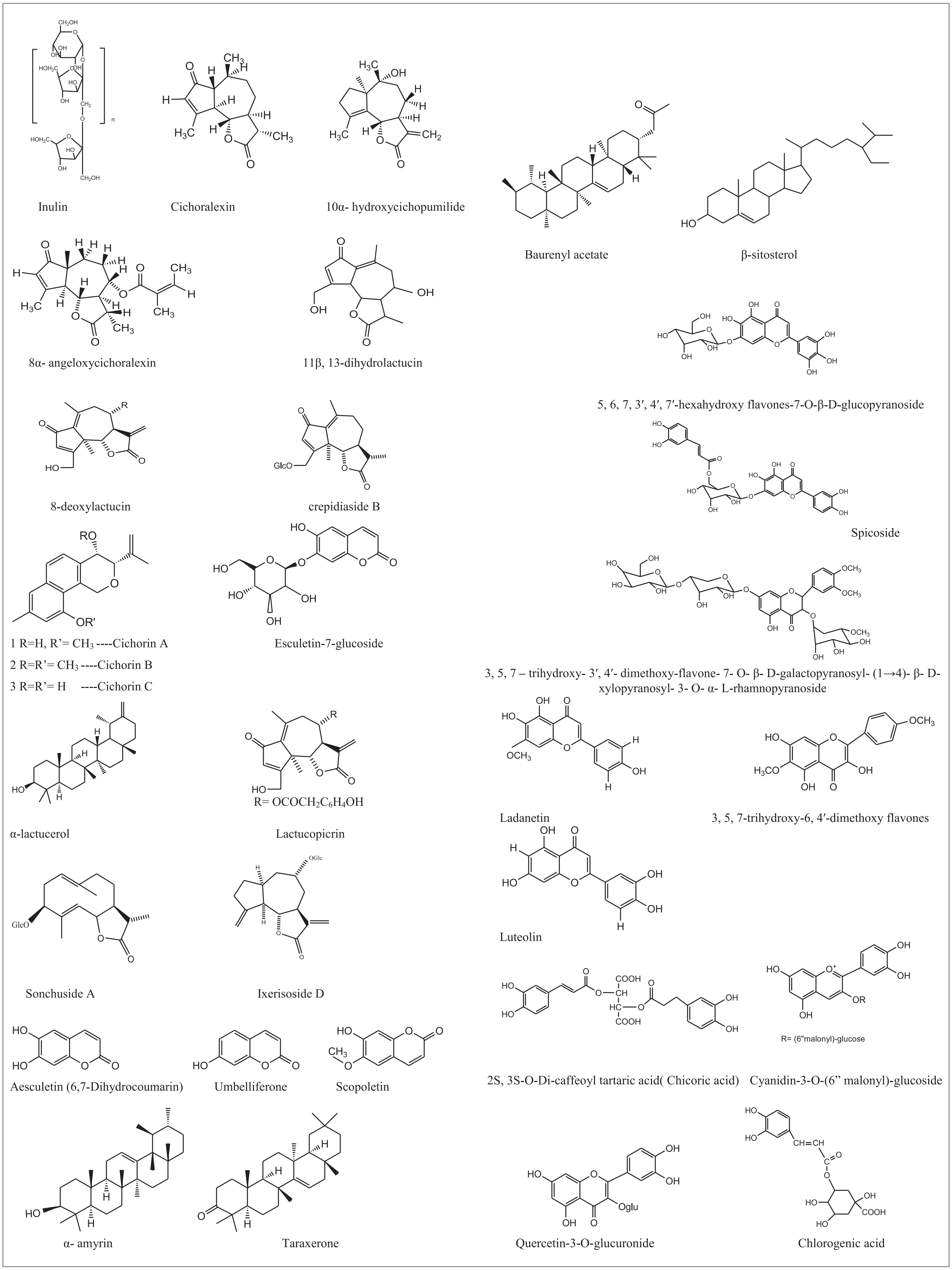

Figure 2: Some identified phytoconstituents of chicory

endocrine cells present in the intestinal mucosa. This effect may play a role in the management of obesity and diabetes through its capacity to promote secretion of endogenous gastrointestinal peptides involved in appetite regulation.[76] Kaskoos found that the induction of diabetes in rats with streptozotocin elevated the circulating lipids levels, and administration of extract of *C. intybus* decreased the levels of circulating lipids. They also lowered the atherogenic index and increased the high-density lipoprotein to much higher level. The aqueous extract possessed antidiabetic activity. Chicory extract (mainly inulin) may have a potential for reducing postprandial hyperglycemia by decreasing intestinal absorption of glucose. This might be due to an increase in the mucosal unstirred layer thickness due to the increased viscosity of chicory extract and inulin.[29,77] Chicory was also widely used to treat diabetes mellitus, and one recent research supported the traditional belief that ethanol extract of *C. intybus* could ameliorate a diabetic state by reducing the hepatic glucose-6-phosphatase activity.[78]

Cardioprotective

The cardioprotective effects of the aqueous extracts of the leaves of *C. intybus* have been proved by Nayeemunnisa on the ageing myocardium of albino rats by administering shade-dried powdered leaves 500 mg twice daily of *C. intybus* for 30 days and found that *C. intybus* ameliorate the age induced injury and offered protection to the heart from oxidative damage, suggestive of ageing.[61]

Antiallergic effects

Kim *et al.* reported that the aqueous extracts of *C. intybus* dose dependently inhibited mast cell immediate-type reactions to compound 48/80 in mice with a dose of 1000 mg/kg. Plasma histamine levels were reduced in a dosage related fashion to antidinitrophenol when administered at concentrations between 1 and 1000 mg/kg. C. intybus aqueous extract inhibits mast cell-mediated immediate-type allergic reactions *in vivo* and *in vitro*.[79]

Antihyperlipidemic effects

Inulin decreases serum triglycerides by decreasing fatty acid synthesis and reducing production of low-density lipoproteins.[80] Chicory root extracts affect reduce cholesterol uptake.[81]

Anti-inflammatory effects

Chicory has been found to inhibit prostaglandin E (2) and cyclooxygenase 2)[82] and prevents immunotoxicity induced by ethanol and have anti-inflammatory properties.[83,84]

Antineoplastic effects

Chicory derived beta (2-1) fructans have been shown to exert cancer protective effects in animal models.[85] The tumor inhibition of chicory root extracts against Ehrlich ascites carcinoma were tested in mice. Significant results were reported for doses obtained between 300 and 700 mg/kg.[1] The chicory fructan supplements inhibit aberrant crypt foci formation, an early preneoplastic marker of malignant potential in the process of colon carcinogenesis.[86,87]

Calcium homeostasis activity

The leaves of chicory maintain calcium levels by heterologous expression of total RNA.[88-90] In addition, inulin also has the capability for enhancement of calcium absorption.[91-93]

Cytochrome P450 activity

Chicory is known to contain guaianolides, eudesmanolides, and germacranolides. The biosynthesis of these sesquiterpene lactones are involved with the cytochrome P450 enzyme.[94,95]

Fecal bulking properties

Inulin and oligofructose are considered dietary fibers. They share the basic common characteristics of dietary fibers including saccharides of plant origin, resistance to digestion and absorption in the small intestine, and fermentation in the colon to produce short-chain fatty acids that are absorbed and metabolized in various parts of the body. Moreover, fermentation induced by difidobacteria has a bulking effect.[96] Fermentation of inulin decreases fecal pH and increases fecal volume.[97]

Immunostimulatory activity

Oligofructose and inulin, selective fermentable chicory fructans, have been shown to stimulate the growth of bifidobacteria, which are regarded as beneficial strains in the colon.[98-100]

Prebiotic effect

Chicory and mannan-oligosaccharide alter fecal microbial populations and certain indices of the immune system.[101]

Menne *et al.* assessed the prebiotic effect of an Fn-type chicory inulin hydrolysate product. The F is for fructose, and n is the number of β(2->1) bound fructose moieties. Fecal samples of eight subjects (5 females and 3 males) who consumed 8 g daily of an Fn-rich chicory inulin product for up to 5 weeks were collected and analyzed for total anaerobes, bifidobacteria, lactobacilli, *Bacteroides*, coliforms, and *Clostridium perfringens*. Both 2 and 5 weeks of oligofructose feeding resulted in a selective increase in bifidobacteria ($P < 0.01$). A daily intake of 8g of Fn-type oligofructose preparation reduced fecal pH and caused little intestinal discomfort.[102]

Protective in pancreatitis

Minaiyan *et al.* demonstrated that *C. intybus* hydroalcoholic extracts possess protective therapy in cerulein-induced acute pancreatitis in mice when given at a dose of 200 mg/kg i.p and suggested a therapeutic potential for pretreatment in this inflammatory disease condition in a clinical setting.[103]

Kocsis *et al*. reported that chicory exhibited a positive effect on the pancreas in experimental dislipidemia.[104]

Antimicrobial activity

The cell wall of Gram-negative bacteria is composed fundamentally of a lipopolysaccharide which stops the accumulation of phenolic compounds in a target cell membrane.[105] The seed extract of *C. intybus* in methanol, ethyl acetate, chloroform, n-butanol, n-hexane and was found to be useful in the treatment of bacterial infections.[106] The antibacterial activity can also be ascribed to the polyphenols, tannins, and coumarins found in crude extracts of herbal plants.[107-109]

Root extracts of chicory in water, ethanol, and ethyl acetate exhibited potent activity against *Escherichia coli*, *Salmonella typhi*, *Bacillus thuringiensis*, and *Staphylococcus aureus* while some reports suggested that inhibitory effect of chicory root extract against *E. coli* was not confirm.[34,110] The fungi *Penicillium* sp. and *Aspergillus* sp. were the most resistant to all the extracts. No inhibition activity was found against *Penicillium* sp. and *Aspergillus* sp. Chicory extracts can inhibit growth of *Sarcina lutea*, *Agrobacterium tumefaciens*, *Erwinia carotovora, Pseudomonas aeruginosa*, *Pseudomonas fluorescens,* zoophilic, and anthropophilic dermatophytes.[42] The root extracts have more intensive antibacterial activity than extracts from whole plant.[110] Phenolic compounds could attack cell walls and cell membranes by affecting their permeability, enabling the release of intracellular constituents, and interfering with membrane functionality of the microbe.[111] Aqueous extracts of red chicory can inhibit cell division, DNA, and RNA synthesis and elongate cells of *Prevotella intermedia*.[112]

Antioxidant

Gazzani has studied the water-soluble antioxidant properties of *C. intybus* var. *silvestre* and found that chicory contained both pro- and antioxidant compounds that can act in both chemical and biological systems.[113] Antioxidants also possess antimicrobial abilities.[114] Lavelli has studied red chicory products (*C. intybus* L.var. *silvestre*) to evaluate the relationship between their polyphenol contents and antioxidant activities. They found that the total amount of phenolics was significantly correlated with antioxidant activity when evaluated with both synthetic radical and enzyme-catalyzed reactions.[115]

Other studies suggesting dosage

Jindal *et al*. examined the toxicity of alcoholic and water extracts of the crude powder and the roasted roots, there was reported to be a mean LD_{50} via the i.p. route of the aqueous extract of 8.7 and 9.3 g/kg for the ethanol extract. Both extracts reported to have significant anticonvulsant activity to a range of compounds that act on the higher centers of the brain. Both ethanolic and aqueous extracts had significant anticotine activity the mean ED_{50} (i.p. mg/kg) was reported to be for aqueous extracts was 510 mg/kg and for ethanol extracts 565 mg/kg. The analgesic effects of both extracts appeared to be similar to morphine. On the neuromuscular junction, the chicory extracts were reported to result in a blockade due to the persistent depolarization.[84] The average daily consumption of chicory fructooligosaccharides (fructans extracted on a commercial basis from the chicory root) in the USA has been reported to be 1–4 g and between 3 and 11 g in Europe.[116]

Reproductive and developmental toxicity

Roy-Choudhury and Venkatakrishna-Bhatt reported on a study where an aqueous suspension of chicory root powder extract was administered to male Swiss mice at 4.3 or 8.7 g/kg for 10 days. A decreased body weight gain was reported for both treated groups. The high dose group also exhibited a decreased testicular weight, degenerated seminiferous tubules with atrophied leydig cells. The seminiferous tubules were reported to be full of desquamated cells and debris. No spermatogenic effect upon the low dose group was reported.[117] Crude ethanol extracts of the seeds of *C. intybus* were tested for their ability to inhibit postcoital conception in adult female Sprague-Dawley rats.[118] The dose not specified was administered to female rats from days 1 to 10 postcoitum, significant contraceptive activity was observed. The activity of the butanol/chloroform insoluble fractions significantly reduced the numbers of implantation.

Dosage

C. intybus generally administered at a dose of 3–6 g of powdered seeds or powdered roots.

Toxicological Assessment

Dermal toxicity

Willi *et al*. reported a 35-year-old Caucasian male cook with a 6-year history of chronic eczema on his hands and distal forearms, which markedly improved on vacations. Skin prick testing gave a strongly positive reaction to *C. intybus* (common chicory). The patient confirmed regular contact with chicory and on avoidance of chicory the patient's eczema disappeared quickly. Sometime later, the patient reported developing generalized pruritus, facial erythema, and dyspnea when standing next to a colleague who was handling chicory, but without any direct contact with himself. The diagnosis of anaphylactic type I-allergy to chicory was confirmed.[119]

Escudero *et al*. reported a study in which sensitization was observed to lettuce and chicory. The patient who had worked in a grocery store for a period of eight years showed symptoms of rhinitis, asthma and chronic eczematous lesions which were clearly related to lettuce and chicory handling, (the patient also gave a positive skin prick test to commercial lettuce extract, leaves and stems of fresh lettuce and chicory). The plants in the *Asteraceae* family may become sensitizing not only through its wind-pollinated members such as mugwort and ragweed, but also through foods such as lettuce or chicory and commented that ‘this is important for elimination diets, for subjects with a known respiratory pollen allergy, and for people highly exposed as a result of their job.[120]

Occupational asthma

Nemery and Demedts reported occupational asthma in a 55-year-old woman that had reported symptoms of wheezing bronchitis due to "chicory allergy." The symptoms were only reported by the patient 2-years after she had stared cultivating chicory. The patient was reported to have a delayed cutaneous reaction to a patch test with chicory root and leaves and also had a slightly positive patch test to substances in the rubber gloves used by the grower. The authors suggested that contact dermatitis to chicory is thought to be due to a sesquiterpene lactone. Bronchospasmic reactions along with irritant dermatitis have been noted in workers from a chicory processing unit, but occupational asthma had not been reported.[121]

Chronic toxicity

The safety of a chicory root extract was evaluated by Schmidt *et al*., on a 28-day sub-chronic toxicity study in male and female Sprague-Dawley rats. The measurements included clinical observations, body weights, food consumption, clinical pathology, gross necropsy and histology. There were no treatment-related toxic effects from chicory extract administered orally at 70, 350, or 1000 mg/kg/day. There were no observed adverse effects of chicory extract in these studies.[5]

General toxicity

The chicory leaves extract were also confirmed without any toxic effects at acute and sub chronic toxicity levels, and free of any cytotoxicity towards rat's lymphocytes.[78]

Conclusion

Chicory has been described in different system of medicine viz., Ayurvedic, Chinese for treatment of various disorders. The toxicity studies reveal it to be a very safe drug. Most of the investigations carried out are directed toward the presence of major constituent inulin in the root. However certain traditional uses as reported in Indian traditional medicine viz., gout, rheumatism, etc., is yet to be scientifically authenticated. More research should be directed towards scientific authentication of these traditional uses.

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Conflicts of interest

There are no conflicts of interest.

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