AN OVERVIEW ON PHYTOCHEMICAL AND PHARMACOLOGICAL PROFILE OF *CICHORIUM INTYBUS* LINN

Tauseef Shaikh, Atar Mujum, Khan Wasimuzzama, Rukhsana A Rub *

Department of Pharmacognosy, M.C.E.Society's Allana College of Pharmacy, 2390, K.B Hidayatullah Road, Azam Campus, Camp, Pune-411001, MS, India.

Summary

Chicory, *Cichorium intybus,* (Asteraceae), is a biennial or perennial herb and is a native of Europe and Asia. Chicory is an important foodstuff appreciated for its bitter taste. Ground roasted powder of the roots is mixed with coffee to impart rich flavor and to decrease caffeine content of the coffee formulation. The plant is a good tonic, cooling and is useful in headache, throat inflammation and enlargement of spleen. The extensive research work claims hypoglycemic, antiallergic, antineoplstic, fecal bulking property for the roots of Chicory. Immunostimulation, mutagenic, probiotic, hepatoprotective,antitibacterial activity etc are the other pharmacological actions attributed to a wide range of phytoconstituents like sesquiterpene lactones, responsible for bitter taste of the plant, eg: lactucin, lactupicrin; coumarines like cichoriin; flavonoids like quercetin 3 galactoside. It also contains, inulin (upto 60%), phlobaphenes, phenolic acids like cichoric acid. The present review summarizes the phytochemical status and pharmacological potential of *Cichorium intybus.*

Keywords: *Cichorium intybus;* hypoglycemic; phytochemical behavior; sesquiterpene lactones, coumarines

Address for correspondence:

Mrs. Rukhsana A. Rub,
Head, Department of Pharmacognosy,
M.C.E. Society's Allana College of Pharmacy,
2390, K.B. Hidayatullah Road,
Azam Campus, Camp, Pune-411001
MS, India.
Email: hailrukhsar@yahoo.com
Contact No.: +91-9890937888

Introduction

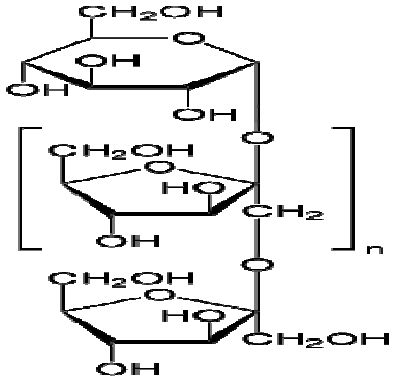
Chicory consists of dried roots and dried above ground parts of *Cichorium intybus* Linn, family Compositeae/ Asteraceae.

Cichorium intybus Linn

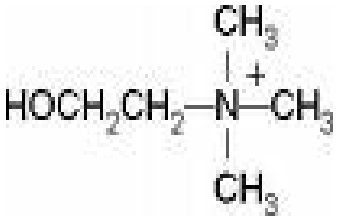
Chicory is a biennial or perennial herb, native to Europe and Asia and can be easily identified by its terminal and auxillary capitulums of lovely blue, lavender, or occasionally white flowers and spindle shaped taproots.[1,2] It is one of earliest mentioned plants in recorded literature. Horace mentions it in reference to his own diet, which he describes it as "Me pascunt olivae, me cichorea, me malvae" (As for me, olives, endives, and mallows provide sustenance).Lord monbodo describes the plant in 1779 as the Chicoree" which the French cultivate as a pot herb[3]. In the United state chicory root has long been used as a substitute for coffee in prisons[4]. The plant is a good tonic; cooling; useful in thirst, headache, opthalmia, throat inflammation, fever, vomotting, diarrhoea, enlargement of spleen etc. Root is the best part of the plant; good stomachic, diuretic, enriches and purifies blood, lessons inflammation and pain in the joints. Leaves are applied topically for the same. The seeds are tonic to the brain, good in biliousness, lumbago and asthma etc.[5]

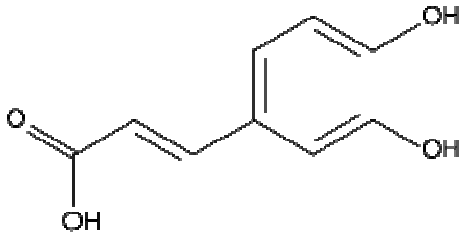
Phytochemical review

1. The roots of *Cichorium intybus* contain sesquiterpene lactones, inulin (up to 60%), phlobaphenes caffeic acid, cichoric acid, sugar, pactin, fixed oil, choline and reducing sugars. [1, 6]



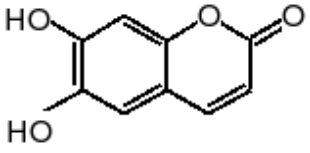
(Inulin)

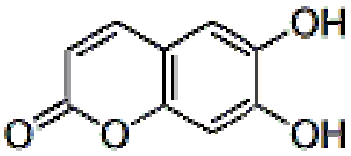




Choline **(Caffeic acid)**

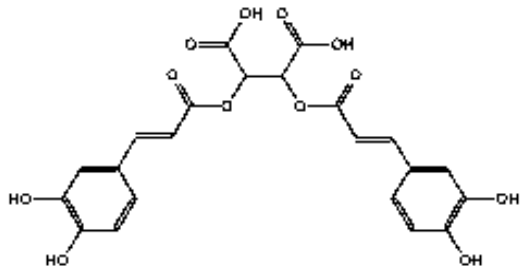
2. The Leaves contain coumarines; esculetin, cichoriin and sesquiterpene lactones.[7] A new coumarin glucoside ester Cichoriin-6'-*p*-hydroxyphenyl acetate, was also isolated from chicory leaves along with cichoriin.[8]





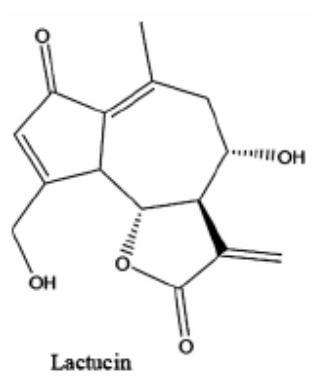
Esculetin **(Cichoriin)**

3. The flowers too contain cichoriin, along with lactucin, intybin and a colourless crystalline glucoside.[9]
4. The seeds contain inulin, phlobaphenes, reducing sugars etc. [10]
5. Water soluble extract of *Cichorium intybus* roots showed the presence of Alkaloids, Flavonoids ,Tannins and saponins.[11]
6. A diacetyl ester, chicoric acid purified from *C. intybus* was able to enhance insulin secretion and glucose uptake in L6 muscular cells. [12]

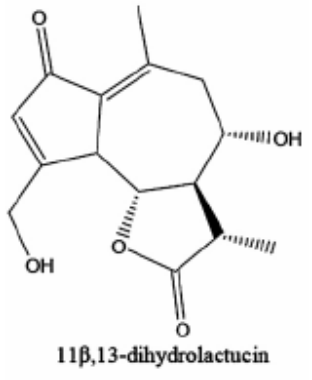


Chicoric acid

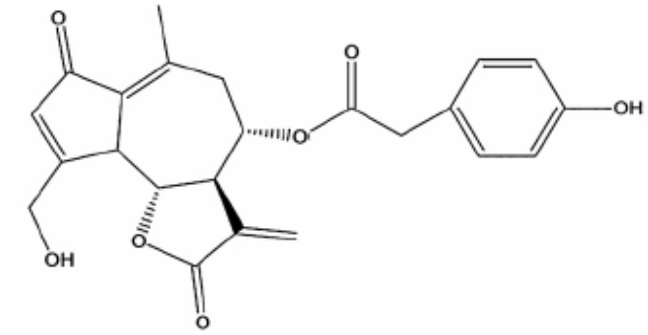
7. A sesquiterpenelactone,lactucin and its derivatives lactucopicrin and 11 beta, 13-dihydrolactucin were found to possess analgesic activity in mice while lactucin and lactucopicrin were found to have sedative properties. [13]



Lactucin



11β,13-dihydrolactucin

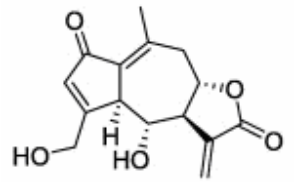


Lactucopicrin

A sesquiterpene lactone 11 beta, 13-dihydrolactucin was quantified for its bitterness value by ELISA in three different varieties of chicory roots which was found to be in the range of 485 to 1720 mg/kg.[14,42,50]

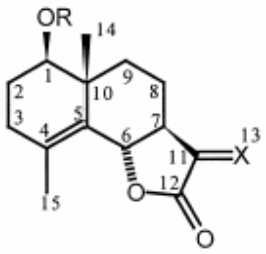
8. Two new triterpenoids; 18 alpha, 19 beta-20 taraxasten-3beta, 21 alpha-diol (cichoridiol) and 17-epi-methyl-6-hydroxyangolelensate (intybusoloid were isolated together with 11 known compound lupeol, friedelin, beta sitosterol, stigmasterol, betulinic acid, betulin, betulinaldehyde, syringic acid, vanilic acid, 6,7- dihydroxy coumarin, and methyl-alpha-d-galactopyranoside from the methanolic extract of seeds of *Cichorium intybus*, having good alpha glucosidase inhibitory activity.[15]

9. The composition of peptic polysaccharides homoglacturonans and rhamnoglacturonan-I (RG-I) in leaf cell wall of chicory were found to be high (about 67%) as compared to cellulose, xyloglucans, heteroxylans, and glucomannans in the leaf lamina while midrib contains high proportion of homoglacturonans, and lower proportion of non peptic polysaccharides. [16]
10. Cichosterol, a new phytosterol have been isolated from seed of *C. intybus* and their structures were determined by using spectral studies.[17]A water soluble enzyme lipooxygenase type III was isolated from *C. intybus.* The results shown by the biochemical properties, kinetic parameters and carotene bleaching activity revealed that the isolated enzyme was found to be lipooxygenase type III depending upon indication given for soyabean isoenzyme. [18]
11. An enzyme Fructane 1 Exohydrolase IIa (1FEH) isolated from *Cichorium intybus* involved in fructane degradation acts as a strong competitive inhibitor with sucrose while 1-kestose acts as an ideal substrate in complex with 1-FEH.[19]



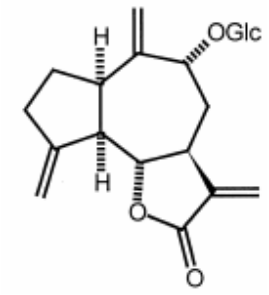
intybulide

12. Three new guaianolides, Eudesmanolide,magnolialide and guaianolide ixerisoside were isolated from aerial part of *Cichorium intybus* along with known sesquiterpene lactones. [20,47]



R = H, X = CH_2

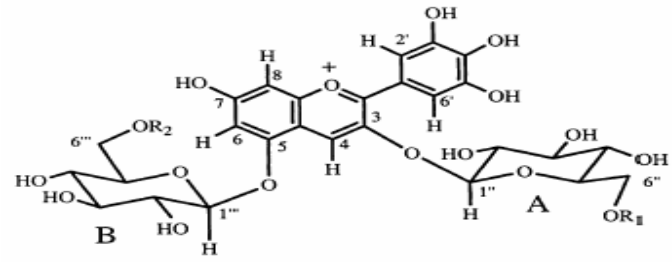
(Magnolialide)



(Ixerisoside)

13. Five principle volatile components octane, n-nanodecane,pentadecanone , hexadecane and pentylsalicylate have been isolated from aerial parts and roots of *Cichorium intybus* and analysed by GCMS.[21]
14. Two new anthocyanins have been isolated from flowers of *Cichorium intybus* and identified as delphinidin- 3, 5-di-O-(6-O-malonyl-beta-D- glucoside) and delphinidin

3-O-(6-O-malonyl-beta-D-glucoside)-5-O-beta-D-glucoside with two known compound delphinidin-3-O-beta-D-glucoside-5-O-(6-O-malonyl–beta-D-glucoside) and delphinidin 3,5- di-O-beta-D-glucoside.[22]



	R_1	R_2
1	malonyl	malonyl
2	malonyl	H
3	H	malonyl
4	H	H

1 Delphinidin 3,5-di-O-(6-O-malonyl-b-D -glucoside)
2 Delphinidin 3-O-(6-O-malonyl-b-D -glucoside)-5-O-b-D -glucoside
3 Delphinidin 3-O-b-D- glucoside-5-O-(6-O-malonyl-b-D-glucoside)
4 Delphinidin 3, 5-di-O-b–D-glucoside.

Pharmacologoical review

1. Water soluble extract of chicory has found to cause reduction in cholesterol uptake in gut-perfused rats, may be due to the increased viscosity of intestinal content, the reason could be presence of inulin in large proportion.[23,46,48]
2. Water extract of *Cichorium intybus* roots has found to have remarkable anti oxidant activity on low density lipoprotein (LDL) oxidation and inhibitory effect on production of thiobarbituric acid reactive substances .[24,43,44]
3. Triterpenoids isolasted from chicory possess a good alpha glucosidase inhibitory activity.[15]
4. Chicoric acid, isolated from *Cichorium intybus* was found to stimulate insulin release from INS- 1E insulin secreting cell line and rat islets of langerhans as well as glucose uptake. [12]
5. Hypoglycemic activity of ethanolic extract of whole plant of *Cichorium intybus* was studied in STZ induced diabetic rats.A dose of 125 mg/kg was found to posses most potent hypoglycemic activity. [25]
6. Tannins present in methanolic extract of *Cichorium intybus* leaves were found to enhance glucose uptake and inhibit adipogenesis in 3T3-L1 adipocytes.[26]
7. Ethanolic extract of chicory roots causes significant inhibition of Ehrlich ascites carcinoma in mice at doses ranging from 300-700mg/kg. [27]

8. The results obtained from toxicological evaluation of chicory root extract revealed that it had no mutagenic activity in Ames test but was found to be cytotoxic to certain strains of Salmonella at higher doses.[9]
9. The lactucin and its derivatives (lactucopicrin and 11 beta, 13-dihydrolactucin) obtained from ethanolic extract of *Cichorium intybus* leaves were investigated for analgesic and sedative activity. Results of study showed that the lactucopicrin had a potent analgesic activity while lactucin and lactucopicrin were found to have good sedative activity. [28]
10. *Cichorium intybus* was evaluated for anti-inflammatory activity. The ethyl acetate extract of roots produced inhibition of prostaglandin E2(PGE2) production in human colon carcinoma HT29 cells by inhibition of expression of cyclooxigenase-2(COX-2) and direct inhibition of COX enzyme activity.[29] The ameliorative effect of ethanolic extract of *Cichorium intybus* was investigated using cisplatin induced nephrotoxicity on rats. The extract was found to reduce nephrotoxicity with no sign of toxicity .[30]
11. Transglucosylases, an enzyme obtained from heads of *Cichorium intybus* was found to convert cichoriin to esculin. [31]
12. Antibacterial activity of chicory root extract was investigated using various solvents. The hexane and ethyl acetate extracts were found to be effective than chloroform and pet ether extracts. [32] Chicory root extract was also found to have potential antifungal activity .[33]
13. Lactucin and lactucopicrin, isolated from *Cichorium intybus* posseses anti-malarial activity.[34]
14. *Cichorium intybus* was found to inhibit mast cell mediated immediate type allergic reactions. [35]
15. The immunotoxicity of ethanolic extract of *Cichorium intybus* was investigated in ICR mice. The results revealed that the immunotixicity induced by ethanol was restored or prevented by *Cichorium intybus* extract.[36]
16. Esculetin, a phenolic compound obtained from *Cichorium intybus* prevents carbon tetrachloride induced liver damage. [37]
17. Root callus of *Cichorium intybus* have better anti-hepatotoxic effect against CCl4 induced liver damage than natural root extract.[38]
18. Also, seeds *of Cichorium intybus* were successively fractioned with acetone, methanol and water and investigated for hepatoprotective activity using CCl_4 and paracetamol induced toxicity in rats. The methanolic fraction exhibited maximum hepatoprotective effect. [39,49]

Toxicity

Chicory extract had no mutagenic activity in the Ames test;although it was cytotoxic to certain strains of salmonella at higher doses with or without metabolic activation [40] .It is also contraindicated to patient with kidney stones since the root is rich in oxalates,people having low blood pressure or with tendency to suffer anemia, It must not be used with gastro duodenal ulcers.[41]

Conclusion

Chicory is one of the most important plants mentioned in different traditional systems of medicine and have been found to have huge pharmacological potential and tremendous scope for its phytochemical research; as suggested in this extensive review on the plant. The review highlights wide range of chemical constituents along with their uses like; inulin, sesquiterpene lactones,phenolics like caffeic acid, chichoric acid , coumarines; esculetin, cichoriin, two new triterpenoids having good alpha glucosidase inhibitory activity. Chicoric acid found to stimulate insulin release whereas esculetin preventing carbon tetrachloride induced liver damage. Thus the plant has great hypoglycemic, hepatoprotective, antioxidant and immunomodulatory potential and the crude extracts or the isolated phytoconstituents of the herb can be exploited for designing effective herbal formulations for aforesaid indications. The areas where still more focus is needed are, pharmacognostic evaluation, enhancement of secondary metabolite production and novel agro-techniques for cultivation of the plant on commercial scale.

References

1) A.N Kalia, Textbook of Industrial Pharmacognosy,CBS Publication. 219.
2) WilliamA.Mitchell, Plant Medicine in Practice, Churchill Livingstone ,79.
3) Letter from Monboddo to john Hope, 29 april,1977,reprinted by william knight 1900.
4) Delaney,John H.New york(state),Dept. of efficiency and economy Annual report. Albany new york,1915,p.673.
5) K.R Kirtikar ,B.D Basu, Indian Medicinal Plant ,2nd edition,Vol-II,international book distributer,1433-1435.
6) Wealth of India, 1950. A Dictionary of Indian Raw Materials and Industrial Products.Council of Scientific and Industrial Research, New Delhi, vol. 3.556-561.
7) Barbura.M,Schmidt.N,a.pouler,I raskin,Toxicological evaluation of chicory root extract,Food and Chemical toxicology,1131-1139.
8) Kisiel W, Michalska K .A new coumarin glucoside ester from *Cichorium intybus*. Fitoterapia 73(2002):544–546.
9) Nadkarni A.K.Indian Materia Medica,3rdEditionVol II, Popular Prakashan ,313-314.
10) Single Dug Standardisation, part I, CCRU publication, 160.
11) Nandagopal.P,Ranjitha B.D,Phytochemical and Anti-bacterial studies of Chicory" Advances in Biological Research.1(1-2):17-21,2007.
12) Tousch.D,Lajoiy.A,Hosy.E,Jacqueline.A,Ferrare.K,Celine.J,Cros.G,Petit.p,Chi-coric acid,a new compound able to enhance insuline release & glucose uptake.
13) William C.MEffect of inulin on lipid parameters in human" Journal of Nutrition.1999:129(7 Suppl);1471S-1473S.
14) Hanee.P,Martin.Y,Vasseur.J,Hilbhert.J,Trotin.F.Quantification of chicory root bitterness by an ELISA for 11ß,13-dihydrolactucin". Food chemistry (2007) vol-105(2)742-748.
15) Rahman.A,Zareen.S,Choudhary.M,Akhtar.M.N,Khan.S.N,Alpha-glucosidase inhibitory activity of triterpenoids from cichorium intybus.Journal of natural product.71(5)910-913.

16) Sun.X,Andrew.I.G,Joblin.K.N,Harris.P.J,McDonald.A,Hoskin S.O.Polysacchari- de compositions of leaf cells walls of forage chicory. Plant science, Vol-170,issue1(2006)18-27.
17) Bahar.A,Sandhya.B,siddiqui.A.B,Tnaveer.A,Shah.A,Components from seeds of Cichorium intybus.Indian journal of Chemistry,41(2002)2701-2705.
18) Daglia.M,Aceti.C,Giorgetti.s,Papetti.A,Gazzani.G.Purification & characterizati- on of soluble cichorium intybus lipoxygenase.Journal of agriculture& food chemistry.2005,53(16) 6448-6454 .
19) Lammens.W,Verhaest.M,Roy.K.L,Ranter.C,Laere.A,Ende.W,Rabijsn.A.Fructan 1-Exohydrolase IIa from cichorium intybus in complex with ligands.Food Research International.vol-29,Issue 5-6(1996)439-444.
20) Kisiel W, Zieli ska K (2001) Guaianolides from *Cichorium intybus* and structure revision of *Cichorium* sesquiterpene lactones. Phytochemistry 57:523– 527.
21) Asta.J,Jurga.B volatile constituents from aerial parts & roots of cichorium intybus (chicory) grown in Luthiana Chemija 2008.vol.19(2).25-28.
22) Rikke.N,Karina N,Tadao.KAnthocyanins from flowers of cichorium intybus.Phytochemistry 60(2002) 357-359.
23) Meehye.kim Ph.DThe water soluble extract of chicory reduces cholesterol uptake in gut-perfused rats.Nutrition Research .vol 20,issue 7,1017-1026.
24) Kim.T.W,Yang.K.S,Oxidative effects of cichorium intybus root extract on LDL oxidation"Archives of Pharmaceutical Research.vol.24(5),431-436(2001).
25) Pushparaj PN, Low HK, Manikandan J, Tan BK, Tan CH,Anti-diabetic effects of Cichorium intybus in streptozotocin-induced diabetic rats".Journal of Ethnopharmacology.111(2007)430-434.
26) Muthusamy VS, Anand S, Sangeetha KN, Sujatha S, Arun B, Lakshmi BS,Tanins presents in *Cinchorium intybus* enhance glucose uptake and inhibit adipogenesis in 3t3-l1 adipocytes through ptp 1b inhibition.Chemico-biological interaction,174(2008)69-78.
27) B. Hazra, R. Sarkar, S. Bhattacharyya and P. Roy, Tumour inhibitory activity of chicory root extract against Ehrlich ascites carcinoma in mice.*Fitoterapia* 73 (2002), 730– 733.
28) Wesolowska.A,Nikiforuk.A,Michalska.K,Kisiel.W,Chojnacka-Wojcik.EAnalgesic and sedative activity of lactucin and some lactucin like aguainolide in mice. Journal of Ethnopharmacology 107(2006)254-258.
29) Cavin,C,Delannoy,M.Malonoe,A,Debefve,E,Touche,A,Courtois,and Schilter,B.Inhibition of the expression and activity of cycloxygenase-2 by chicory extract.Biochem,Biophys.Res Commun.2-18-2005:327(3):742-749.
Cyanidin 3-malonylglucoside in Cichorium intybus. Phytochemistry 23, 2968–2969.
30) Shafaq N,Tabassum.M,Ameliorative effect of ethanolic extract of cichorium intybus on Cisplatin-Induced Nephrotoxicity in Rats.Pakistan Journal of scientific & Industrial Research.2009:52(4) 208-216.
31) Sato.M,Hasegawa.MTransglucosylases in Cichorium intybus converting cichoriin to esculin.Phytochemistry.vol.11,issue 11,(1972).3149-3156.
32) Nandagopal.P,Ranjitha B.D,Phytochemical and Anti-bacterial studies of Chicory" Advances in Biological Research.1(1-2):17-21,2007.
33) Mares, D., C.B. Romagnoli, B. Tosi, E. Andreotti, G. Chillemi and F. Poli, 2005. Chicory extracts from *Cichorium intybus* L. as potential antifungals. Mycopathologia, 160: 85-92.

34) Bischoff,T.A.Kelley,c,J,Karchesy,Y.Lauantose,M,Nguyen Dinh,P andArefi,A.G.Antimalar ial activity of lactucin and lactucopicrin: sesquiterpene lactones isolated from Cichoriun intybus L.Journal of Ethnopharmacology.2004:95(2-3):445-457.
35) Kim,HM,Kim,HW,Lyu,Y.S.Won,J.H.Kim,d.K,Leo,Y.m.Morii,Jippo,t.Kitamera,Y and An,N.H.Inhibitory effect of mast cell mediated immediate type allergic reaction by Cichorium intybus".pharmacological Research.1999:40(1):61-65.
36) Kim. J.H., Y.J. Mun, W.H. Woo, K.S. Jeon, N.H. An and J.S. Park,Effects of the ethanol extract of *Cichorium intybus* on the immunotoxicity by ethanol in mice" International. Immunopharmacology. **2** (2002), 733–744.
37) Gilani.A.H,Janbaz.K.H,Shah.B.H,Esculetin prevents liver damage induced by paracetamol and CCL4".Pharmaological Research.37(1998) 31-35.
38) Zafar and S.Mujahid ali,Antihepatotoxic effect of roots and root callus extract of Cichorum intybus"Journal of Ethnopharmacology.63(1998)227-231.
39) Gadgoli, C. and Mishra, S.H. (1997). Antihepatotoxic activity of *Cichorium intybus"* Journal of Ethnopharmacology.58(1997).131-134.
40) Schmidt.B.M,Ilic.N,Poulev.A,Raskin.I,Toxicological evaluation of a chicory root extract".Food & Chemical Toxicology 45(2007) 1131-1139.
41) www.botanicalonline.com
42) Beek.T.A,Maas.P,King.B.M,Leclercq.E,voragen.A.G.J.Groot.A,Bitter sesquiter- pene lactones from chicory roots.Journal of Agriculture Food Chemistry.38(1990) 1035-1038.
43) Boeuf G,Bauw G,Legrand B, Rambour S (2000) Purification and characterization of a basic peroxidase from the medium of cell suspension cultures of chicory. Plant Physiol Biochem 38:217–224.
44) Daglia.A,Gazzani.G,Anti & pro-oxidant activity of water soluble component in cichorium intybus".Journal of pharmaceutical & Biomedical analysis.vol 30,Issue 4(2002) 939-945.
45) Daglia.M,Aceti.C,Giorgetti.s,Papetti.A,Gazzani.G.Purification & characterizati- on of soluble cichorium intybus lipoxygenase.Journal of agriculture& food chemistry.2005,53(16) 6448-6454 .
46) Delzenne,N,M.Cani,P.D.Daubioul,C, and Neyrinck,A.M.Impact of inulin and oligofructose on gastrointestinal peptides"Journal of.Nutrition.2005;93 Suppl 1:S157-S161.
47) El-Feraly, F.S., Chan, Y.M., Benigni, D.A., 1979.Magnolialide, a novel eudesmanolide from the root bark of Magnolia grandi.ora.
48) Elly Den Hond,Benny .G,Ghoos.Y,Effect of high performance chicory inulin on constipation.Nutrition Research.vol.(20) 731-736.
49) Handa, S.S., Sharma, A., Chakraborti, K.K., 1986. Natural products and plants as liver protecting drugs. Fitoterapia 57, 307-349.
50) Mahmoud,Z., El-Masry, S., Amer, M., Ziesche, J., Grenz, M., 1984.Sesquiterpene lactoness from Sonchus macrocarpus. Phytochemistry23,1105–1107.