Pharmacognostical Studies and Pharmacological Investigations for Anti-diabetic Activities of *Taraxacum officinale* Weber (Dandelion)

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***Abstract- Taraxacum officinale* (dandelion) contains active pharmaceutical agents with various medicinal activities. This research work was an attempt to establish scientific protocols to perform pharmacological investigation / research on *Taraxacum officinale* for antidiabetic effect against STZ induced diabetes in rats. Plant parts were analysed pharmacognostically and authenticated showed the presence of resin, glycosides, phenolic compounds, flavanoids, steroids, and amino acids. High total phenolic content and total flavonoid content were found in the EETOL extract then EETOR extract. *In-vivo* pharmacological investigation for anti-diabetic activity of EETOL / EETOR against streptozotocin induced diabetes was performed and it was found that both EETOL-B extract and EETOL-A extracts produced significant anti-diabetic effects. EETOL-B extract lowered the blood glucose level, LDL and VLDL significantly and produced better action than EETOL-A. Anti-diabetic potential was comparable with glipizide (Standard drug). Extract EETOL-B repaired beta cells, revitalized damaged cells, extracts rejuvenates cells and induce insulin secretion. Finally, much more elaborated pharmacological research is recommended.**

Keywords: **Anti-diabetic, dandelion, glipizide, lipoproteins, Oral glucose tolerance test, quercetin, total phenolic content, total flavonoid content, streptozotocin.**

Introduction

Diabetes mellitus (DM) is a metabolic disorder (endocrine) caused due to impaired insulin secretion, insulin action, or both. Herbal medicine is currently enjoying a revival in popularity in the west and in many parts of the world. Now a day, various Ayurvedic formulations / herbal formulations / phyotoformulations are commercially available for the prevention and treatment of type-2 diabetes.

WHO (2016) has made the prediction that 371 million will be suffering from diabetes in 2030 and India will become Diabetics Capital of the world (95% of total diabetic population is suffering with NIDDM). Allopathic drugs used in diabetes include sulphonylureas, thiazolidinedione, glucagon-like peptide-1 analogs, biguanides, dipeptidyl peptidase-IV inhibitors and insulin. Overdoses and prolonged therapy of these drugs resulted in side effects like excess sweating, slurred talk, tachycardia, seizures, and daze state, clouded vision, hypoglycaemia, weight gain, anorexia and hepatic & renal dysfunction **(Liu *et al*., 2004)**.

Mukherjee *et al*., 2009, illustrated that various medicinal plants phyoto-formulations are clinically proven as anti-diabetic and their use is strengthened due to their promptly accessibility, complete cure and minimal side effects. There are more than 500 anti-diabetic medicinal plants which include *Gymnema sylvestre, Momordica charantia, Aegle marmelos, Trigonella foenum, Syzygium cumini, Combretum micranthum, Tinospora cordifolia, Berberis aristata, Curcuma longa, Elephantopus scaber, Aegle marmelos, Pterocarpus marsupium, Glycyrrhiza glabra, Liriope spicata, Azadirachta indica, Commiphora wighti, Syzygium cumini, Phyllanthus emblica, Ficus glomerata, Terminalia chebula, Asparagus racemosus, Tribulus terrestris, Piper nigrum, Plumbago zeylanica, Picrorrhiza kurroa,* etc.

Grover *et al*., 2002 revealed that in India unconventional medicines / natural medicines are used to cure diabetes. World wellbeing association has likewise prescribed the assessment of conventional plant separates treatment for diabetes.

Damylo *et al*., 1984 illustrated that *Taraxacum officinale* Weber (called "dandelion"; "lion's tooth"; Asteraceae (Compositae), perennial herb / weed.

Vašut *et al*., 2015 reported that the genus *Taraxacum* (30–57 varieties ; many microspecies; divided into 9 sections; dandelion : plant's jagged-edged leaves / toothed leaves; 3–35cm height; single yellow flowers; florets).

Koo *et al*., 2004 summarised that TO has terpenoid; sterol (taraxacin; taraxacerin); terpene/sterol (taraxasterol); free sterols (sitosterin, stigmasterin, and phytosterin). Further, **Ali *et al*., 1989** reported that dandelion contains vitamins A, B, C and D; iron. It contains flavonoids, phenolics, coumarins, sterols, sequiterpenes, high beta-carotene, vitamin C and iron (more iron and calcium than spinach) as main constituents and shown various pharmacological activities. *T. officinale* is commercially cultivated and used as a traditional medicine and food (soup/salad) in Europe, North America, and China.

Figure 1: Photograph of dandelion with flowers, stems, and leaves.


Figure 2: Dandelion Edible young leaves and flower (right).


Figure 3: Dandelion flower (left) and ripe fruits (right).

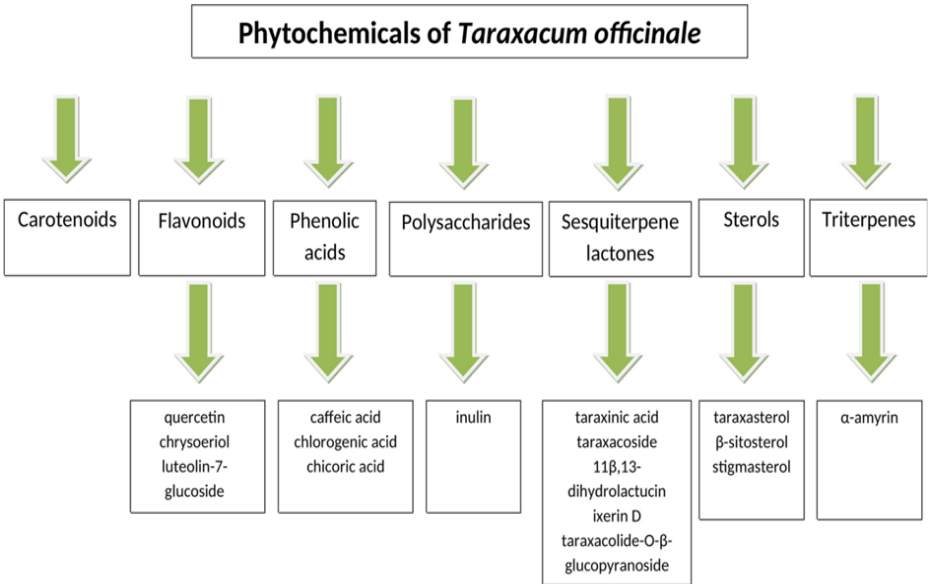

Figure 4: Phytochemicals present in *Taraxacum officinale*.

Objectives

Modaresi, 2012 summarised that dandelion is nontoxic and possess anti-inflammatory and diuretic properties. But, surprisingly, no significant pharmacological investigations have been reported in literature for anti-diabetic activities on dandelion leaves, aerial parts and roots against streptozotocin (STZ). So, this pharmacognostical and phramacological research work was undertaken on *Taraxacum officinale* (dandelion) herb with following objectives:

- ❖ Phytochemical screening and physio-chemical evaluation of ethanolic extract of *T. officinale* leaves (EETOL), ethanolic extract of *T. officinale* aerial parts (EETOP) and ethanolic extract of *T. officinale* roots (EETOR),
- ❖ HPLC chromatography of various extracts of dandelion,
- ❖ Anti-diabetic activity of EETOP, EETOL and EETOR against STZ.
- ❖ Comparison of anti-hyperglycemic effects of dandelion extracts with glipizide.

Methodologies / Testing Technologies Used

(i) Various research papers were scientifically reviewed for literature search, summarised, assessed, statistically analysed to establish research protocols.

(ii) Phytochemical analysis techniques (chromatographic methods, IR, UV etc.) were used for qualitative/quantitative analysis.

(iii) Blood glucose level analysis were performed for anti-diabetic activity.

Procurement & Authentication of Dandelion Plant Material

Fresh entire plants of *Taraxacum officinale* Weber (dandelion) were harvested and collected from Medicinal Plant Garden of the IEC-GI campus in January 2020. Dandelion plants were washed to clean, dried under shade and finally coarsely pulverised in grinder. Dandelion parts were scientifically analysed by pharmacognostical methods for its authentication. Phytochemical screening was done to detect PPMs and SPMs and herbarium specimens were also deposited.

Phytochemical Screening of Dandelion Plant Material

Extracts of dandelion were subjected to preliminary phytochemical screening using standard procedures described by **Sofowora (1993); Khandelwal (2008);** (Table 1):

Table 1: List of qualitative chemical tests.

PPMs / SPMs	Test
Alkaloid	a. Mayer's Reagent Test;
	b. Dragendorff's Reagent Test;
	c. Hager's Reagent Test;
	d. Wagner's Reagent Test;
Carbohydrate	Molisch's Reagent Test;
Reducing Sugar	a. Fehling's Reagent Test;
	b. Benedict's Reagent Test;
Saponins	a. Foam Test;
	b. Forth Test;
Phytosteroids	a. Salkowski's Test;
	b. Libbermann Buchard's Test;
Phenols	Ferric Chloride Test;
Tannins	Lead Acetate Reagent Test;
Flavonoids	a. Alkaline Reagent Test;

	b. Lead Acetate Test;
Cardiac Glycosides	Killer-KIllani Test;
Proteins & Amino Acids	a. Millon's Reagent Test;
	b. Biuret's Test;
	c. Ninhydrin Reagent Test;
Terpenoids	Salkowski's Test;
Fixed Oils and Fats	a. Spot Test;
	b. Saponification Test;
Gum and Mucilage	Ruthenium Red Solution Test
Glycosides	Liebermann's Test;

Physico-chemical Parameters Analysis

In the experiment freshly procured, washed, air-dried and pulverised / powdered aerial parts, leaves and roots of dandelion were subjected to physico-chemical analysis for parameter like foreign matter, extractive values (alcohol / water), swelling index, ash value (acid insoluble / water soluble), fluorescence analysis in various solvents (normal light / UV light), and loss on drying (LOD) etc.

Preparation of EETOP, EETOL and EETOR Extract of Dandelion

Dandelion shade dried and coarsely pulverized aerial parts, leaves, and roots (1000 gm each) were Soxhlet extracted with crude ethanol (80%; Soxhletion; separately) for 16 hours, filtered, distilled, vacuum evaporated and finally lyophilized.

HPLC Analysis of EETOL, EETOP and EETOR Extracts

System Used: HPLC – diode array detector (DAD) - electrospray ionization (ESI) - tandem mass spectrometry (6410B HPLC-DAD-ESI-MS/MS; Agilent Technologies).
Mobile Phase: Acetonitrile (eluent A) with formic acid (1.0% v/v, eluent B).
Gradient Elution Flow Rate: 1 ml/min.
Injection volume: 10 µl.
Detection wavelength: 280 nm & 320 nm.
ESI source was kept at 110˚C with desolvation temperature at 400˚C. Nebulizer pressure, fragmentor voltage, and capillary voltage were maintained at 35 psi, 135 V, and 3,000 V, respectively and spectra were recorded in the negative ionization mode over the m/z range of 100-1,000 Da.

Anti-diabetic Activity of EETOP, EETOL and EETOR against Streptozotocin

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Grouping of Animals

Table 2 : Groups of animals for anti-diabetic assessment.

Group	Treatment with Dose	Animals
I	Normal	6
II	Toxic Control : STZ : 100 mg/kg i.p.	6
III	STZ (100 mg/kg; 07 days) + EETOL - 200 mg/kg p.o. for 03 weeks	6
IV	STZ (100 mg/kg; 07 days) + EETOL - 400 mg/kg p.o. for 03 weeks	6
V	STZ (100 mg/kg; 07 days) + EETOP -200 mg/kg p.o. for 03 weeks	6
VI	STZ (100 mg/kg; 07 days) + EETOP -400 mg/kg p.o. for 03 weeks	6
VII	STZ (100 mg/kg; 07 days) + EETOR - 200 mg/kg p.o. for 03 weeks	6
VIII	STZ (100 mg/kg; 07 days) + EETOR -400 mg/kg p.o. for 03 weeks	6
IX	STZ: 100 mg/kg for 07 days - Standard Glipizide for 21 days	6

(i) Effect of "EETOL", EETOP and "EETOR" on Glucose level

Animals were treated with EETOL, EETOP and EETOR and the normal group received water. Animals were anaesthetised with Ketamine+Xylazine ((80 mg/kg+10 mg/kg i.p.) and blood was withdrawn from retro orbital plexus and blood glucose levels were estimated with Glucometer or by GOD/POD method at 1, 2, and 3 h.

(ii) Effect of EETOL, EETOP and EETOR on "Oral Glucose Tolerance Test"

Oral glucose tolerance test (OGTT) was estimation was carried out in overnight fasted normal rats. Animals were administered EETOL, EETOP and EETOR (400 mg/kg). Glucose (2 g/kg b.w.) was given orally (60 min after dosing) and glucose levels were estimated.

(iii) Comparison of anti-diabetic effects of EETOL, EETOP, EETOR with Glipizide

STZ in 0.1M citrate buffer (pH 4.5) was given to animals and glucose levels were analyzed after 07 days. Animals were treated with EETOL, EETOP and EETOR (Group III-VIII) and Glipizide (Standard, Group IX) as prescribed and after 21 days blood glucose levels were analysed.

Determination of Effect of EETOL, EETOP and EETOR on Lipid Profile in diabetic rats
Total cholesterol : Cholesterol estimated with Agappe Liqui CHEK kit (CHOD –PAP method.

Formula :

$$\text{Cholesterol conc. (mg/dl)} = \frac{\text{Absorbance of sample}}{\text{Absorbance of standard}} \times 200$$

Where 200 is the standard concentration

Serum Triglyceride
Enzymatic determination of triglycerides based on the following reactions:

$$\text{Triglycerides} + H_2O \xrightarrow{\text{Lipoprotein lipase}} \text{Glycerol} + \text{fatty acid}$$

$$\text{Glycerol} + ATP \xrightarrow{\text{Glycerol kinase}} \text{Glycerol} - 3\text{-Phosphate} + ADP$$

$$\text{Glycerol} - 3\text{-Phosphate} + O_2 \xrightarrow{\text{Glycerol Phosphate Dehydrogenase}} \text{Dihydroxyacetone Phosphate} + H_2O_2$$

$$H_2O_2 + 4\text{-Aminophenazone} + p\text{-Chlorophenol} \xrightarrow{\text{Peroxidase}} \text{Quinone} + H_2O$$

Estimation of Triglycerides (mg /dl)

$$\text{Triglycerides in (mg /dl)} = \frac{\text{Absorbance of sample}}{\text{Absorbance of standard}} \times 200$$

Where, 200 is the standard concentration

Results and Discussions
Morphology of dandelion leaf showed spatula-like leaf (lion's-tooth), oblanceolate / oblong / obovate, length: 2.0–17.7 in; width 0.39–3.94 inch with shallow, lobed margin. Besides, morphology of flower of dandelion florets (rosette; 40 to over 100 per head), ligulate and bisexual, 12-18 segments. The procured plant drug was authenticated as dandelion with herbarium specimen number IEC/Pharm/Herb/2020/102.
Qualitative analysis of dandelion aerial parts, leaves and roots showed the presence of PPMs and SPMs like glycosides; alkaloids; amino acids; tannins; saponins; flavanoids; steroids; phenolics; reducing sugars; anthraquinones.

Table 3 : Physicochemical analysis of aerial parts, leaves and roots of dandelion.

Quantitative parameter	Values obtained (%) w/w		
	Dandelion Aerial Parts	Dandelion Leaves	Dandelion Roots
Alcohol Soluble Extractive Value (ASEV)	6.82±0.46	7.94±0.72	5.26±0.32
Water Soluble Extractive Value (WSEV)	10.42±0.84	12.62±0.46	7.86±0.42
Total Ash Value (TAV)	4.26± 0.18	4.68± 0.24	3.82± 0.20
Acid Insoluble Ash Value (AIAV)	1.96±0.06	2.26±0.08	1.42±0.04
Water Soluble Ash Value (WSAV)	2.42±0.06	2.92±0.08	2.12±0.04
Sulphated Ash Value (SAV)	4.82±0.14	6.12±0.14	3.78±0.16
Swelling Index (SI)	NIL	NIL	NIL
Loss on Drying (LOD)	6.32±0.04	6.68±0.04	5.76±0.04
Foreign Matter Content (FMC)	0.96%	0.78%	0.56%

Table 4 : Physicochemical parameters of leaves of dandelion.

Solvent used	Observation	
	UV light (200 nm)	UV light (400 nm)
Benzene	Green	Reddish Brown
Acetone	Green	Orange
Ethyl acetate	Yellowish Green	Orange
Chloroform	Green	Creamish Green
H_2O (Distilled)	Green	Blackish Brown
Dil. HNO_3 Soln.	Green	Bluish Green
Dil. H_2SO_4 Soln.	Green	Dark Green
Conc. HCL Soln.	Yellowish Green	Yellowish Brown
Aq. NaOH solution	Green	Brown
NaOH in CH_3OH	Light Green	Yellowish Brown

Physico chemical constant parameters were establish the purity and quality of the drug. Ash values indicated the inorganic salts or any extraneous matter (oxidation of the component of the crude drug; include carbonate, phosphates, silicates, and silica). Low ash value indicated drug was free from contamination. Low acid-insoluble ash values indicated that the drug was free from siliceous matters or sand. Water soluble ash value indicated presence of water soluble salts whereas sulphated ash showed oxides were converted into sulphates. Solvent extractive values depend upon the presence of phyto-constituents and useful for the determination of exhausted and adulterated drug (any addition of exhausted material to the pure drug will be reflected by lowering of these extractive values). LOD was performed to assess moisture content (percentage) as it cause enzyme hydrolysis, growth of microbes and leads to deterioration of PPMs and SPMs.

Practical yield EETOL, EETOP and EETOR extracts were 1.86%, 1.54% and 1.12% respectively. Different concentrations of EETOL, EETOP and EETOR extracts (200 / 400 mg in 1 % carboxymethylcellulose) were used in pharmacological studies.

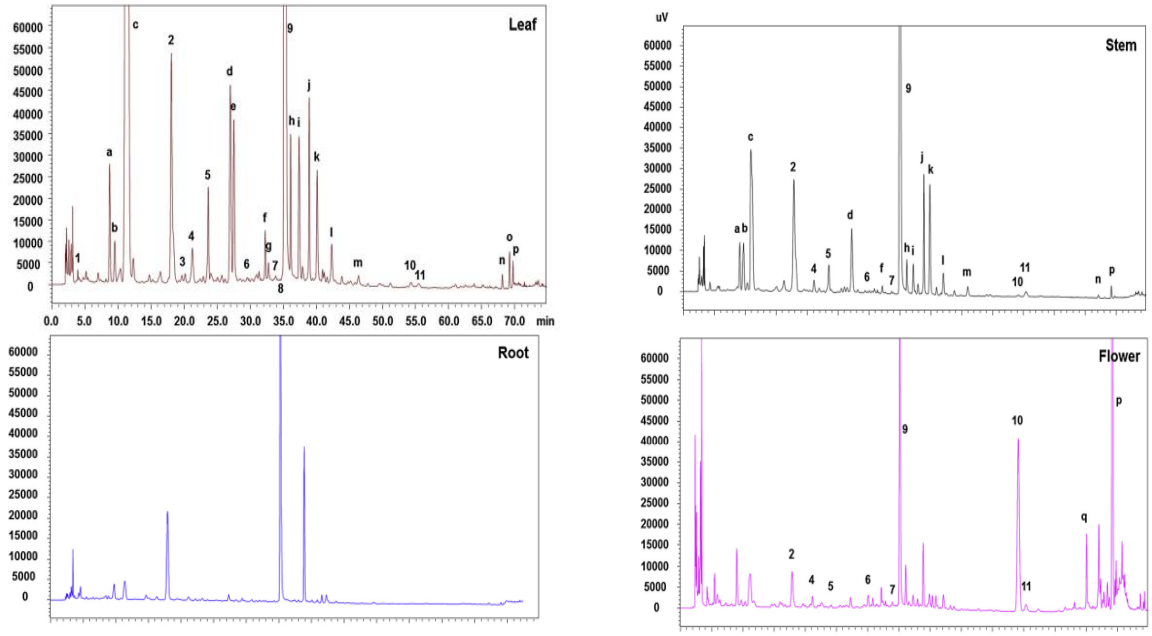

Figure 5: Dandelion EETOL, EETOR, and EETOP HPLC chromatographs. (1. gallic acid; 2. chlorogenic acid; 3. vanillic acid; 4. caffeic acid; 5. syringic acid; 6. 4-coumaric acid; 7. ferulic acid; 8. Rutin; 9. chicoric acid; 10. Quercetin; 11. trans-cinnamic acid.)

Table 5 : SPMs in EETOL, EETOR, and EETOP HPLC chromatographs.

S. No.	SPMs in HPLC Leaves, Stem, flower and roots of Dandelion			
	Leaves	Stem	Flower	Roots
1.	Gallic acid	---	---	---
2.	Chlorogenic acid	Chlorogenic acid	Chlorogenic acid	Chlorogenic acid
3.	Vanillic acid	---	---	Vanillic acid
4.	Caffeic acid	Caffeic acid	Caffeic acid	Caffeic acid
5.	Syringic acid	Syringic acid	Syringic acid	Syringic acid
6.	4-coumaric acid	4-coumaric acid	4-coumaric acid	luteolin
7.	Ferulic acid	Ferulic acid	Ferulic acid	isorhamnetin
8.	Rutin	---	---	---
9.	Chicoric acid	Chicoric acid	Chicoric acid	apigenin
10	Quercetin	Quercetin	Quercetin	Quercetin
11.	T-cinnamic acid	T-cinnamic acid	T-cinnamic acid	---

HPLC profile of EETOL indicated ferulic acid, caffeic acid and quercetin (detection was improved in chromatograms with absorbance at 320 nm compared that detected at 280 nm), high chlorogenic acid and chicoric acid contents (chicoric acid and chlorogenic acid in leaves were as high as 24.03 mg/g DW and 2.82 mg/g DW). Concentration of caffeic acid in EETOL was 0.237 ± 0.025 mg/g DW. Rutin and quercetin were also present. EETOL also contains flavonoids like luteolin-7-O-glucoside, luteolin-7-O-rutinoside and quercetin-7-O-glucoside.

HPLC profile of EETOP confirmed flavonoids, rutin, quercetin (flower at 5.43 mg/g DW). Chlorogenic, syringic, caffeic and vanillic acid were found in EETOR fraction. Besides, flavonoids like isorhamnetin, luteolin, apigenin, and quercetin derivatives were found in EETOR.

Dandelion EETOL has induced glucose lowering effect after 2 hr. Besides, sugar levels were restored after 3 hr in all treatment groups (Table 6). EETOL had alleviated blood glucose (maximum reduction after 21 days) and produced better action than EETOP and EETOR ($P < 0.001$; Table 7; Figure 6-7).

Table 6: Normoglycaemic effects of EETOL, EETOP, EETOR.

Groups	Blood glucose (mg/dl)			
	0 hr	1 hr	2 hr	3 hr
Control (DW)	76.2 ±.2	75.4 ±.2	73.6 ±.2	72.6 ±.8
EETOL (400 mg/kg)	78.2±.4	74.2±.2	72.6±.8	74.6±.4
EETOP (400 mg/kg)	74.6±.4	76.2±.2	80.2±.8	78.8±.2
EETOR (400 mg/kg)	75.4±.4	78.2±.4	83.4±.6	82.6±.6

Note: Mean ± SEM (triplicate measurements)

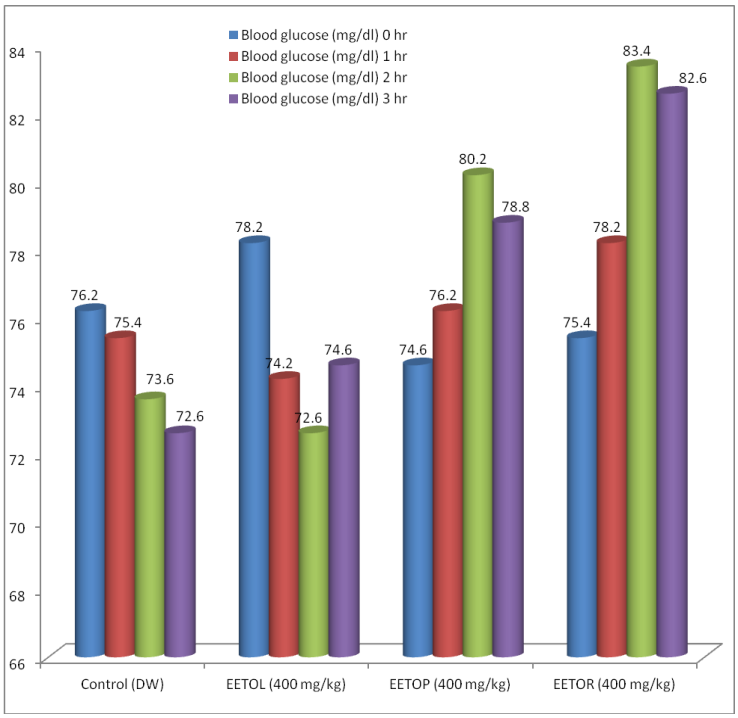

Figure 6: Effect of EETOL and EETOR on blood glucose in normo-glycaemic rats.

Table 7 : EETOL, EETOP and EETOR effect on glucose tolerance. (Figure 7)

Groups	Blood glucose (mg/dl)				
	0 min	30 min	60 min	90 min	120 min
Control	80.6±.42	138.2±.42	164.8±.22	138.6±.22	128.3±.32
EETOL (400 mg/kg)	77.4±.20	127.26±.22	112.4 ±.18	96.3±.28	84.2±.28
EETOP (400 mg/kg)	82.6±.64	128.6±.24	122.6± .32	108±.1.8	102.8±.24
EETOR (400 mg/kg)	82.4±.64	130.2±.32	124.2± .30	112±.2.6	106.8±.32

Note: Mean ± SEM.

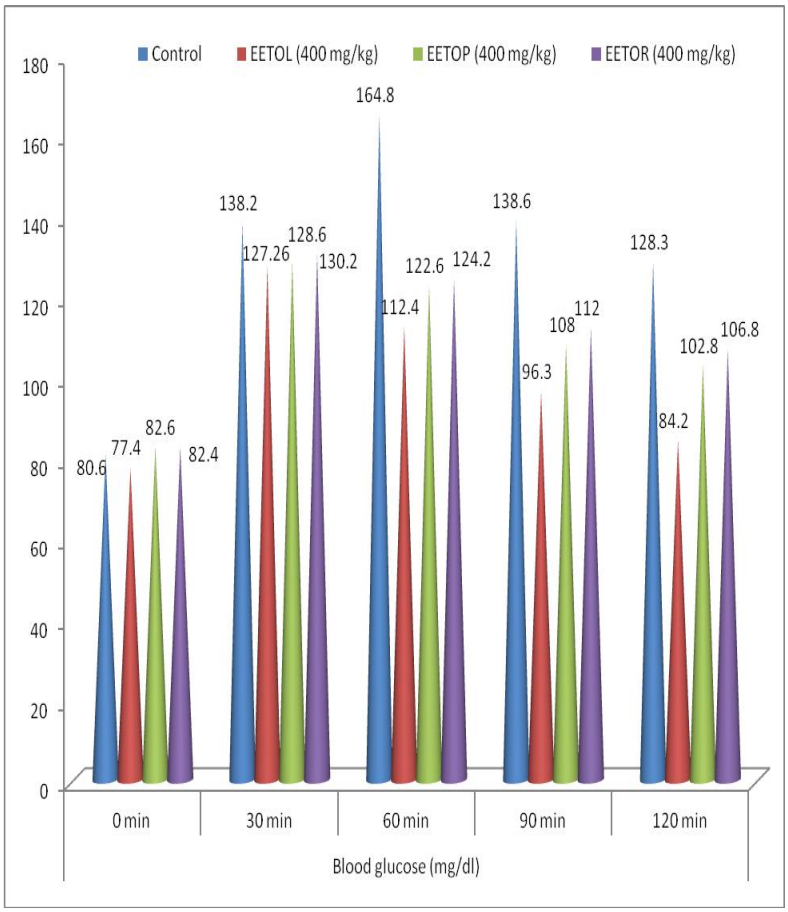

Figure 7 : EETOL, EETOP and EETOR effects on glucose-tolerance.

Table 8: EETOL, EETOP and EETOR effects on blood glucose against STZ.

Group	Blood Glucose (mg/dl)			
	Day 1	Day 7	Day 14	Day 21
Control	92.2 ± 4.34	95.2 ± 3.84	94.4 ± 3.92	94.8 ± 4.22
Toxic Control	212.4 ± 6.34	206.4 ± 5.72	202.6 ± 6.14	198.4 ± 4.32
EETOL	206.2 ± 4.36	170.4 ± 3.84	134.6 ± 4.14	108.6 ± 2.86
EETOP	204.6 ± 8.24	194.2 ± 4.56	148.6 ± 4.36	132.2 ± 4.32
EETOR	204.2 ± 6.26	182.4 ± 3.52	162.6 ± 3.52	154.8 ± 4.64
Glipizide	206.4 ± 5.22	162.2 ± 3.84	124.6 ± 3.24	98.4 ± 2.72

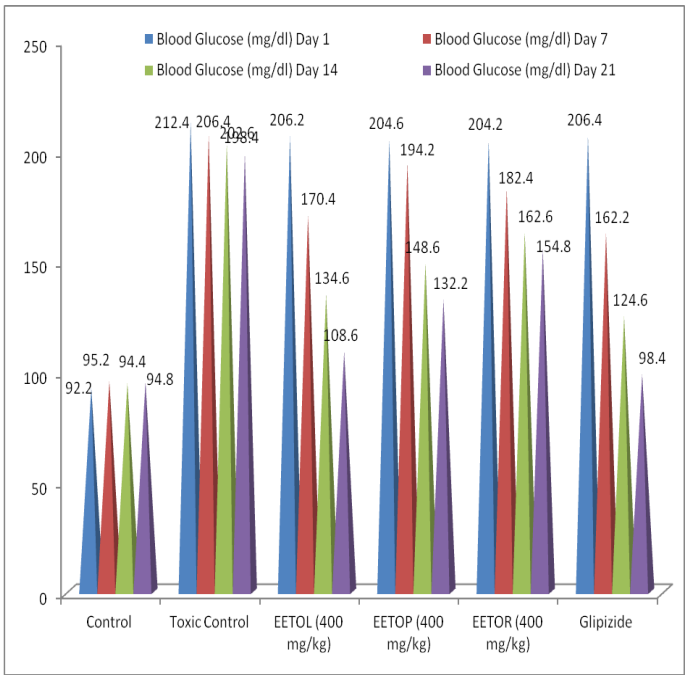

Figure 8: Anti-diabetic effects of extracts and Glipizide (Std.) against STZ.

Further, EETOL lowered blood glucose significantly from 206.2 (1st day), 170.4 (7th day), 134.6 (14th day) to 108.6 (21st day) (Table 8; Figure 8). On the other hand blood glucose in animals treated with EETOR was 204.2 (Day-1), 182.4 (day-7), 162.6 (day -14) and 154.8 on day-21. Glipizide (standard drug) significantly lowered glucose level from 206.4 (day 1)-162.2 (day -7)-124.6 (day-14) to 98.4 mg/dl after 21 days.

Table 9: Effect of EETOL and EETOP on cholesterol and triglycerides in diabetic rats.

Groups	After 7 days		After 21 days	
	Cholesterol	Triglyceride	Cholesterol	Triglyceride
Control	114.2± 1.4	102.2±.2.8	108.6±1.26	98.8±2.24
Diabetic control	266.4±2.4	200.2±1.2	221.6±2.84	174.8±2.4
EETOL (400mg/kg)	142.4±2.4	132.4±1.54	120.0±1.82	84.4±2.26
EETOP (400mg/kg)	154.6±2.8	148.6±2.24	134.6±1.26	92.4 ± 2.14
EETOR (400mg/kg)	184.4±2.8	168.2±2.24	154.8±1.64	142.6 ± 2.14
Glipizide (5mg/kg)	112.6±1.52	98.6±1.28	98.4±1.24	88.6 ± 1.12

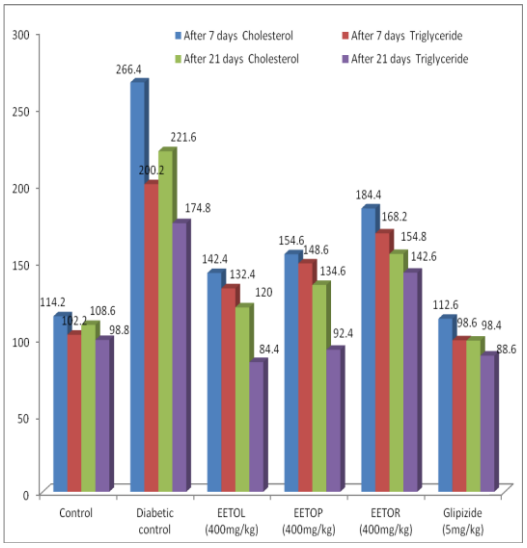

Figure 9: Effect of Extracts on cholesterol and triglycerides in diabetic animals.

Observations recorded in Table 9 (Figure 9) indicated the effect of EETOL, EETOP and EETOR on cholesterol and triglycerides level in STZ induced diabetic rats. STZ toxicity induced increase in serum cholesterol (after 7 days 266.4; after 21 days 221.6), triglycerides [200.2 (7 days); 174.8 (21 days)] ($P < 0.0001$). EETOL treatment alleviated the level serum cholesterol [142.4 (7days); 120.0 (21 days)], triglycerides [132.4 (7 days); 84.4 (21 days)]. Treatment with EETOP alleviated cholesterol [154.6 (7days); 134.6 (21 days)], triglycerides [148.6 (7 days); 92.4 (21 days)]. Standard reference drug glipizide (5mg/kg) decreased

cholesterol the [112.6 (7 days); 98.4 (21 days)], triglycerides [98.6 (7 days); 88.6 (21 days)]. EETOL has prominent hypolipidemic / hypocholesterolemic activity but lesser than Standard drug ($P < 0.0001$).

Table 10 : Effect of EETOL, EETOP and Glipizide on lipoproteins.

Groups	After 7th day			After 21st day		
	HDL	LDL	VLDL	HDL	LDL	VLDL
Control	60.4±0.4	32.4±0.46	20.6±0.14	40.4±0.22	36.0±.64	14.4±.02
Toxic	21.2±0.2	192±2.42	41.2±0.12	27.2±1.44	134.4±1.2	40.2±.16
EETOL	34.4±.16	80.6±.84	26.4±.16	42.6±1.6	58.2±1.2	15.6± 0.4
EETOP	32.4±.22	91.2±.32	27.6±.12	43.2±1.2	62.4±1.84	18.8±0.12
EETOR	28.8±.24	96.4±.36	27.2±.18	36.4±1.4	66.2±1.76	18.2±0.14
Glipizide	38.6±.26	72.8±.74	24.2±.32	46.8±1.6	48.6±1.24	14.2± 0.6

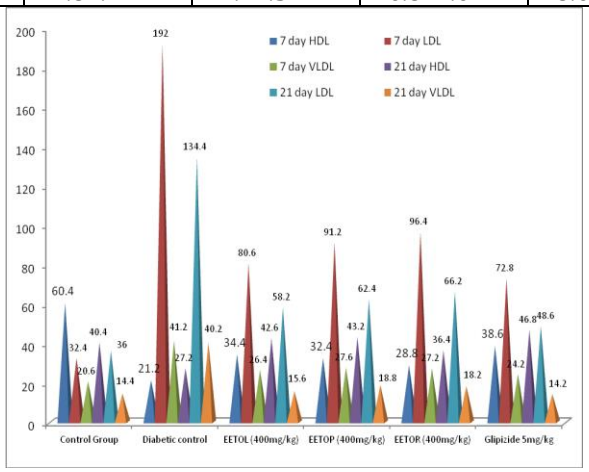

Figure 10: Effect of extracts on lipoproteins in STZ induced diabetic rats.

In normal animals HDL (good cholesterol) level were found to be 60.4 (7 days) and 40.5 (after 21 days). In diabetic control / toxic control group HDL level were 21.2 (7 days) and 27.2 (21 days). HDL was significantly lowered in diabetic rats when compared to normal control ($P < 0.0001$). EETOL restored HDL level 34.4 (7 days) and 42.6 (21 days) and EETOP treatment the produced HDL level 32.4 (7 days) and 43.2 (21 days). In glipizide (5mg/kg) treated group serum HDL was 38.6 (7 days) and 46.8 (21 days). Beneficial effect of EETOL and EETOP on HDL level in treated animals was therapeutic. (Table 10; Figure 10).

In healthy animals (normal group) LDL (bad cholesterol) level were found to be 32.4 (7 days) and 36.0 (after 21 days). In toxic control group LDL level were 192 (7days) and 134.4 (21 days). LDL was significantly increased in STZ toxic group animals ($P < 0.0001$). EETOL alleviated LDL level 80.06 (7 days) and 58.2 (21 days) and EETOP treatment the produced LDL level 91.2 (7 days) and 62.4 (21 days). In glipizide treated group serum LDL was 72.8 (7days) and 48.6 (21 days). Beneficial effect (LDL alleviating effect) of EETOL, EETOP and Standard on LDL level in treated groups was good. In normal group VLDL level were found to be 20.6 (7 days) and 14.4 (21 days). In diabetic toxic control group VLDL were 41.2 (7days) and 40.2 (21 days). EETOL alleviated VLDL level 26.4 (7 days) and 15.6 (21 days) and EETOP treatment the produced VLDL level 27.6 (7 days) and 18.8 (21 days). In glipizide treated group serum VLDL level was 24.2 (7days) and 14.2 (21 days). VLDL alleviating effect of EETOL and EETOP on LDL level group III-IV were therapeutically positive. (Table 10; Figure 10).
EETOL has prominent hypolipidemic / hypocholesterolemic activity but lesser than Standard drug ($P < 0.001$). Possible mechanisms of action (MoA) for anti-diabetic activity include restoration / repairing beta cells (protective effect) in diabetic animals; revitalization of damaged beta cells; flavonoids rejuvenate damaged beta cells (insulin secretagogues effect). In diabetic control group, HDL was significantly lowered in diabetic rats when compared to normal control. EETOL, EETOP and glipizide treatment restored / elevated HDL level. In STZ toxic control group LDL level was significantly increased. EETOL and EETOP extracts treatment alleviated LDL level. Standard glipizide alleviated LDL level. LDL alleviating effect of standard, dandelion EETOL and EETOP was good.

Conclusions

Both EETOL and EETOP produced significant anti-diabetic activity by repairing and revitalization of damaged beta cells and insulin secretagogues effect (lowered blood glucose level significantly). EETOL, EETOP and glipizide treatment induced prominent hypolipidemic activity with restored HDL level and alleviated LDL and VLDL level. In future, it is proposed that research work is to be conducted to isolate and characterize the pharmacologically active principles of EETOL and EETOP extracts *T. officinale* Weber.

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