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Original Research Article

Evaluation of phytochemicals, antioxidant property and effects of *cichorium intybus* cultivated at foothilarea of Uttarakhand on hyperglycemic rats

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ABSTRACT

Cichorium (C.) intybus is an important medicinal herb has been used in Ayurveda, Unani and Siddha System of Medicine for treatment of liver, stomach, kidney and skin diseases. It is also used as blood purifier, antipyretic and antibacterial. Free radicals or highly reactive oxygen species are capable of inducing various degenerative diseases through oxidative damage to cells/organs in human being. The study was aim to determinate the phytochemical characterization and evaluates the antioxidant property and effects of *C. intybus* cultivated in foothill area of Uttarakhand on hyperglycemic rats. The antioxidants compounds of the *C. intybus* were also determined. Leaves and roots of Kasni plant are rich in phytochemicals and antioxidant compounds, but significant ($P<0.05$) difference in phytochemicals and antioxidant property were observed between two parts leaves and roots of the plants. The leaf extract of the plant was also exhibited significantly ($P<0.05$) effects on hyperglycemic rats. Hence, both parts leaf and root of chicory plant can be used in prevention and treatment of hyperglycemia, hyperlipidemia, and maintaining normal blood biochemical parameters as well as in reduction of oxidative stress in human being.

1. Introduction

Free radicals or highly reactive oxygen species formed in the human body by exogenous chemicals or endogenous metabolic processes. These are capable to oxidize bio-molecules viz nucleic acids, proteins, lipids and DNA. They can initiate different degenerative diseases like neurological disorders, diabetes, cancer, cirrhosis, atherosclerosis, arthritis etc.[1,2] Diabetes is a chronic disorder in the metabolism of proteins, fats, and carbohydrates.[1,2] It is characterized by chronic hyperglycemia due to defects in insulin secretion, insulin action or both.[3] Free radicals inducing oxidative damage are the important factors to enhance risk of hyperglycemia in human being. Nowadays, different treatments, such as insulin therapy, pharmacotherapy and diet therapy are available to control diabetes. These treatments have some disadvantages such as drug resistance (reduction of efficiency), side effects, and even toxicity. Antioxidants are the compounds, which terminate the attack of free radicals and thus reduce the risk of diabetic disorder.[3] Prior and Cao, (1999)[4] reported that antioxidant supplements or dietary antioxidants protect against the damaging effects of free radicals. Presently, much attention has focused on the use of natural antioxidants to protect the human body from the oxidative damage caused by free radicals. In last decades, several medicinal plants have shown such effectiveness through the traditional methods.[5] Therefore, it is better for diabetes patients to use the medicinal plant for controlling and treating the diabetes symptoms.

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Cichorium (C.) intybus L., commonly known as chicory belonging to family Asteraceae is an erect fairly woody perennial herb, approx. 1m in height with a fleshy taproot of up to 75 cm in length and large basal leaves and it is widely distributed in Asia and Europe.[6,7] Chicory plant is considered important domestic plant usually grown for food, animal fodder, and to make traditional medicines. It contain various important constituents such fructo-oligosaccharides prebiotic, sesquiterpene lactones, caffeic acid derivatives (chicoric acid, chlorogenic acid, isochlorogenic acid, dicaffeoyl tartaric acid), inulin, proteins, hydroxycoumarins, flavonoids, alkaloids, steroids, terpenoids, oils, volatile compounds, vitamins.[8,9] They have possessed lot of benefits for the human health like hepato-protective, gastro-protective, cardioprotective, antioxidant, hypolipidemic, anticancer, reproductive, anti-inflammatory, analgesic, sedative, immunological, antimicrobial, anthelmintic, anti-protozoal, antidiabetic, wound healing and many other pharmacological effects.[6,10] Presently, the chicory plants were cultivated at foothill area of Kumaun region of Uttarakhand for the evolution of their medicinal property for the development of herbal product. Hence, the current study was aimed to determine the phytochemical characterization, antioxidant activity, and effects on hyperglycemic rats of *C. intybus*. The antioxidants compounds such as total phenols, flavonoids, tannins and ascorbic acid were also determined to correlate with their antioxidant activity.

2. Material and Methods

2.1. Plant material and extract preparation

The leaves and roots of *C. intybus* were collected from the farm of DIBER, DRDO Haldwani, Nainital, Uttarakhand (India). The leaves and roots were shade dried and grinded into fine powder with the help of mechanical grinder. The freshly prepared dried powder of plant material was subjected to overnight in 20% ethanolic solution for hydroalcoholic extract (HAE) over a period of 48 h for cold extraction. The HAE was filtered and the solvent was removed by evaporation using rotary evaporator under reduced pressure at 40 ºC. The samples were stored in an airtight container at (-) 4 ^{0}C for further use.

2.2. Chemicals

Aluminium chloride, Potassium acetate, Methanol, Folin–Ciocalteau solution, Folin-Denis solutuion, 2, 6-dichlorophenolindophenolwere purchased from E. Merck. Catechol, 1,1-diphenyl-2-picryl-hydrazyl (*DPPH*), Ascorbic acid, D-glucose, Bovine serum albumin, Quercetin, streptozotocin, Tannic acid and Oxalic acid were purchased from Sigma Chemical Co. Ltd, USA.

2.3. Phytochemical characterization of roots and leaves extract of C. intybus

The analysis of phytochemicals such as carbohydrates, proteins, total phenols, flavonoid, tannins, ascorbic acids in hydro-alcoholic extracts of leaves and roots of *C. intybus* were carried out.

Carbohydrates are the important components of storage and structural material in the plants. They exist as free sugars and polysaccharides. Carbohydrate contents can be measured by hydrolysis of polysaccharides into simpler sugars by acid hydrolysis and estimating the resultant monosaccharaides. Estimation of Total carbohydrate was done by Anthrone method.[11] Total carbohydrate was calculated with the help of reference curve using D-glucose as standard.

Proteins are present in the living word, irrespective of size of the organism, since from the structural and functional basis of the cell. In some cases, identification of presence or absence of proteins is very necessary. Now a day different methods are available for the determination of total proteins. Estimation of total protein was done by Lowry's method.[12] In this method the blue colour developed by the reduction of the phosphomolybdic–phosphotungstic components in the Folin-Ciocalteau reagent with the amino acids present in the protein. The amount of protein present in the sample was calculated by using the standard graph. The bovine serum albumin (BSA) was used as standard.

Phenols, the another important aromatic compound are wide spread in plant kingdom having free radical scavenging ability due to presence of hydroxyl group.[13] Natural polyphenolic compounds have inhibitory effects on mutagenesis and carcinogenesis in humans.[14] Phenolic compounds include phenolic acids, flavonoids, tannins, stilbenes, curcuminoids, coumarins, lignans, quinones, etc are found in medicinal herbs and dietary plants. Phenols play important roles in resistance power of the plants against disease and pests. High amount of polyphenols to give resistant against bird attack. Total phenols were determined by Folin–Ciocalteau method. The standard curve was prepared by using different concentrations of catechol.[15] The total amount of phenol present in the test samples was estimated by using the standard curved and expressed as mg phenols/100 g.

Flavonoids were determined by Aluminium chloride colorimetric method.[16] 1.0 mg/ml extract was mixed with 0.1 ml 10% aluminium chloride, 0.1 ml of 1.0 M potassium acetate and 2.8 ml distilled water. The mixture was vortexed for 30 seconds and then allowed to stand for 30 minutes at room temperature. The absorbance was recorded at 415 nm. Quercetin used as standard and standard curve was plotted. Flavonoid contents were represented as mg Quercetin equivalent/gm of dry weight

Tannins also possess very high antioxidant activity due to their tremendous free radical scavenging ability and thus

they protect the body from harmful effect of free radicals. Tannin is an astringent, polyphenolic biomolecule that binds to and precipitates proteins and various other organic compounds including amino acids and alkaloids. The tannin compounds are widely distributed in many species of plants, where they play a role in protection from predation, and perhaps also as pesticides, and might help in regulating plant growth. Tannins were estimated by Folin-Denis method.[17] Tannin like compounds reduces phosphotungstomolybdic acid in alkaline solution to produce blue colour, the intensity of which is proportional to the amount of tannins and measured in a spectrophotometer at 700 nm. The tannin content present in the test samples was calculated from the standard graph using tannic acid.

Ascorbic acid is a naturally occurring antioxidant compound found in medicinal plants, vegetables, fruits and whole grains. Total ascorbic acid content in plant extract was determined by 2, 6- dichlorophenolindophenol method.[18] 2 g dried powdered sample was extracted with 4% oxalic acid and the volume was made up to 100 ml. It was centrifuged at 10,000 rpm for 10 min. 5 ml supernatant liquid was transferred to a conical flask and 10 ml of 4% oxalic acid was added. It was titrated against standard dye solution (2, 6-dichlorophenolindophenol) to a pink end point. The procedure was repeated with a blank solution (without adding sample). 5 ml ascorbic acid of 100 ppm was used as standard. Ascorbic acid content was calculated using the formula:

Ascorbic acid (mg/100 g) = [0.5 mg x titer vol against test x 100 ml/titer vol. against ref. x 5 ml x weight of sample] x 100

2.4. Screening of antioxidant activity as free radical scavenging activity (FRSA) by DPPH method in roots and leaves extract of C. intybus

The stable 1,1-diphenyl-2-picryl hydrazyl radical (DPPH) was used for determination of FRSA of the plant extract. Different aliquots of hydroalcoholic extract were taken in test tubes and volume was made upto 1 ml with methanol. Then added 2 ml methanolic solution of DPPH (0.1 Mm) in all test tubes. After 30 minute at room temperature, the absorbance was recorded at 517 nm. Ascorbic acid was used as standard.[19,20] Percentage inhibition was calculated as % free radical scavenging activity = [(Abs $_{control}$ — Abs $_{sample}$)/Abs $_{control}$ x 100]

Where, Abs control is the absorbance of DPPH radical with methanol; Abs sample is the absorbance of DPPH radical with sample extract/standard. All test were performed in triplicates.

2.5. Effects of C. intybus on hyperglycemic rats

2.5.1. Animals used

Male Wistar rats (180-250 gm, age 10-14 w) were selected from the Experimental Animal House of the Institute for this study. They were kept in the polycarbonate plastic cages under standard management conditions (Temperature 25±3 °C, Relative Humidity - 50–70 %, and 12 h/12 h dark/light cycle). The animals had ad libitum access to food and drinking water. All procedures in the present study were carried out under strict compliance of approved directions of CPCSEA, Ministry of Environment and Forest, Government of India, New Dehli. The experiments were conducted according to protocols given below.

2.5.2. Acute toxicity study

The extract of Chicory leaf was administered orally to different groups of rats at different dosage viz 50, 500 and 2000 mg/kg body weight for acute toxicity. Acute toxicity study was carried out according to the OECD Guideline 423[21] and animals were observed for 14 days for any toxic symptoms and mortality.

2.5.3. Streptozotocin induced hyperglycemia in rats

Diabetes was induced in the rats (overnight fasted) by a single injection of streptozotocin (60 mg/kg b.w., i.p.). After 72 hrs of STZ injection, blood sample was collected from the retro-orbital of the rat eyes and plasma glucose level were determined. The confirmed hyperglycemic animals (plasma glucose levels ≥200 mg/dl) were separated and used for evaluate the effects of *C. intybus* on hyperglycemic rats[22] in groups II-IV.

The selected rats were divided into following groups. Each group contains five rats.

1. *Group I.* Normal control group: Normal rats were treated with 0.5 mL saline orally for 21 days.
2. *Group II.* Hyperglycemic (diabetic) control group: Hyperglycemic rats were treated with 0.5 mL saline orally for 21 days.
3. *Group III.* Hyperglycemic test group: Hyperglycemic rats were treated with extract of *C. intybus* (50 mg/kg b.w.) orally for 21 days.
4. *Group IV.* Hyperglycemic test group: Hyperglycemic rats were treated with extract of *C. intybus* (200 mg/kg b.w.) orally for 21 days.
5. *Group V.* Hyperglycemic standard group: Hyperglycemic rats were treated with glibenclamide (5 mg/kg body weight) as standard drug orally for 21 days.

During the experimental period, body weight, food intake and water intake of all treated animals were monitored weekly. At the end of experimental period, the rats were fasted overnight, euthanized and the blood was withdrawn

by retro-orbital puncture, collected and allowed to stand for 30 min at 37°C. Then the serum was separated from blood with the help of centrifugation at 3000rpm for 10 min, transferred to eppendorf tubes and stores at -20 ^{0}C for further estimation of serum biochemical parameters.

2.5.4. Blood serum biochemical parameters analysis

The serum biochemical parameters such as glucose, serum glutamic pyruvic transaminase (SGPT), alkaline phosphatase (ALP), serum glutamic oxalacetic transaminase (SGOT), total bilirubin (TB,) direct bilirubin, total protein, albumin, cholesterol, triglycerides, creatinine, uric acid and BUN were measured of all treated animals by commercial kit with the help of biochemistry analyzer (MEDICA).

2.6. Statistical analysis

The results in the study were expressed as Mean ± S.D. Statistical analysis of the results were done by using one way ANOVA followed by post-hoc analysis by Dunnett's 't' test for all groups compared vs. control group and Student-Newman-Keuls Test for compared all pairs of groups.

3. Results and Discussion

3.1. Screening of phytochemicals

Phytochemicals such as total carbohydrate, total proteins, total phenolics, ascorbic acid, flavonoids and total tannins contents were quantitatively analysed in hydro-alcoholic extracts of leaves and roots of *C. intybus*. The results of analysis of above phytochemicals are shown in Table 1.

The total carbohydrate content in leaf and roots of *C. intybus* was found 6.314±0.38 g/100 g and 32.78±0.206 g/100 g respectively (Table 1). Similarly, in previous studies carbohydrate was reported 4.7 g/100g in leaves[23] and average 21% in roots.[24] Hence, locally cultivated chicory plants shows good amount of carbohydrates in both leaf and root parts, but high content observed in leaf as compared to roots. The varied content of carbohydrates found in the chicory plant, which depend on their cultivation, climates, extraction method, and parts of the plant. Chicory plant is containing carbohydrates like saccharose, glucose and fructose, fructooligosaccharides, inulin etc. in leaves and roots parts. Inulin is a soluble polyfructan and belongs to a group of dietary fibre. Fructooligosaccharides is having prebiotic activity in humans.[25] Use of chicory plant as food supplement will be beneficial for human being.

Along with carbohydrates, the Chicory plant is also good source of proteins and amino acids. Total protein content of *C. intybus* was recorded 1.89±0.01 g/100 g in leaf and in root 3.68±0.10 g/100 g showed inTable 1. Maximum content of protein was recorded in roots part than leaf part of *C. intybus*. In similar study, done by Saeed M *et al*., 2017[22] in *C. intybus* plant, the protein content was found to be 1.7 g/100 g in leaves.

Phenolics or polyphenols are secondary plant metabolites and ubiquitously present in plants and their products.[26] In this study, total phenolics were found in leaves (55.4±2.2 mg Catechol equivalent (CE)/g) than roots (28.43±0.87mg CE /g) of *C. intybus* (Table 1). A study done by Shad *et al*. (2013)[27] on *C. intybus*, total phenolic content was reported 25.2±2.6 mg GAE /g in methanolic extract (30%) of leaf and 4.7±0.7 mg GAE /g in methanolic extract (30%) of roots. Similarly Malik *et al*., 2017[28] reported total phenolic content 19.21±0.60 mg GAE /g in 80% methanolic leaf extract of cultivated *C. intybus*. Hence, results showed that the leaves are good source of phenolics than roots of *C. intybus*. Tanaka *et al*., (1998)[14] suggested that the natural polyphenolic compounds are having inhibitory effects on mutagenesis and carcinogenesis in humans. Phenolics or polyphenols are having antioxidant property due to the presence of hydroxyl groups and it has protective role against the oxidative damage caused by endogenous free radicals.[26,29] They act through scavenging or chelating process.[30,31]

In present study, maximum content of flavonoids was found in the leaf part (3.2±0.09 mg Quercetin equivalent (QE) /g) as compared to roots part (1.26± 0.103mg QE/g) of *C. intybus* shown in Table 1. Shad *et al*. (2013)[27] has reported flavonoid 1.0±0.2 mg catechin equivalent (CE) /g in methanolic extract (30%) of leaf and 0.5±0.3 CE mg/g in methanolic extract (30%) of roots of *C. intybus*. Similarly, Malik *et al*., (2017)[28] has reported total flavonoids 9.51±0.43 mg GAE /g in methanolic extract (80%) of leaves of cultivated *C. intybus*. Hence, results show that the both parts leaves and roots of *C. intybus* are good source of flavonoids, but leafs are having high amount than roots. Therefore, *C. intybus* has been found to have high medicinal value due to rich source of phenolics and flavonoid compounds.

Tannins are polyphenolic compounds with high molecular weight and having protective role against harmful effects of free radicals. They are also having protective role in plants against micro-organisms, unfavourable climatic conditions and damage by animals/birds' attack.[32] In present study, total tannins content was recorded 0.73±0.1 mg Tannic acid equivalent (TAE) /g in leaf extract and 0.052±0.01 mg TAE/g in roots extract of *C. intybus* (Table 1). Abaas *et al*., (2015)[33] has reported total tannin content 0.59±0.04 mg/g in leaf extract of chicory plant. While, Shad *et al*. (2013)[27] has reported total tannin content 6.6±0.2 mg/g in methanolic extract (30%) of leaf and 15.1±0.3 mg/g in methanolic extract (30%) of roots of *C. intybus*. The leaf of chicory plant is also a good source of total tannins.

The leaves and roots of chicory plant are a good source of ascorbic acid, which was recorded 89.9 ± 0.75 mg/g and 71.1±0.122 mg/g in the leaves and roots respectively

Table 1: Screening of phytochemicals in *C. intybus*

Name of Sample	Carbohydrate (g/100g)	Proteins g/100g)	Tannins (mg/g)	Phenolic (mg/g)	Ascorbic Acid (mg/100 g)	Flavonoids (mg/g)
C. intybus (leaf)	6.314±0.38	1.89±0.01	55.4±2.2	0.73±0.1	89.9±0.75	3.2±0.09
C. intybus (root)	32.78±0.206*	3.68±0.10*	28.43±0.87*	0.052±0.01*	71.1±0.122*	1.26± 0.10*

[Values expressed as mean ± S.D. from three observations. p values <0.05 significant difference between leaf and root]

(Table 1). Hence, leaves and roots of chicory plant are good source of antioxidant compound like phenolics, flavonoids, tannins, and ascorbic acid. Antioxidants are the compounds, which terminate the attack of free radicals and reduce the risk of diseases that are capable of inducing oxidative damage to human body.

3.2. *Evaluation of antioxidant activity as FRSA*

The DPPH method is most widely used method for *in-vitro* estimating Free Radical Scavenging Activity (FRSA) of the plant extracts. In this method DPPH are the free radicals, which neutralized by the antioxidant compound like ascorbic acid, total phenolics, tannins etc. In this study DPPH radical scavenging based antioxidant potential of the extracts was evaluated using the parameter IC_{50}. Here, IC_{50} means the concentration of antioxidant required for 50% scavenging of DPPH radicals.

The HAE of leaf of *C. intybus* exhibited FRSA 67.61 %, whereas, root (HAE) exhibited FRSA 32.26 % at dose of 400 μg. The IC_{50} value was recorded in chicory leaf 295.78 μg/ml, while, in root 619.94 μg/ml. Lower IC_{50} value in leaf of chicory as compared to root indicates high antioxidant property inleaf. Milala *et al*., (2009)[24] has reported high antioxidant activity in leaf (51.8 mg TAEC/g) than root (6.5 mg TAEC/g) of chicory plants. Whereas, Malik *et al.*, (2017)[28] has reported IC_{50} value 46.81 μg/ml in 80% methanolic extract of leaves of cultivated *C. intybus*. The root and leaf extracts of plant were also showed dose-dependent FRSA increased proportionate to the increase in concentration of the extracts. The present results of the study indicates that plant cultivated at foothill area of Himalayas showed higher antioxidant activity as compared to earlier reports[33] on antioxidant property of chicory leaf. Hence, we concluded that leaf and roots of chicory plant showed very good antioxidant activity may be due to presence of high amount of phenolics, flavonoids, tannins, and ascorbic acid in the leaf part of the plants. Shad *et al*. (2013)[27] also showed the similar tendency in leaves showing good free radical scavenging capacity against DPPH radicals.

3.3. *Acute toxicity study*

A preliminary toxicity study was designed to demonstrate the appropriate safe dose range that could be used for subsequent experiments rather than to provide complete toxicity data on the extract. In acute toxicity study, no significant changes in food intake, body weight and behaviour parameters such as alertness, motor activity, sluggishness, paralysis, breathing, restlessness, diarrhoea, convulsions, coma etc. All rats were found physically active and normal in health as well as neurological behaviors. There was no signs of toxicity and mortality found in oral dose of hydroalcoholic leaf extract of *C. intybus* up to 2 g/kg body weight during observation period of 14 days.

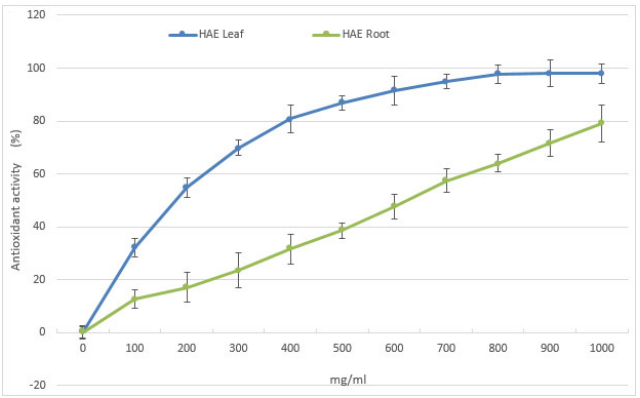

Chart 1: Antioxidant activity or FRSA in leaf and root extracts of *C. intybus*.

3.4. *Effects of C. intybus on hyperglycemic rats*

The various plants traditionally have been used as anti-diabetes, and some have been proven to have hypoglycemic effects. These plants are having some important phytochemicals such as polysaccharides,[34] inulin,[35] terpenoids and tannins,[36] and alkaloids,[37] which are responsible for antidiabetic effect. Administration of STZ in rats caused rapid destruction of pancreatic β-cells, which led to impaired glucose stimulated insulin release and insulin resistance, both of which are marked feature of type II diabetes.[38] Oral hypoglycemic agents and insulin are currently available for treating diabetes, but in present scenario of world population, there is a growing interest in herbal remedies due to side effects associated with the existing drugs.[39] The present investigation indicates the hypoglycemic, anti-lipidemic and liver & kidney protective effects of HA leaf extract of *C. intybus* on STZ induced hyperglycemic rats. The *C. intybus* plant contains several medicinally important compounds such as polysaccharides, coumarins, alkaloids, steroids, terpenoids, inulin, proteins, caffeic acid derivatives, flavonoids, vitamins etc. They

Table 2: Antioxidant activity or FRSA of *C. intybus* by DPPH method

S.No.	Name of Sample	% FRSA	DPPH FRSA (mg Ascorbic acid equivalent/g sample	Avg IC_{50}
1	HAE of *C. intybus* leaf	67.61 at 400 μg/ml	40.91 mg/g	295.78 μg/ml
2	HAE of *C. intybus* root	32.26 at 400 μg/ml	19.52 mg/g	619.94 μg/ml*
3	Std Drug (Ascorbic acid)	82.63 at 20 μg/ml	—	12.10 μg/ml

[Values expressed as mean from three observations. p values <0.05 significant difference between leaf and root]

Table 3: Effect of *C. intybus* on body weight of hyperglycemic rats

S. No.	Name of Group	Weekly Body Weight Change (gm)			Total body weight change (g) in 21 days
		1^{st} week	2^{nd} week	3^{rd} week	
1	Normal control	4	3.6	4.8	12.4
2	Hyperglycemic (Diabetic) control	- 30*	-21*	- 26*	-77*
3	Std Drug (5 mg/kg)	-14.8*#	- 8.2*#	- 0.2*#	- 23.2*#
4	*C. intybus* 50 mg/kg	-16.0*#	- 6.0*#	- 0.4*	- 22.4*#
5	*C. intybus* 200 mg/kg	- 14.2*#	3#	9.2#	-2*#

[Values expressed as mean from five animals in each group. *p values <0.05 significant value vs. control group and #p values <0.05 significant value vs. hyperglycemic control (diabetic animals) group using one way ANOVA followed by post-hoc analysis by Dunnett's t test]

have used in traditional medicine as hepatoprotective, gastroprotective, liver tonic, cholagogue, antioxidant, hypolipidemic, diuretic and also is used as a tonic and anticancer agent.[6,8,10,40]

3.4.1. Effect of C. intybus on food intake of hyperglycemic animals

To evaluation of effect of orally administration of *C. intybus* leaf extract (50 mg/kg and 200 mg/kg) and glibenclamide (5 mg/kg) for 21 days on food intake of STZ induced hyperglycemic animals was cited in Table 4. The Food intake of hyperglycemic (induced by STZ) rats was significantly and continuously increased till the end of the study as compared to normal control (non hyperglycemic) animals. While, food intake of *C. intybus* extract and glibenclamide (5 mg/kg) treated hyperglycemic animals was not significantly change during study period as compared to hyperglycemic animals. Food intake of hyperglycemic animals treated with *C. intybus* extract (50 mg and 200 mg/kg was not increased similar to glibenclamide treated hyperglycemic animals. Hence, increases in food intake of STZ treated hyperglycemic animals was declined by sub-chronic administration of leaf extract of *C. intybus* in hyperglycemic (STZ treated) animals. A researcher has suggested that *C. intybus* may be used for nutritional and pharmaceutical purposes in livestock.[23] Therefore, we can concluded that hydroalcoholic extract *C. intybus* leaf may have important role in appetite of hyperglycemic rats.

3.4.2. Effect of C. intybus on water intake of hyperglycemic animals

The effect of *C. intybus* leaf extract (50 mg/kg and 200 mg/kg, orally for 21 days) and glibenclamide (5 mg/kg, orally for 21 days) on water intake of hyperglycemic (STZ induced) animals is presented in Table 5. The water intake was found significantly high during the study in hyperglycemic (STZ induced) rats as compared to normal control (non STZ treated) rats. While, water intake of *C. intybus* extract (50 mg/kg and 200 mg/kg) treated hyperglycemic animals was not significantly change as compared to non-treated hyperglycemic animals and found similar to standard drug glibenclamide (5 mg/kg) treated animals during study period. Hence, water intake induced by STZ in hyperglycemic animals, was significantly declined by administration of leaf extract of *C. intybus* at both doses (50 and 200 mg). Azay-Milhau (2013)[41] suggests that the whole-plant methanolic extract of chicory positively influences glucose transport, while not inducing adipogenesis at the same time. Therefore, it was concluded that leaf extract of *C. intybus* might have important role in utilization/transportation of glucose in diabetic rats.

3.4.3. Effect of C. intybus on body wt of hyperglycemic animals

The effect of sub-chronic administration of *C. intybus* leaf extract and glibenclamide on body weight of STZ induced hyperglycemic animals is given in Table 3. The body weight of hyperglycemic (STZ induced) rats was significantly and continuously decreased till the end of the study as compared to normal control (non hyperglycemic) rats. Whereas, body weight of *C. intybus* leaf extract (50 mg/kg) and standard drug glibenclamide (5 mg/kg) treated hyperglycemic animals was also decreased up to two weeks and then constant up to third week as compared to hyperglycemic animals. In *C. intybus* extract (200 mg/kg) treated hyperglycemic animals, body weight was

Table 4: Effect of *C. intybus* on food intake of hyperglycemic rats

S. No.	Name of Group	Food Intake (gm)				Avg Food Intake (g) per animal
		1^{st} Day	7^{th} Day	14^{th} Day	21^{st} Day	
1	Normal control	13.88	16.63	17.0	16.6	16.02
2	Diabetic control	17.78	20.75	22.5	21.05	20.52*
3	Std drug (5 mg/kg)	13.75	14.75	17.75	13.63	14.97#
4	*C. intybus* 50 mg/kg	14.33	15.24	17.5	16.25	15.83#
5	*C. intybus* 200 mg/kg	15.0	15.88	17.5	15.33	15.92#

[Values expressed as mean from five animals in each group. *p values <0.05 significant value vs. control group and #p values <0.05 significant value vs. hyperglycemic control (diabetic animals) group using one way ANOVA followed by post-hoc analysis by Dunnett's t test]

Table 5: Effect of *C. intybus* on water intake of hyperglycemic rats

S. No.	Name of Group	Water Intake (ml)				Avg WI (ml) per animal
		1^{st} Day	7^{th} day	14^{th} day	21^{st} Day	
1	Normal control	24.75	26	22	22.5	23.82
2	Diabetic control	29	46.25	35.5	55	41.44*
3	*C. intybus* 50 mg/kg	28	29.5	21.75	21.33	25.15#
4	*C. intybus* 200 mg/kg	31.25	39.5	28	19.25	29.5#
5	Std drug (5 mg/kg)	22.25	37.5	22.5	37	29.82#

[Values expressed as mean from five animals in each group. *p values <0.05 significant value vs. control group and #p values <0.05 significant value vs. hyperglycemic control (diabetic animals) group using one way ANOVA followed by post-hoc analysis by Dunnett's t test]

significantly decreased in first week, but it was recovered in third week. Hence, sub-chronic treatment of leaf extract of *C. intybus* in hyperglycemic animals, initially decreased body weight of hyperglycemic animals was recovered similar to previous study of Abdel-Rahim *et al*., (2016),[42] who has suggested that the improvement in body weight of hyperglycemic animals treated with chicory leaf extract was observed as compared to the hyperglycemic non treated animals. Urias-Silvas *et al*. (2007)[43] has reported that chicory inulin is useful for regulation of appetite. Therefore, we can conclude that hydro-alcoholic extract *C. intybus* leaf might affect digestion of carbohydrates, proteins and lipid and their utilization in hyperglycemic rats.

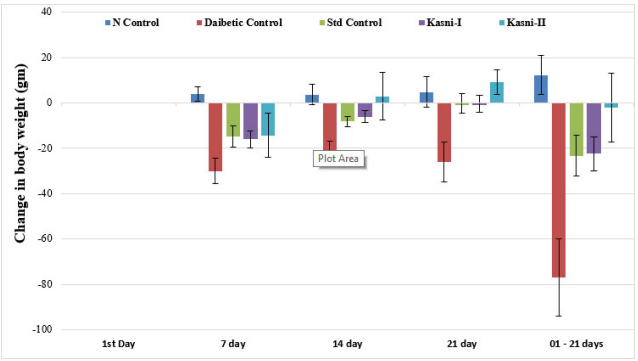

Chart 2: Effect of *C. intybus* on body weight of hyperglycemic animals**.**

3.4.4. Effect of C. intybus on serum glucose of hyperglycemic animals

The effect of sub-chronic administration of *C. intybus* leaf extract (50 mg/kg and 200 mg/kg, orally) and glibenclamide (5 mg/kg, orally) on serum glucose level in blood of STZ induced hyperglycemic animals was evaluated (Table 6). The blood serum glucose level was found significantly high in hyperglycemic rats as compared to normal control animals (no hyperglycemic animals) during the whole study period. While, serum glucose level was significantly decreases in *C. intybus* extract (50 mg/kg and 200 mg/kg) and glibenclamide (5 mg/kg) treated hyperglycemic animals as compared to non treated hyperglycemic animals at the end of the study. In hyperglycemic control animals, level of glucose in blood of rats did not decreased on 21st day as compared to normal control (non hyperglycemic) animals. Hence, increased blood serum glucose in hyperglycemic animals by STZ treatment was significantly declined by sub-chronic administration of both doses (50 mg/kg and 200 mg/kg) of leaf extract of *C. intybus* similar to standard drug glibenclamide (5 mg/kg) treated hyperglycemic animals at the end of the study. Therefore, it was observed that the both doses (50 mg/kg and 200 mg/kg) of hydro-alcoholic leaf extract of chicory plant exhibited hypoglycemic effect in hyperglycemic rats similar to effect of glibenclamide (5 mg/kg) in hyperglycemic rats. This result was similar to previous result of studies of Abdel-Rahim *et al*., (2016)[42] and Mubeen *et al*., (2013).[44] The hypoglycemic effects of *C. intybus* leaf extract in STZ hyperglycemic animals may be through potentiating pancreatic secretion of insulin or enhanced transport/utilization of blood glucose or inhibition of endogenous glucose production.[35] A scientist Ghamarian

Table 6: Effect on glucose and other serological parameters of hyperglycemic rats

S. No.	Parameters	Normal Control	Diabetic Control	Std drug (5 mg/kg)	*C. intybus* 50 mg/kg	*C. intybus* 200 mg/kg
1	GLU (mg/dL) Initial	101.6±13.31	398.6±87.37*	359.3±69.08*	418.0±22.51*	363.3±84.57*
	On last day	126.9±30.70	324±74.6*	132.0±18.52#	170.0±41.94#	143.6±24.68#
2	CHOL (mg/dl)	51.4±10.6	83±9.82*	54±11.38#	63.4±11.88#	57±19.76#
3	TRIG (mg/dl)	47±10.84	99.6±12.34*	46±13.45#	71±10.29#	69.4±8.47#
4	SGOT (U/L)	48.2±13.49	136.4±19.04*	108±13.07#	104±17.90#	90±16.22#
5	SGPT (U/L)	24.6±6.58	50.6±10.85*	26.6±10.35#	33±3.87#	33±6.70#
6	ALP (U/L)	66.4±11.84	169±11.66*	98±17.36#	108±14.3#	80±10.77#
7	TBIL(mg/dl)	0.52±0.26	0.97±0.162*	0.74±0.08#	0.69±0.11#	0.48±0.13#
8	DBIL (mg/dl)	0.25±0.18	0.56±0.15*	0.31±0.02#	0.33±0.05#	0.34±0.08#
9	TP (g/dl)	7.32±0.32	6.22±0.32	6.3±1.21	7.1±0.48	6.7±0.07
10	ALB (g/dl)	3.1±0.32	2.82±0.08	2.82±0.35	3.06±0.36	3.02±0.13
11	BUN (mg/dl)	24.12±5.09	41.02±7.10*	33±7.90#	25±7.10#	32.96±12.67#
12	CRTN (mg/dL)	1.66±0.18	4.6±0.54*	3±0.28#	3.3±0.36#	3.12±0.08#
13	URIC (mg/dl)	1.02±0.16	3.76±0.23*	1.96±0.75#	2.36±0.69#	2.36±0.23#

[Values expressed as mean from five animals in each group. *p values <0.05 significant value vs. control group and #p values <0.05 significant value vs. hyperglycemic control (diabetic animals) group using one way ANOVA followed by post-hoc analysis by Dunnett's t test]

et al. [2012][45] suggested that chicory has insulin-sensitizing activity.

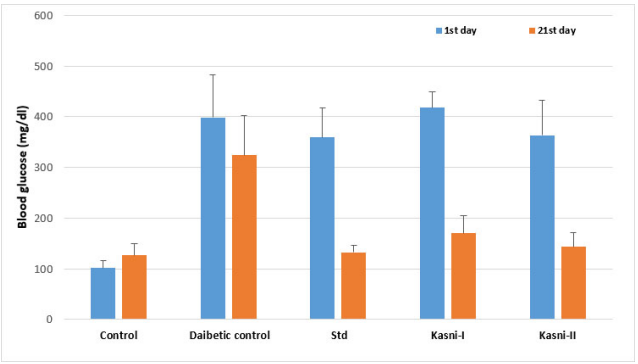

Chart 3: Effect of *C. intybus* on blood serum glucose level of hyperglycemic animals

3.4.5. Effect of C. intybus on lipid profile of hyperglycemic animals

The effect of sub-chronic administration of *C. intybus leaf extract* (50 mg/kg and 200 mg/kg, orally) and glibenclamide (5 mg/kg, orally) on lipid profile of hyperglycemic animals is presented in Table 6. The levels of blood serum cholesterol and triglycerides were found significantly high in hyperglycemic rats as compared to normal control animals (no hyperglycemic animals) on last (21st) day of the study. In *C. intybus* extract (50 mg/kg and 200 mg/kg) treated hyperglycemic animals, levels of blood serum cholesterol and triglycerides were significantly low as compared to hyperglycemic animals and the result was observed similar to glibenclamide (5 mg/kg) treated hyperglycemic animals. Therefore, it was indicates that the hydro-alcoholic extract of chicory leaf exhibited hypolipidemic effect in hyperglycemic similar to previous study of Abdel-Rahim *et al*., (2016)[42] and Mubeen *et al*., (2013).[44] Diabetes is associated with hyperlipidemia due to destruction of β-cells leads to depletion of plasma insulin. Insulin activates enzyme lipoprotein lipase, which hydrolyzes triglyceride under normal conditions. Diabetogenic agents significantly increase the cholesterol and TG levels.[46] The significant control of plasma lipid levels suggests that the chicory leaf extract may produce its action by improving insulin secretion. A study on 150 type 2 diabetes mellitus patients confirmed that ingestion of *C. intybus* seed extract has significantly decreased inflammation, oxidative stress, and hypertriglyceridemia.[47] Cholesterol synthesis may be decreased via the action of chicory inulin that inhibits hydroxymethyl glutaryl-CoA reductase.[48] Hence, we can conclude that increases levels of blood serum cholesterol and triglycerides in STZ-hyperglycemic animals, were significantly decreased by treatment of leaf extract of *C. intybus* (50 mg/kg and 200 mg/kg).

3.4.6. Effect of C. intybus on liver functions of hyperglycemic animals

The serum levels of SGOT, SGPT, Total bilirubin and direct bilirubin were found significantly high in blood of hyperglycemic rats as compared to normal control animals (no hyperglycemic animals) (Table 6). While, blood serum levels of SGOT, SGPT, Total bilirubin and direct bilirubin were significantly decreased in hyperglycemic animal streated with *C. intybus* extract (50 mg/kg and 200 mg/kg) and glibenclamide (5 mg/kg) as compared to non treated hyperglycemic animals. Hence, increased levels of SGOT, SGPT, total bilirubin and direct bilirubin in blood serum of hyperglycemic animals were significantly reduced by sub-chronic administration of both doses (50 mg/kg and

200 mg/kg) of leaf extract of *C. intybus* similar to standard drug glibenclamide treated hyperglycemic animals. This study was support by Abdel-Rahim *et al*., (2016),[42] who has reported that the activities of AST, ALT and LDH were observed significant low in the diabetic rats administrated balanced diet with 20% of either chicory leaves in comparison to diabetic rats which feed on either high fat diet or balanced diet.

No significant changes were observed in the blood serum levels of total proteins and albumins in any treated hyperglycemic animal with *C. intybus* and glibenclamide as compared to control (non hyperglycemic) animals. Therefore, it was concluded that the hydro-alcoholic extract of chicory leaf exhibited hepato-protective effects in STZ hyperglycemic animals.

3.4.7. Effect of C. intybus on kidney functions of hyperglycemic animals

The levels of uric acid, creatinine and BUN in blood serum were found significantly high in hyperglycemic rats as compared to normal control animals (no hyperglycemic animals) on 21st day of the study. Whereas, *C. intybus* extract (50 mg/kg and 200 mg/kg) and glibenclamide (5 mg/kg) treated hyperglycemic animals, levels of uric acid, creatinine and BUN in blood of animals were significantly low as compared to hyperglycemic animals (Table 6). Hence, increased levels of uric acid, creatinine and BUN in blood serum of STZ- hyperglycemic animals were significantly reversed by sub-chronic administration of both doses (50 mg/kg and 200 mg/kg) of leaf extract of *C. intybus* similar to glibenclamide (5 mg/kg, for 21 days) treated hyperglycemic animals. This result was found similar to result of the study of Abdel-Rahim *et al*., (2016),[42] who has reported that the serum levels of creatinine and urea were significant decrease in the hyperglycemic rats administrated balanced diet with 20% of chicory leaves. Therefore, it was indicated that the hydroalcoholic extract of chicory leaf enhanced kidney functions in hyperglycemic rats.

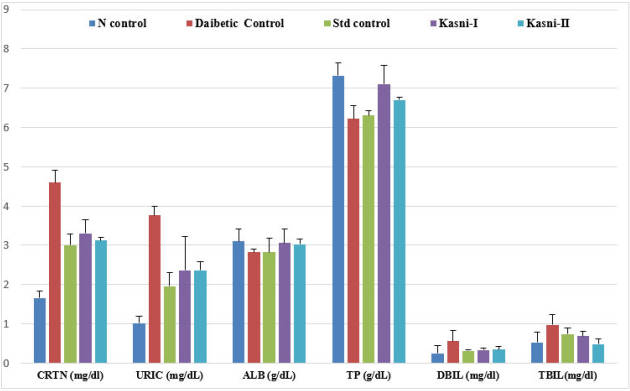

Chart 4: Effect of *C. intybus* on blood biochemical parameters of hyperglycemic animal

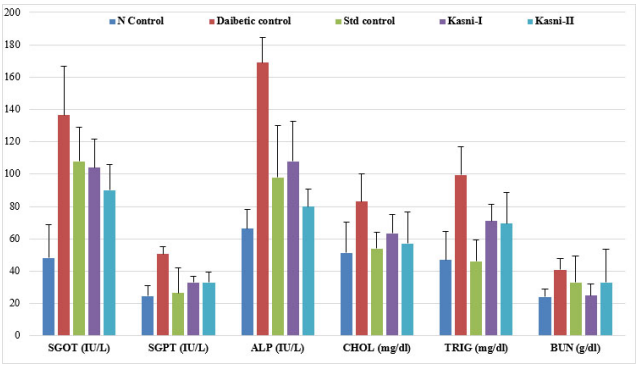

Chart 5: Effect of *C. intybus* on blood biochemical parameters of hyperglycemic animals

4. Conclusion

In view of above the result we conclude that the root and leaf parts of *C. intybus* locally cultivated in foothill area of Uttarakhand are found rich in total carbohydrate, proteins and antioxidant compounds like phenolics, tannins, ascorbic acid, and flavonoid and having antidiabetic, kidney and liver protective properties, but both parts are having significant difference bio-chemically and medicinally. The root part of the plant has high amount of carbohydrates and proteins than leaf part, while leaf part has high amount of antioxidant compounds such as phenolics, tannins, ascorbic acid, and flavonoid than root part. The *C. intybus* has also very good antioxidant properties that are high in leaf as compared to root. Hence, leaf part may be more beneficial in oxidative damaged related disorders. While, in metabolism related disorders, root part might be more effective than leaves.

Results of animal trials on hydro-alcoholic leaf extract of *C. intybus* have shown very good hypoglycemic properties that also improve the liver and kidney functions in hyperglycemic animals. The body weight, food and water intake of hyperglycemic animals were regulated at normal level by continued administration of leaf extract. It might regulate metabolism via enhance the sensitivity/production of insulin. It also suggest that further investigation to identify the mechanism action of active principle of the plant for hypoglycemic activity and improvement of liver and kidney functions to be required.

5. Source of Funding

DRDO.

6. Conflicts of Interest

The author declares that there is no Conflict of interest.

References

1. Halliwell B, Gutteridge JM. Oxygen toxicity, oxygen radicals, transition metals and diseases. *Biochem J*. 1984;219(1):1–14. doi:10.1042/bj2190001.
2. Maxwell SR. Prospect for the use of antioxidant therapies. *Drugs*. 1995;49(3):345–61. doi:10.2165/00003495-199549030-00003.
3. Rice-Evans CA, Miller NJ, Paganga G. Structure antioxidant activity relationships of flavonoids and phenolic acids. *Free Radic Biol Med*. 1996;20(7):933–56. doi:10.1016/0891-5849(95)02227-9.
4. Prior RL, Cao G. Variability in dietary antioxidant related natural product supplements: The need for methods of standardization. *J Am Nutraceutical Assoc*. 1999;2:46–56.
5. Dhawan BN. Decade of the Brain: India/USA Research in Mental Health and Neurosciences. SH K, RS M, GV C, editors. Rockville: National Institute of Mental Health; 1995. p. 197–202.
6. Bais HP, Ravishankar GA. Cichorium intybus L. cultivation, processing, utility, value addition and biotechnology, with an emphasis on current status and future prospects. *J Sci Food Agric*. 2001;81(5):467–84. doi:https://doi.org/10.1002/jsfa.817.
7. Van Wyk BE, Oudtshoorn B, Van Gericke N. Medicinal Plants of South Africa. Pretoria, South Africa: Briza Publications; 1997. doi:10.4102/sajs.v105i7/8.120.
8. Koesis I. Effects of chicory on pancreas status of rats in experimental dyslipidemia. *Acta Biologica Szegediensis*. 2003;47(1-4):143–6.
9. Saini M, Khan AA, Bala M, Abdin MZ, Farooqi H. Development of a validated HPTLC method for quantification of esculin in different fractions of Cichorium intybus leaf extract. *Int J Pharm Pharm Sci*. 2014;6(1):278–82.
10. Esmail A. Medical importance of Cichorium intybus - A review. *IOSR J Pharm*. 2016;6(3):41–56.
11. Sadasivam S, Manickam A. Determination of total carbohydrate by anthrone method. In: Biochemical methods. New Delhi: New Age International (P) Limited Publishers; 2008. p. 7–8.
12. Sadasivam S, Manickam A. Protein estimation by Lowry's method. In: Biochemical methods. New Delhi: New Age International (P) Limited Publishers; 2008. p. 51–53.
13. Hatano T, Edamatsu R, Hiramatsu M, Mori A, Fujita Y, Yasuhara T, et al. Effects of interaction of tannins with co-existing substances VI. Effects of tannins and related polyphenols on superoxide anion radical and on DPPH radical. *Chem Pharm Bull*. 1989;37(5):2016–37. doi:10.1248/cpb.38.1224.
14. Tanaka M, Kuei CW, Nagashima Y, Taguchi T. Application of antioxidative maillrad reaction products from histidine and glucose to sardine products. *Nippon Suisan Gakkaishi*. 1998;54:1409–14. doi:https://doi.org/10.2331/suisan.54.1409.
15. Sadasivam S, Manickam A. Protein estimation by Lowry's method. In: Biochemical methods. New Delhi: New Age International (P) Limited Publishers; 2008. p. 51–53.
16. Ponnusamy K, Mohan M, Nagaraja HS. Protective antioxidant effect of Centella asiatica bioflavonoids on lead acetate induced neurotoxicity. *Med J Malaysia*. 2008;63:102.
17. Sadasivam S, Manickam A. Tannins. In: Biochemical methods. 2008;p. 205–6.
18. Sadasivam S, Manickam A. Ascorbic Acid. In: Biochemical methods. New Delhi: New Age International (P) Limited Publishers; 2008. p. 193–4.
19. Hatano T, Edamatsu R, Mori A, Fujita Y, Yasuhara E. Effect of tannins and related polyphenols on superoxide anion radical and on DPPH radical. *Chem Pharm Bull*. 1988;37:2016–2037.
20. Meena H, Pandey HK, Pandey P, Arya MC, Ahmed Z. Evaluation of antioxidant activity of two important memory enhancing medicinal plants Baccopa monnieri and Centella asiatica. *Indian J Pharmacol*. 2012;44(1):114–21. doi:10.4103/0253-7613.91880.
21. OECD (Organization for Economic Cooperation and Development) . Acute Oral Toxicity-Acute Toxic Class Method; 1996. Guidelines for Testing of Chemicals,Guidelines 423.
22. Arunachalam K, Parimelazhagan T. Antidiabetic activity of Ficus amplissima Smith. Bark extract in streptozotocin induced diabetic rats. *J Ethnopharmacol*. 2013;147(2):302–312. doi:10.1016/j.jep.2013.03.004.
23. Saeed M, El-Hack MA, Alagawany M, Arain MA, Arif M, Mirza MA, et al. Cichorium intybus) Herb: Chemical Composition, Pharmacology, Nutritional and Healthical Applications. *Int J Pharmacol*. 2017;13(4):351–60. doi:10.3923/ijp.2017.351.360.
24. Milala J, Grzelak K, Krol B, Juskiewicz J, Zdunczyk Z. Composition and properties of chicory extracts rich in fructans and polyphenols. *Pol J Food Nutr Sci*. 2009;59(1):35–43.
25. L'homme C, Peschet JL, Puigserver A, Biagini A. Evaluation of fructans in various fresh and stewed fruits by high-performance anion-exchange chromatography with pulsed amperometric detection. *J Chrom A*. 2001;920(1-2):291–8. doi:10.1016/s0021-9673(00)01262-0.
26. Razali N, Razab R, Junit M, S, Aziz A, A. Radical scavenging and reducing properties of extracts of cashew shoots Anacardium occidentale. *Food Chem*. 2008;111(1):38–44. doi:http://dx.doi.org/10.1016/j.foodchem.2008.03.024.
27. Shad MA, Nawaz H, N RTI. Determination of some biochemicals, phytochemicals and antioxidant properties of different parts of cichorium intybus l.: a comparative study. *J Animal Plant Sci*. 2013;23(4):1060–6.
28. Malik B, Pirzadah TB, Tahir I, Rehman RU. Chemo-profiling, Antioxidant potential and Ionomic analysis of Cichorium intybus L. *Pharmacog J*. 2017;9(6):917–28. doi:10.5530/pj.2017.6.144.
29. Saggu S, Sakeran MI, Zidan N, Tousson E, Mohan A, Rehman H, et al. Ameliorating effect of chicory (Cichorium intybus L.) fruit extract against 4-tert-octylphenol induced liver injury and oxidative stress in male rats. *Food Chem Toxicol*. 2014;72:138–84. doi:10.1016/j.fct.2014.06.029.
30. Kessler M, Ubeaud G, Jung L. Anti and pro-oxidant activity of rutin and quercetin derivatives. *J Pharm Pharmacol*. 2003;55(1):131–42. doi:10.1211/002235702559.
31. Cook NC, Samman S. Flavonoids-chemistry, metabolism, cardioprotective effects, and dietry sources. *Nutr Biochem*. 1996;7:66–76.
32. Reed JD, Soller H, Woodward A. Fodder tree and straw diets for sheep: intake, growth, digestibility and the effects of phenolics on nitrogen utilization. *Anim Feed Sci Technol*. 1990;30(1-2):39–50.
33. Abbas ZK, Saggu S, Sakeran MI, Zidan N, Rehman H, Ansari AA, et al. Phytochemical, antioxidant and mineral composition of hydroalcoholic extract of chicory (Cichorium intybus L.) leaves. *Saudi J Biol Sci*. 2015;22(3):322–6. doi:10.1016/j.sjbs.2014.11.015.
34. Tomoda M, Shimada K, Konno C, Hikino H. Structure of panaxan B, a hypoglycaemic glycan of Panax ginseng roots. *Photochem*. 1985;24(10):2431–3. doi:10.1055/s-2007-969758..
35. Azorin-Ortuno M, Urban C, Ceron JJ, Tecles F, Allende A, Barberan FA, et al. Effect of low inulin doses with different polymerisation degree on lipid metabolism, mineral absorption, and intestinal microbiota in rats with fat-supplemented diet. *Food Chem*. 2009;113:1058–65.
36. Reher G, Slijepcevic M, Krans L. Hypoglycemic activity of triterpenes and tannins from Sarcopoterium spinosum and two Sanguisorba species. *Planta Medica*. 1991;57(2):57–68.
37. Schimizu M, Ito T, Rshima S, Mayashi T, Arisawa M, Morita-Kurokowa S, et al. Inhibition of lens aldose reductase by flavonoids. *Phytochem*. 1984;23:1885–8.
38. Farswan M, Mazumder PM, Parcha V. Modulatory effect of an isolated compound from Syzygium cumini seeds on biochemical parameters of diabetes in rats. *Int J Green Pharm*. 2009;3:128–33.
39. Holman RR, Turner RC, Pickup J, Williams G. Textbook of Diabetes. Oxford: Blackwell Science; 1991.
40. Liu H, Wang Q, Liu Y, Chen G, Cui J. Antimicrobial and Antioxidant Activities of Cichorium Intybus Root Extract Using Orthogonal Matrix Design. *J Food Sci*. 2013;78(2):258–63. doi:10.1111/1750-3841.12040.
41. Azay-Milhau J, Ferrare K, Leroy J, Aubaterre J, Ournier M, Lajoix A.): A Comparative in Vitro Study with the Effects of Caffeic and Feruli Acids. *J Ethnopharmacol*. 2013;150:755–60.

42. Abdel-Rahim E, Rashed MM, El-Hawary ZM, Abdelkader MM, Kassem SS, Rasha SM, et al. Anti-diabetic Effect of Cichorium intybus Leaves and Plantago ovate Seeds in High Fat Diet-streptozotocin Induced Diabetic Rats. *J Food Nutr Res*. 2016;4(5):276–81. doi:10.12691/jfnr-4-5-2.
43. Urias-Silvas JE, Cani PD, Delmee E, Neyrinck A, Lopez MG, Delzenne MN, et al. Physiological effects of dietary fructans extracted from Agaves tequilana and Dasylirion spp. *Br J Nutr*. 2007;99(2):254–61. doi:10.1017/S0007114507795338..
44. Mubeen F, Pandey H, K D. Anti-Diabetic Activity of Methanolic extract of chicory roots in streptozocin induced diabetic rats. *Int J Pharm*. 2013;3(1):211–217.
45. Ghamarian A, Abdollahi M, Su X, Amiri A, Ahadi A, Nowrouzi A, et al. Effect of chicory seed extract on glucose tolerance test (GTT) and metabolic profile in early and late stage diabetic rats. *DARU J Pharm Sci*. 2012;20(1):56–64. doi:10.1186/2008-2231-20-56.
46. Bothayna MA. Production of bakery products using two sources of inulin. *Ann Agric Sci Moshtohor*;38(1):361–78.
47. Chandra K, Jain V, Jabin A, Dwivedi S, Joshi S, Ahmad S. Effect of Cichorium intybus Seeds Supplementation on the Markers of Glycemic Control, Oxidative Stress, Inflammation, and Lipid Profile in Type 2 Diabetes Mellitus: A Randomized, Double-Blind Placebo Study. *Phytother Res*. 2020;34:1609–1618.
48. M AEMN. Hepatoprotective effect of feeding celery leaves mixed with chicory leaves and barley grains to hypercholesterolemic rats. *Pharmacog Magaz*. 2020;7(26):151–7.

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