



Received on 08 May 2018; received in revised form, 19 June 2018; accepted, 13 July 2018; published 01 January 2019

EFFECT OF ETHANOLIC EXTRACTS OF INDIAN MEDICINAL PLANTS ON THE NON-ENZYMATIC ANTIOXIDANT SYSTEM IN STREPTOZOTOCIN INDUCED DIABETIC RATS IN COMPARISON WITH GLIBENCLAMIDE

R. Kavitha

Department of Biotechnology, Periyar University PG Extension Centre, Dharmapuri - 636701, Tamil Nadu, India.

Keywords:

Trichosanthe dioica, *Clitoria ternatea*, Non-enzymatic antioxidants, Glibenclamide, Histopathology

Correspondence to Author:

Dr. R. Kavitha

Associate Professor and Head,
Department of Biotechnology,
Periyar University PG Extension
Centre, Dharmapuri - 636701,
Tamil Nadu, India.

E-mail: erokavi_vasu@yahoo.com

ABSTRACT: Objective: To investigate the effects of ethanolic extracts of leaf and fruit of *Trichosanthes dioica* and leaf of *Clitoria ternatea* were studied on the altered non-enzymatic antioxidant system such as reduced glutathione (GSH), Vitamin E, C and A in streptozotocin-induced diabetic Wistar rats. **Methods:** Male adult Wistar albino rats divided into eleven groups of six rats each were assigned to non-diabetic and diabetic groups (Group I to XI). Diabetes was induced in Albino rats by single intraperitoneal administration of STZ (60 mg/kg body weight), on confirming diabetes after 48 h of injection. Group I and II were kept as non-diabetic and diabetic control. The other diabetic groups (Group III to Group X) were treated with both individual and combined ethanolic extracts of *T. dioica* and *C. ternatea* at the doses of 200, and 400 mg/kg of body weight were administered orally at a single dose per day for 28 consecutive days. Group XI was treated with Glibenclamide (600 µg/kg body weight), a standard oral hypoglycemic drug used as a reference drug for comparison. After completion of experimental period serum, liver and kidney were used for estimating GSH, plasma, and liver for estimating Vitamin E, C and A, and pancreas, liver and kidney were used for histopathological changes in the diabetic rats. **Results:** A significant increase in GSH, Vitamin E, C and A levels were observed in diabetic rats treated with ethanolic extracts of *T. dioica* (leaf and fruit) and *C. ternatea* (leaf) compared to diabetic control rats. Histopathological studies demonstrated the reduction in the pancreas, liver and kidney damage and confirmed the biochemical findings. **Conclusion:** These results suggest that *T. dioica* and *C. ternatea* are beneficial in the control of diabetes by the noticeable antioxidant property.

INTRODUCTION: Diabetes mellitus persistent hyperglycemia causes increased production of free radicals *via*, auto-oxidation of glucose. It may lead to the disruption of cellular functions, affects antioxidant reactions catalyzed by reactive oxygen species (ROS) scavenging enzymes¹ and endothelial dysfunction^{2,3}.

Scavengers of oxidative stress may have an effect in reducing the increased serum glucose level in diabetes and may alleviate diabetes as well as reduce its secondary complications⁴.

Antioxidants are the substances that prevent or slow down the oxidation reactions. All organisms possess the most important antioxidant system includes enzymatic such as superoxide dismutase, catalase, and glutathione peroxidase and the non-enzymatic group includes reduced glutathione, Vitamins A, C and E. They are located in the cell and in the extracellular fluid which is produced either endogenously or derived from dietary sources.

<p>QUICK RESPONSE CODE</p> 	<p>DOI: 10.13040/IJPSR.0975-8232.10(1).418-30</p>
<p>The article can be accessed online on www.ijpsr.com</p>	
<p>DOI link: http://dx.doi.org/10.13040/IJPSR.0975-8232.10(1).418-30</p>	

These are responsible for scavenging and to protect the human body against ROS generated in the cells⁵. They stop the free radical generation by trapping the free radicals, and thus they inhibit the chain reactions which can lead to the destruction of healthy cells⁶. Supplementation of exogenous antioxidants or boosting endogenous antioxidant defenses of the body is a promising way of combating the undesirable effects of ROS induced oxidative damage. Plants have an innate ability to biosynthesize a wide range of some chemical substances especially secondary metabolites and non-enzymatic antioxidants which serve as sources of antioxidants and do scavenging activity^{7,8}.

Diabetes mellitus is a multifactorial disease, and therefore, it would require more than a single drug agent to reverse all or the majority of the aspects of the disease. The human body is much better suited to treatment with herbal remedies than with the isolated chemical medicines. Polyherbal therapy which is the use of a combination of various agents from different plant sources for a therapeutic approach in the management of diabetes and has the advantage of producing maximum therapeutic efficacy with minimum side effects⁹. In the traditional system of Indian medicinal plant formulations and several cases, combined extracts of plants are used as a drug of choice rather than individual¹⁰.

In the present investigation, the first plant *Trichosanthes dioica* Roxb (family: Cucurbitaceae) is a dioecious (male and female) vine (creeper) perennial herb distributed in the plains of tropical Asia, Polynesia and Australia¹¹. It is extensively cultivated as a vegetable crop in the Eastern part of India, particularly in Orissa, West Bengal, Assam, Bihar, Uttar Pradesh Tripura and also in Tamil Nadu^{12, 13, 14}. It has been used for fever, constipation, diuretics, skin infection, dysentery, diarrhea, convalescents, bronchitis and cancer like conditions. The plant extract has shown a significant reduction in liver enzymes (alanine transaminase and alkaline phosphatase) and serum creatinine¹⁵. The leaves and fruits of the plant have been reported to have hypoglycemic activity¹⁶.

The second plant *Clitoria ternatea* Linn (family Fabaceae) is a perennial twining herb found in Africa, Australia, America, India, China,

Philippines, and Madagascar. In traditional Ayurvedic medicine, it has been used to treat infertility, urinogenital disorder, bronchitis, purgative and diuretic^{17, 18, 19, 20}. A recent study showed that it has anti-hyperglycemic, anti-hyperlipidemic²¹, anti-inflammatory²² and anti-helminthic²³ activities.

Hence, the objective of the present study is to investigate the above-mentioned plant materials are used individually and in combination to evaluate the anti-diabetic, non-enzymatic antioxidant effectiveness and histological studies in STZ-induced diabetic rats and compared to the effect of standard drug Glibenclamide.

MATERIALS AND METHODS:

Chemicals: Streptozotocin (STZ) was purchased from Siga Chemical Company (USA). Glibenclamide was obtained from Aventis Pharmaceuticals Limited (India). All the chemicals and reagents used in the experiments were of analytical grade obtained from BDH (England and India), E. Merck (Germany), Siga Chemical Company (U.S.A), LOBA - Chemie Indo Austranol Co., (India) whenever necessary the solvents were redistilled before use.

Collection and Authentication of Plant

Materials: Fresh unripe fruit and leaf of *T. dioica* and the leaf of *C. ternatea* were collected from SKM Herbal Research Centre, Erode, Tamil Nadu, India. With the help of local flora, a voucher specimen (no. VOCB 2307 and VOCB 2453) was retained in Ethnopharmacology Unit, Research Department of Botany, V. O. Chidambaram College, Tuticorin, Tamil Nadu for further reference.

Preparation of Ethanolic Extracts of *T. dioica*

and *C. ternatea*: Freshly collected leaf and fruit of *T. dioica* and leaf of *C. ternatea* were washed with distilled water, and the fruits were cut into small pieces. Both fruits and leaves were dried under shade for two weeks. The shade dried leaves and fruits were coarsely powdered separately. The powdered materials were kept in airtight containers to use. About 500 g of dried coarse powdered samples were weighed and subjected to 1250 ml of ethanol in a Soxhlet extractor for 24 h. All the extracts were filtered through Whatmann no. 41

filter paper separately and the extracts were concentrated in vacuum at 60 °C using a rotary evaporator. To evaporate the remaining solvent, the extracts were kept in an oven at a temperature of 40-50 °C for 8h that were used in the present study.

Collection of Experimental Animals: Healthy male adult Albino rats of Wistar strain approximately of the same age, weighing around 160-180 g were procured from Nandha College of Pharmacy. The entire process was approved by the Institutional Animal Ethics Committee (IAEC) which is certified by the Committee for Control and Supervision of Experiments on Animals, (CPCSEA), India (Proposal number: NCP/IAEC/PHD/01/2007-2008), Nandha College of Pharmacy, Erode, Tamil Nadu, India.

Preparation of Streptozotocin-induced Diabetic Wistar Rats: Diabetes was induced by single dose intraperitoneal administration of streptozotocin at a dose of 60 mg/kg body weight in 0.1 M citrate buffer (pH 4.5) and then injected into the tail of the sixty rats. The injection volume was prepared to contain 1 ml/kg bw¹⁸. After 72 h of STZ administration, the blood glucose content was measured. The animals with blood glucose levels \geq 250 mg/dl were considered to be diabetic and used for the experiment.

Experimental Design of Animals: In the present investigation, the rats were divided into eleven groups of six rats in each group as follows:

Group I: Normal control rats received normal saline (0.9% sodium chloride).

Group II: STZ-induced diabetic control rats received normal saline.

Group III: Diabetic rats received ethanolic leaf extract of *T. dioica* (200 mg/kg body weight).

Group IV: Diabetic rats received ethanolic leaf extract of *T. dioica* (400 mg/kg body weight).

Group V: Diabetic rats received ethanolic fruit extract of *T. dioica* (200 mg/kg body weight).

Group VI: Diabetic rats received ethanolic fruit extract of *T. dioica* (400 mg/kg body weight).

Group VII: Diabetic rats received ethanolic leaf extract of *C. ternatea* (200 mg/kg body weight).

Group VIII: Diabetic rats received ethanolic leaf extract of *C. ternatea* (400 mg/kg body weight).

Group IX: Diabetic rats received combined ethanolic extracts of *T. dioica* leaf (200 mg/kg body weight) and *C. ternatea* leaf (200 mg/kg body weight).

Group X: Diabetic rats received combined ethanolic extracts of *T. dioica* fruit (200 mg/kg body weight) and *C. ternatea* leaf (200 mg/kg body weight).

Group XI: Diabetic rats received standard drug glibenclamide (600 μ g/kg body weight) for 28 d orally by using an intragastric catheter tube.

Determination of Blood Glucose Level (Electronic Glucometer Method): The blood collected from the tail vein was used to determine the glucose level. As bleeding starts, the animal was held to the blood glucose test strip and allowed the drop of blood to fall on the strip which reacted with the blood. After a few seconds the blood glucose level was displayed on the screen of the glucometer. The blood glucose was estimated every 7 days in control as well as experimental animals for 28 days.

Collection of Blood and Preparation of Tissue Homogenate: At the end of the treatment, all rats were sacrificed by cervical dislocation. Blood was collected from the experimental animals by direct cardiac puncture. Serum was separated by centrifugation at 2500 rpm for 10 min and stored at -20°C until used for the non-enzymatic antioxidant assays. Liver and kidney of the sacrificed animals were excised immediately and thoroughly washed with cold physiological saline and kept in a deep freezer at -20 °C till used. The homogenate was filtered and then centrifuged at 10,000 rpm for 20 min at 4 °C.

Quantification of Phytochemicals in Ethanolic Extracts of Leaf and Fruit of *T. dioica* and Leaf of *C. ternatea*: Total phenolic content was measured by the method²⁴, flavonoids was estimated by the method²⁵, tannins and saponins were determined by the method^{26, 27}, alkaloids was determined according to the method²⁸, and Vitamin C was measured by the method²⁹.

Estimation of Non-Enzymatic Antioxidants Activities: The changes in the levels of the most important non-enzymatic antioxidants includes GSH (reduced glutathione) activity was studied by

the method³⁰, Vitamin E, Vitamin C, and Vitamin A were estimated according to the methods^{31, 32, 33}.

Histopathological Studies: The pancreas, liver, and kidney of the sacrificed rats were dissected, removed and fixed in 10% formalin solution. The fixed specimens were then trimmed, washed and dehydrated in ascending grades of alcohol. These specimens were cleared in xylene, embedded in paraffin, sectioned at 4-6 microns thickness and stained with hematoxylin and eosin then to observe histopathological changes by microscopically.

Statistical Analysis: All the experimental values are expressed as means \pm SD for groups of six animals each. Student's t-test performed statistical analyses. The values are statistically significant at three levels, *** $p < 0.001$, ** $p < 0.01$, * $p < 0.05$. But NS if $p > 0.05$.

RESULTS:

TABLE 1: QUANTITATIVE ANALYSIS OF PHYTOCHEMICALS AND VITAMIN C IN ETHANOLIC EXTRACTS OF LEAF AND FRUIT OF *T. DIOICA* AND LEAF OF *C. TERNATEA*

Phytochemicals	<i>T. dioica</i>		<i>C. ternatea</i> leaf
	Leaf	Fruit	
Flavonoids (mg RE/ g extract)	36.1 \pm 2.02	48.2 \pm 1.06	74.5 \pm 3.03
Total phenolics (mg GAE/ g extract)	26.0 \pm 0.03	38.1 \pm 0.03	98.2 \pm 1.02
Tannins (mg TAE/ g extract)	38.26 \pm 3.81	65.72 \pm 7.10	78.75 \pm 2.09
Saponins (%)	0.38 \pm 0.02	0.78 \pm 0.01	0.66 \pm 0.06
Alkaloids (gm/ 100 g)	0.11 \pm 0.01	0.21 \pm 0.01	0.18 \pm 0.01
Vitamin C (mg AAE/ g extract)	52.26 \pm 0.13	60.03 \pm 0.17	118.83 \pm 0.47

Values are mean of three independent analyses of the extract \pm standard deviation (n = 3). RE-Rutin equivalent; GAE – Gallic acid equivalent; TAE-Tannic acid equivalent; AAE–Ascorbic acid equivalent

TABLE 2: DETERMINATION OF BLOOD GLUCOSE LEVEL IN NORMAL AND EXPERIMENTAL RATS AT DIFFERENT TIME INTERVALS (DAYS)

Treatment groups	Dose (mg/kg bw)	Blood glucose level (mg/dl)				
		Days of Treatment				
		0	7	14	21	28
I Normal control	Normal saline	81.67 \pm 2.91	79.23 \pm 2.14	85.92 \pm 4.08	80.14 \pm 2.84	86.91 \pm 2.48
II DC	Normal saline	196.85 \pm 8.43**	218.56 \pm 1.32**	234.68 \pm 5.99***	238.63 \pm 7.94***	231.57 \pm 2.56***
III D+TDL	200	178.45 \pm 4.81*	167.56 \pm 3.87*	143.43 \pm 3.95 ^{NS}	136.95 \pm 6.11 ^{NS}	123.91 \pm 4.62 ^a
IV D+TDL	400	187.56 \pm 3.74**	154.66 \pm 2.85*	141.49 \pm 9.34 ^{NS}	132.78 \pm 3.71 ^{NS}	126.75 \pm 3.56 ^a
V D+TDF	200	194.66 \pm 5.86**	143.56 \pm 4.87*	130.04 \pm 2.91 ^{NS}	121.42 \pm 5.67 ^{aa}	109.48 \pm 2.74 ^a
VI D+TDF	400	189.29 \pm 4.67*	141.93 \pm 2.39 ^{NS}	125.99 \pm 2.58 ^{aa}	116.83 \pm 3.55 ^{aa}	102.69 \pm 2.45 ^{aa}
VII D+CTL	200	191.54 \pm 6.45**	164.76 \pm 6.34*	153.94 \pm 5.93 ^{aa}	143.54 \pm 3.04 ^a	131.87 \pm 4.39 ^a
VIII D+CTL	400	182.87 \pm 2.50*	141.56 \pm 2.82 ^{NS}	121.08 \pm 2.94 ^{aa}	116.87 \pm 2.56 ^{aa}	99.26 \pm 2.53 ^{aa}
IX D+ TDL+ CTL	200 +200	198.45 \pm 5.23**	151.46 \pm 3.78*	132.87 \pm 3.87 ^{aa}	127.59 \pm 3.02 ^{aa}	116.78 \pm 2.45 ^a
X D+TDF +CTL	200 +200	187.45 \pm 2.97*	135.77 \pm 3.67 ^{NSa}	126.76 \pm 2.95 ^{aa}	118.26 \pm 2.79 ^{aa}	102.56 \pm 2.95 ^{aa}
XI D+Glibenclamide	0.6	192.67 \pm 3.51**	143.56 \pm 2.85 ^a	135.68 \pm 2.11 ^{aa}	120.59 \pm 3.14 ^{aa}	108.77 \pm 2.05 ^{aa}

DC: Diabetic control, D: Diabetic, TDL: *T. dioica* leaf, TDF: *T. dioica* fruit, CTL: *C. ternatea* leaf

Blood Glucose Level: Blood glucose level was determined in various groups of experimental animals at frequent intervals of 7 days for 28 days. The results were illustrated in **Table 2**. The levels of glucose in blood of STZ-induced diabetic rats

Quantification of Phytochemicals and Vitamin C: The quantitative analysis of phytochemicals in the ethanolic extracts of the investigated plants were given in **Table 1**.

Among the studied plant samples, *C. ternatea* leaf extract was found to contain an appreciable amount of flavonoids, total phenolics and tannins whereas *T. dioica* fruit was found to contain a higher amount of saponins and alkaloids. But *T. dioica* leaf contained lesser amounts of flavonoids, total phenolics, tannins, saponins, and alkaloids.

Total flavonoid content was expressed as rutin equivalent, total phenolics and tannin content were expressed as gallic acid equivalent and tannic acid equivalent respectively. *C. ternatea* leaf contained a rich amount of Vitamin C when compared to the other two samples.

(Group II) were found to be significantly ($p < 0.001$; $p < 0.01$) elevated when compared with normal control rats (Group I). Oral administration of individual and combined ethanolic extracts of test samples to the experimental groups (Group III to

Group X) showed a significant ($p<0.01$; $p<0.05$) reduction in blood glucose level when compared with diabetic control rats (Group II). At the 28th day of treatment, a maximum reduction of blood glucose level was seen in Group VI, VIII, Group X, and XI. On the other hand, low dose (200 mg/kg bw) of *T. dioica* leaf (Group III) treated group the treatment was less effective in all the different durations.

Effect of Ethanolic Extracts of Leaf and Fruit of *T. Dioica* and Leaf of *C. Ternatea* on Serum, Liver and Kidney of Non-Enzymatic Antioxidant (GSH) levels in STZ-induced Diabetic Rats: Table 3 represented the concentration of GSH in the serum, liver, and kidney of normal

control, diabetic control, and diabetic treated groups of rats.

There was a significant ($p<0.05$) decrease in the activity of GSH in the serum, liver, and kidney of STZ-induced diabetic rats (Group II) compared to the normal group (Group I). A significant ($p<0.05$) elevation of serum, hepatic and kidney GSH level were observed in the extracts treated diabetic rats which were dose-dependent. Among these group of animals a significant ($p<0.01$) increase in the levels of GSH were found in serum of Group VIII and IX, liver of Group VI, VII, and VIII), kidney of Group VIII and standard drug glibenclamide treated Group XI, when compared with diabetic control group (Group II).

TABLE 3: EFFECT OF ETHANOLIC EXTRACTS OF LEAF AND FRUIT OF *T. DIOICA* AND LEAF OF *C. TERNATEA* ON REDUCED GLUTATHIONE IN SERUM, LIVER, AND KIDNEY OF CONTROL AND EXPERIMENTAL RATS

Treatment groups	Dose (mg/kg bw)	GSH		
		Serum [#]	Liver ^{##}	Kidney ^{##}
I Normal control	Normal saline	34.59±1.24	53.21±2.63	21.78±1.34
II DC	Normal saline	16.26±1.08*	14.50±2.11*	13.93±1.09*
III D+TDL	200	19.31±1.24 ^{NS}	42.67±2.07	17.38±1.21
IV D+TDL	400	27.26±1.73 ^{NS}	46.55±2.93	19.69±0.92 ^a
V D+TDF	200	26.33±1.69 ^{NS}	49.14±2.36	15.08±1.24*
VI D+TDF	400	30.11±1.09 ^a	55.11±2.07 ^{aa}	18.28±1.38 ^a
VII D+CTL	200	29.19±1.34 ^a	51.14±1.93 ^{aa}	19.36±1.76 ^a
VIII D+CTL	400	35.26±1.53 ^{aa}	53.91±2.84 ^{aa}	24.84±1.33 ^{aa}
IX D+TDL+CTL	200 + 200	33.99±1.27 ^{aa}	48.59±2.93 ^a	21.87±1.59 ^a
X D+TDF+ CTL	200 + 200	37.56±1.19 ^a	50.91±2.07 ^a	20.01±0.48 ^a
XI D + Glibenclamide	0.6	34.27±1.73 ^a	56.33±2.29 ^{aa}	22.59±1.64 ^a

DC: Diabetic control, D: Diabetic, TDL: *T. dioica* leaf, TDF: *T. dioica* fruit, CTL: *C. ternatea* leaf. Values are reported as mean ± SD for six animals in each group. * $p<0.05$, ** $p<0.01$, *** $p<0.001$ significance between normal control vs. diabetic control and drug-treated groups; ^a $p<0.05$, ^{aa} $p<0.01$ significance between diabetic control vs. drug-treated groups; NS: Not significant. # mg of glutathione/ dl ^{##} Units/ mg protein

TABLE 4: EFFECT OF ETHANOLIC EXTRACTS OF LEAF AND FRUIT OF *T. DIOICA* AND LEAF OF *C. TERNATEA* ON NON-ENZYMIC ANTIOXIDANTS IN PLASMA AND LIVER OF CONTROL AND EXPERIMENTAL RATS

Treatment groups	Dose (mg/kg bw)	Vitamin-E		Vitamin-C		Vitamin-A	
		Plasma [#]	Liver ^{##}	Plasma [#]	Liver ^{##}	Plasma [#]	Liver ^{##}
I Normal control	Normal saline	1.89±0.12	0.87±0.02	1.48±0.02	1.21±0.05	1.56±0.03	1.87±0.04
II DC	Normal saline	0.67±0.04*	0.46±0.03*	0.51±0.04**	0.62±0.06*	0.34±0.04**	0.56±0.05*
III D+TDL	200	0.89±0.02	0.53±0.05	0.78±0.02	0.81±0.04	0.45±0.02	0.74±0.04
IV D+TDL	400	1.54±0.06 ^a	0.61±0.08 ^{NS}	1.21±0.05 ^a	1.03±0.02 ^{NS}	0.98±0.07 ^a	1.23±0.06 ^a
V D+TDF	200	0.71±0.02*	0.56±0.06	0.92±0.07	0.93±0.06	0.67±0.04*	0.91±0.05
VI D+TDF	400	1.68±0.07 ^a	0.72±0.04 ^a	1.36±0.04 ^a	1.19±0.02 ^{NS}	1.31±0.04 ^{aa}	1.59±0.03 ^a
VII D+CTL	200	0.93±0.05	0.69±0.01	0.83±0.06	0.93±0.06	0.86±0.02	0.87±0.06
VIII D+CTL	400	1.72±0.06 ^a	0.74±0.04 ^a	1.21±0.05 ^a	1.12±0.04 ^a	1.23±0.07 ^a	1.48±0.07 ^a
IX D+TDL+CTL	200+200	1.76±0.03 ^a	0.88±0.03 ^a	1.28±0.07 ^a	1.26±0.08 ^a	1.12±0.05 ^a	1.34±0.06 ^a
X D+TDF+ CTL	200+200	1.96±0.08 ^a	0.91±0.07 ^a	1.42±0.03 ^a	1.30±0.03 ^a	1.49±0.03 ^a	1.67±0.08 ^a
XI D + Glibenclamide	0.6	1.83±0.04 ^a	0.87±0.04 ^a	1.39±0.07 ^a	1.48±0.08 ^a	1.21±0.04 ^a	1.55±0.05 ^{NS}

DC: Diabetic control, D: Diabetic, TDL: *T. dioica* leaf, TDF: *T. dioica* fruit, CTL: *C. ternatea* leaf. Values are reported as mean ± SD for six animals in each group. * $p<0.05$, ** $p<0.01$, *** $p<0.001$ significance between normal control vs diabetic control and drug-treated groups; ^a $p<0.05$, ^{aa} $p<0.01$ significance between diabetic control vs drug-treated groups; NS: Not significant. #mg/ dl; ^{##}µg/ mg protein

Effect of Ethanolic Extracts of Leaf and Fruit of *T. dioica* and leaf of *C. ternatea* on Plasma and Liver of Non-Enzymatic Antioxidants (Vitamin E, C and A) levels in STZ-induced Diabetic Rats: Free radicals inactivate the enzymic antioxidants, and hence the presence of non-enzymic antioxidant is presumably essential for the removal of these radicals³⁴. The results of the non-enzymic antioxidants vitamin E (α -tocopherol), vitamin C (ascorbic acid) and vitamin A (total carotenoids) in plasma and liver of normal control and an experimental group of rats were depicted in **Table 4**.

The levels of these non-enzymic antioxidants in plasma and liver were decreased significantly ($p < 0.01$ and $p < 0.05$) in STZ-induced diabetic rats. On the other hand, treatment of diabetic rats with ethanolic extracts significantly ($p < 0.05$) increased the non-enzymic antioxidant (vitamin E, C, and A) levels to near normal and was found to be dose-

dependent. The plasma level of vitamin E was found to be maximum in diabetic rats treated with combined extracts of *T. dioica* fruit and *C. ternatea* leaf (Group X) (1.96 ± 0.08 mg/dl) which is very near to normal control group I (1.89 ± 0.12 mg/dl).

Histopathological Studies:

Histopathological Studies of Experimental Rat Pancreas: Histopathological changes were noted in pancreatic tissue. The results were presented in **Fig. 1 (a- h)**.

(a) The pancreas of normal control rats (Group I) showed patches of abundant β -cells. (b) The pancreas of diabetic control rats (Group II) showed a severe reduction in the number of pancreatic β -cells that confirmed the destruction of islets and cells due to the effect of streptozotocin. (c) The pancreas of diabetic rats treated with high dose (400 mg/kg bw) of *T. dioica* leaf (Group IV) showed partial recovery of pancreatic β -cells.

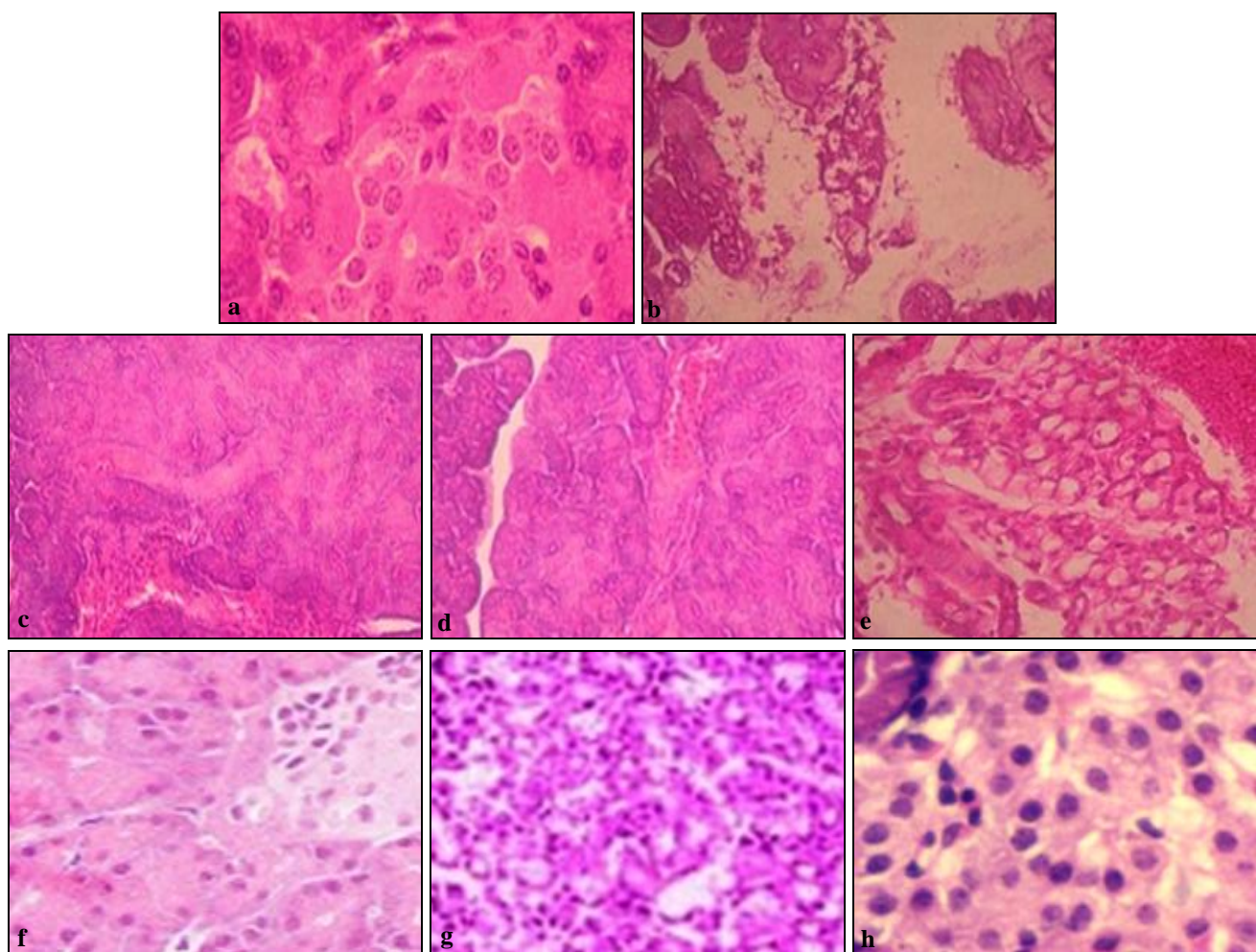


FIG. 1: HISTOLOGICAL EXAMINATIONS OF PANCREAS OF CONTROL AND EXPERIMENTAL RATS AFTER 28 DAYS OF TREATMENT

(d), (e), (f) and (g) pancreas of diabetic rats after treated with high doses (400 mg/kg bw) of *T. dioica* fruit (Group VI) and *C. ternatea* leaf (Group VIII) and combined extracts of *T. dioica* leaf + *C. ternatea* leaf (Group IX) and *T. dioica* fruit + *C. ternatea* leaf (Group X) showed more or less as *T. dioica* leaf. (h) The pancreas of diabetic rats after treated with standard drug glibenclamide (Group XI) showed pancreatic β -cells similar to that of the control.

Histopathological Studies of Experimental Rat Liver: Histopathological changes were noted in the liver. The results were depicted in **Fig. 2 (a-h)**.

(a) Liver of normal control rats (Group I) showed the normal architecture of hepatocytes with central lobule. (b) Liver of diabetic control rats (Group II) showed congestion and cellular necrosis. (c) Liver

of diabetic rats treated with high dose (400 mg/kg bw) of *T. dioica* leaf (Group IV) showed the mild congestion. (d) Liver of diabetic rats after treated with high dose (400 mg/kg bw) of *T. dioica* fruit (Group VI) showed the moderate congestion of hepatocytes with mild necrosis. (e) Liver of diabetic rats after treated with high dose (400 mg/kg bw) of *C. ternatea* leaf (Group VIII) showed the normal architecture of hepatocytes with mild congestion. (f) Liver of diabetic rats after treated with a combined extract of *T. dioica* leaf + *C. ternatea* leaf (Group IX) showed normal architecture with prominent hepatocytes. (g) Liver of diabetic rats after treated with a combined extract of *T. dioica* fruit + *C. ternatea* leaf (Group X) showed normal cellular arrangement. (h) Liver of diabetic rats after treated with the standard drug (Group XI) showed normal cell arrangement.

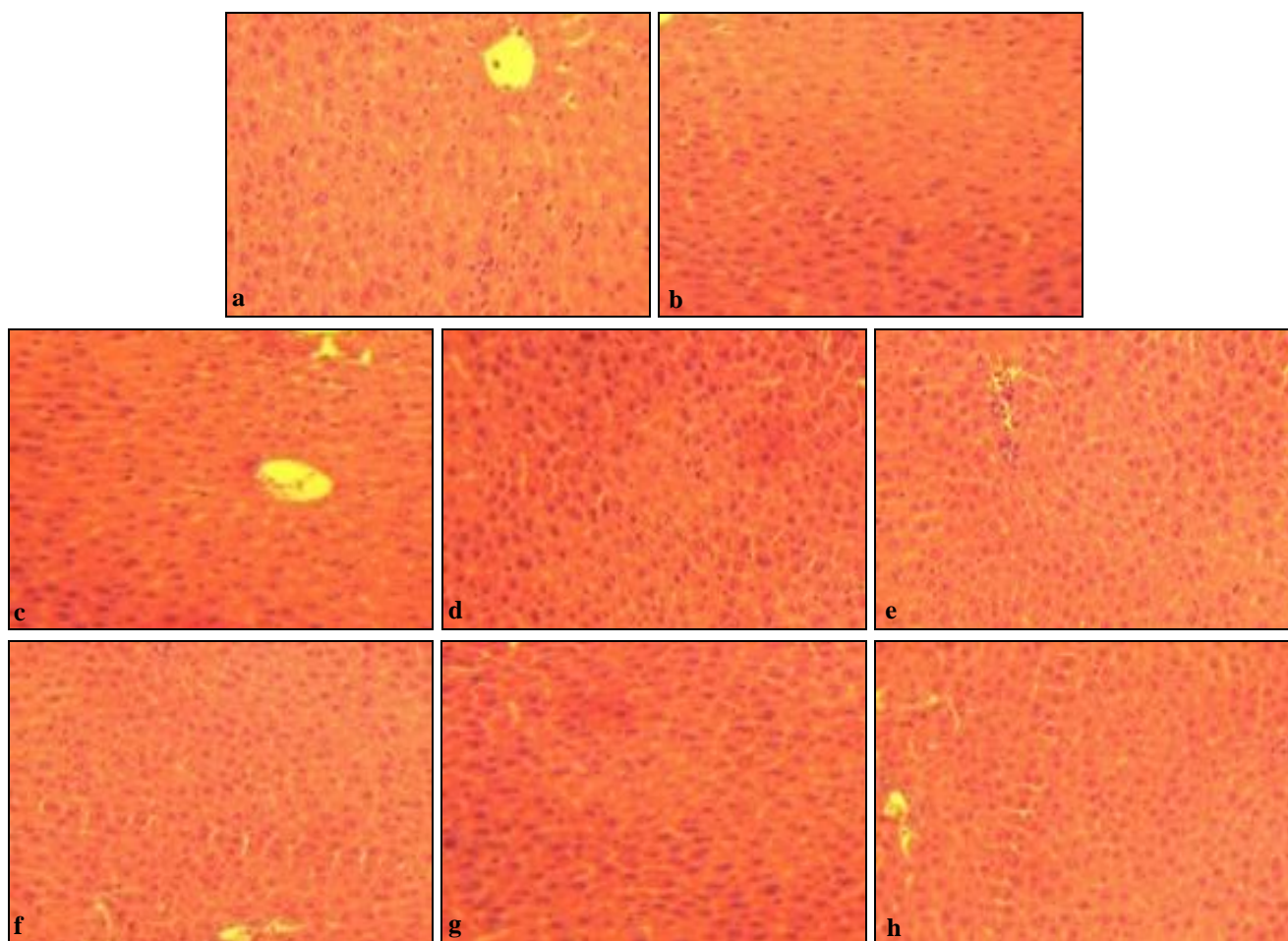


FIG. 2: HISTOLOGICAL EXAMINATIONS OF LIVER OF CONTROL AND EXPERIMENTAL RATS AFTER 28 DAYS OF TREATMENT

Histopathological Examinations of Experimental Rat Kidney: Histopathological changes were noted in the kidney. The results were shown in **Fig. 3 (a-**

h). (a) Kidney of normal control rats (Group I) showed normal alternating areas of convoluted tubules glomeruli and straight tubules. (b) Kidney

of diabetic control rats (Group II) showed congestion of convoluted tubules, deranged glomeruli. (c) Kidney of diabetic rats treated with high dose (400 mg/kg bw) of *T. dioica* leaf (Group IV) showed the mild congestion of tubules and necrosis of cells. (d) Kidney of diabetic rats after treated with high dose (400 mg/kg bw) of *T. dioica* fruit (Group VI) showed the moderate congestion of tubules and necrosis of cells with clear glomeruli. (e) Kidney of diabetic rats after treated with high dose (400 mg/kg bw) *C. ternatea* leaf (Group VIII) showed the normal architecture of

tubules and glomeruli. (f) Kidney of diabetic rats after treated with a combined extract of *T. dioica* leaf + *C. ternatea* leaf (Group IX) showed distinguishable renal corpuscle, glomerulus, and glomerular capsule. (g) Kidney of diabetic rats after treated with a combined extract of *T. dioica* fruit + *C. ternatea* leaf (Group X) showed normal convoluted tubules with distinguishable renal corpuscle, glomerulus, and glomerular capsule. (h) Kidney of diabetic rats after treated with the standard drug (Group XI) showed normal cell arrangement.

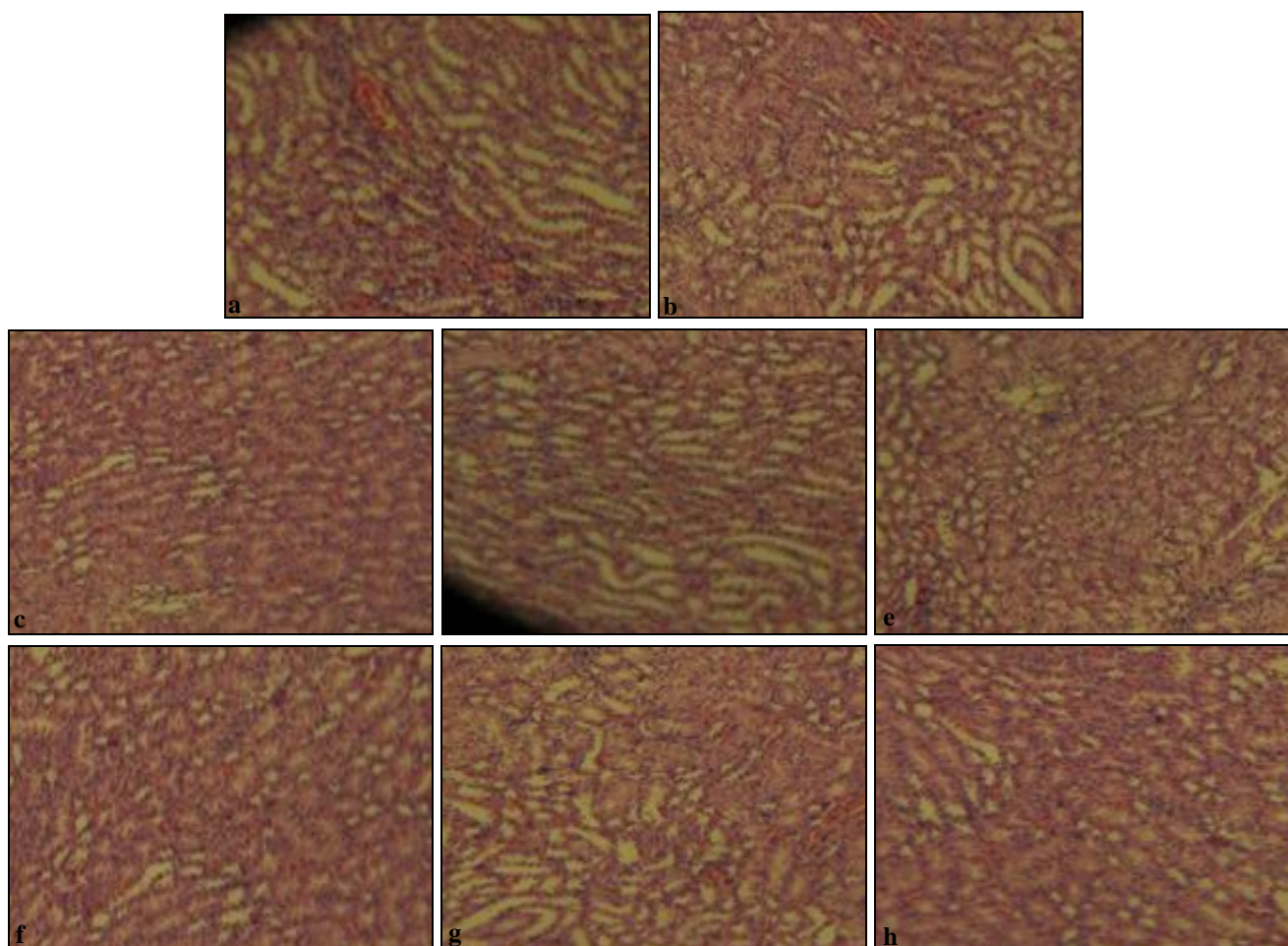


FIG. 3: HISTOLOGICAL EXAMINATIONS OF LIVER OF CONTROL AND EXPERIMENTAL RATS AFTER 28 DAYS OF TREATMENT

DISCUSSION: Medicinal plants consist of a number of biologically active chemical constituents which are formed during the plant's normal metabolic processes. These chemicals are often referred to as “phytochemicals or secondary metabolites.” They have two categories, *i.e.*, primary and secondary constituents. Primary constituents have chlorophyll, proteins, sugar, and amino acids and secondary constituents contain terpenoids, flavonoids, coumarins, glycosides,

phenols, tannins, terpenes, terpenoids and alkaloids³⁵. The WHO is encouraging, promoting and facilitating the effective use of herbal medicine, only a small percentage (5-15%) of the estimated 400,000 - 500,000 plant species have been scientifically and systematically evaluated for their pharmacological activities. Medicinal plants maintain the health and energy of individuals and treat various diseases, including diabetes without causing toxicity³⁶.

The phytotherapeutic effects of plant materials are unique to the particular plant species, and its medicinal effects are due to the combination of secondary product present in plant³⁷. Many conventional drugs have been derived from prototypic molecules in medicinal plants. In the present study, flavonoids, total phenolics, tannins, saponins, alkaloids, and vitamin C were present in considerable quantity in the plant extracts. Flavonoids are a large family of bioactive compounds synthesized by plants. They are the promising alternative for diabetes and its associated complications. It improves and stabilizes the secretion of insulin from pancreatic beta cells, keeping the blood glucose level optimum, reduced aldose reductase activity and compromising continued damage of human islets as well as stabilizing the cellular components is more essential for effective diabetic management. "Insulinomimetic" activities of flavonoids, which are beneficial and desirable effects for diabetics^{38, 39}. It acts as protectors for a wide variety of environmental stresses and is responsible for the radical scavenging effect in humans.

Polyphenols are widely distributed in plant foods. They are the most abundant antioxidants in the diet of human beings⁴⁰. Dietary polyphenol is associated with lower rates of diabetes and cardiovascular disease^{41, 42}. Phenolic compounds have strong *in-vitro* and *in-vivo* antioxidant activities associated with their ability to scavenge free radicals, break radical chain reactions and chelate metals ions⁴³. Several plant polyphenols were reported to inhibit α -amylase and sucrase activity and decreasing postprandial blood sugar level^{44, 45}. Plant tannins are natural polyphenolic compounds of high molecular weight. They have a high antioxidant activity⁴⁶; improved body antioxidant status can protect against degenerative diseases. They have been considered to be cardio-protective, anti-carcinogenic, anti-inflammatory and anti-mutagenic activities. It enhances glucose uptake and inhibits adipogenesis. It can improve the pathological oxidative state of a diabetic situation⁴⁷. Largest and most prevalent of photochemical groups are the alkaloids, terpenes, and phenolics can often have anti-diabetic effects⁴⁸. Saponins reduce the uptake of glucose and cholesterol at the gut and delay glucose transfer from the stomach to the small intestine⁴⁹.

The study showed that the ethanolic extracts of test drugs possess a good amount of vitamin C. It also shows antioxidant activity. Phytochemicals working together with nutrients may help to reduce the risk of many diseases, including diabetes mellitus, cancer, heart disease, stroke and high blood pressure⁵⁰. A blood glucose level of the diabetic rats treated with individual and combined ethanolic extracts of leaf and fruit of *T. dioica* and leaf of *C. ternatea* produced a significant reduction when compared with diabetic control rats. *C. ternatea* leaf extract indicated a maximum reduction in blood glucose level nearly to the level of normal control rats at 28th day of treatment. This might be due to the antihyperglycemic activity of the plant extracts.

The antidiabetic effect of ethanolic extracts of leaf and fruit of *T. dioica* and leaf of *C. ternatea* could be due to the possible presence of the constituents mentioned above in the above said part of the plants used in this particular study, which could act independently or synergistically to enhance the activity of glycolytic and gluconeogenic enzymes. The study revealed that the ethanolic extracts of test drugs possess a good amount of vitamin C. It also exhibits antioxidant activity. Phytochemicals working together with nutrient vitamin C may help to slow the aging process and reduce the risk of many diseases, including diabetes mellitus, high blood pressure, cancer, heart disease and stroke⁵⁰.

Non-enzymic antioxidants such as reduced glutathione (GSH), vitamin C, E and A play an excellent role in protecting the cells from oxidative damage⁵¹. Reduced glutathione is a major endogenous non-enzymic antioxidant which counterbalance free radicals mediated damage. It has a multifaceted role in the antioxidant defense system. It is a direct scavenger of free radicals as well as a co-substrate for peroxide detoxification⁵².

It is well established that GSH is involved in the protection of normal cells and tissue structure and function by maintaining the redox homeostasis, quenching of free radicals, participation in detoxification of xenobiotic reactions, regulation of immune function and keeps up the cellular levels of the active forms of vitamin C and E by neutralizing the free radicals⁵³.

The decreased levels of GSH in the serum, liver, and kidney of STZ-induced diabetic rats were due to chronic oxidative stress is seen in diabetic condition. GSH protects the cells against oxidative stress by reacting with peroxides and hydroperoxides. Decreased activity of GSH is due to decrease GSH formation which requires NADPH and glutathione reductase⁵⁴. Maintenance of NADPH/NADP⁺ ratio plays a crucial role in the regeneration of GSH from GSSG⁵⁵. GSH is also used by aldose reductase for the reduction of glucose to sorbitol through the polyol pathway. The competition for NADPH could be responsible for the decreased glutathione levels found in diabetes mellitus⁵⁶.

A significant elevation of serum, liver, and kidney GSH level were observed in the extracts treated diabetic rats (Group III-Group X). This indicated that the extracts could either increase the biosynthesis of GSH or reduce the oxidative stress leading to less degradation of GSH or have both effects. Administration of ethanolic extracts of leaf and fruit of *T. dioica* and leaf of *C. ternatea*, combined leaf extracts of *T. dioica* + *C. ternatea* and fruit extract of *T. dioica* + leaf extract of *C. ternatea* to the diabetic rats, maintained the levels of non-enzymic antioxidants to near normal by improving the GSH status in serum, liver and kidney.

A non-enzymic antioxidant like reduced glutathione, ascorbate and α -tocopherol play an excellent role in protecting the cells from oxidative damage⁵¹. All these acts synergistically as cellular antioxidants. The most important antioxidant in the cell membrane is α -tocopherol⁵⁷. This molecule is known as chain-breaking antioxidant because its function is to intercept lipid peroxy radicals (LOO^o) and so terminate lipid peroxidation chain reactions. The resultant radical is relatively stable and in normal circumstances, insufficiently reactive to initiate lipid peroxidation itself. This is an essential criterion of a good antioxidant thus protecting cell structures against damage. It helps to build normal and red blood cells as well as working as an antioxidant.

In the present study, the level of vitamin E is lower in diabetic rats which represented an increased utilization of the vitamin due to oxidative stress in

diabetes. This Vitamin exists in interconvertible (reduction and oxidized) form. Thus the reduction in the level of antioxidant Vitamin E can be attributed to reduced regeneration from their oxidized form. People with diabetes may also have greater antioxidant requirements because of increased free radical production with hyperglycemia^{58,59}.

Elevated levels of Vitamin E in experimental groups documented that it prevented the destructive damage that may occur in diabetes. It also may be effective in reducing glycosylation^{60,61}. Ascorbic acid is known to act as an antioxidant both *in-vivo* and *in-vitro*. It functions as a free radical scavenger and successfully prevents detectable oxidative damage under all types of oxidative stress. It plays an important role in the detoxification of reactive intermediates produced by cytochrome P₄₅₀, which detoxify xenobiotics. Reduction in tissue ascorbic acid was observed in STZ-induced diabetic rats. The decrease could have been due to increased utilization of ascorbic acid as an antioxidant defense against increased reactive oxygen species or to a decrease in the GSH level since GSH is required for the recycling of ascorbic acid⁶².

The significant increase of Vitamin C in ethanolic extracts and glibenclamide treated groups when compared to diabetic control might be due to the potent antioxidant effect of the plant extracts. It can protect cell membranes and lipoprotein particles from the oxidative damage by regenerating the antioxidant form of vitamin E. Vitamin C and E act synergistically in scavenging a wide variety of ROS⁶³. The total carotenoids (Vitamin A) have been shown to inhibit tissue lipid peroxidation⁶⁴. Beta-carotene and other carotenoids are also believed to provide antioxidant protection to lipid-rich tissues. Research suggests beta-carotene may work synergistically with vitamin E⁶⁵.

In the present study, the decreased level of Vitamin A observed in untreated diabetic groups might be due to the liberation of lipid peroxide. It is known to be an important natural antioxidant capable of counteracting oxygen free radicals and exerts a protective effect of antioxidant⁶⁶. Increased levels of vitamin A in plant extracts treated rats might be due to decreased levels of lipid peroxides. This can be attributed to the free radical scavenging

potential of the plant extracts shown by the *in-vitro* analysis of the study. The reference drug Glibenclamide treated diabetic group also showed increased levels of non-enzymic antioxidants.

Histopathological Studies:

Histopathological Studies in Pancreatic Tissues:

One of the major findings of this study is that the histopathological investigation along with the biochemical evaluations demonstrated the possibility of the pancreatic tissue regeneration upon combined extract treatment. The regeneration of the pancreas of the STZ destructed islets is probably because pancreas contains few stable cells which have the capacity of regeneration. In this regard, both the plant extracts may contain progenitors cell which may be mobilized into injured pancreatic tissue. On the other hand, progenitor cells may be participating in this repair mechanism. However, the source and nature of these progenitor cells were not determined in this study.

The findings of histopathological investigations in liver and kidney revealed a normal cellular architecture in the normal control group. Cellular necrosis in liver and congestion of convoluted tubules along with deranged glomeruli in kidney were noticed in the diabetic control group. Combined plant extracts treated diabetic groups presented a pattern similar to normal control group however individual extracts revealed the same pattern with some modifications. In the present findings, combined plant extract more effectively stimulate tissue repair than the other individual plant extract treatment and may be clinically beneficial as an agent to restore or maintain tissues after injury.

CONCLUSION: From the present study, it can be concluded that the combined extract of *T. dioica* fruit and *C. ternatea* leaf have potent antidiabetic activity. In this sense, the antihyperglycemic effect may be due to the presence of phytochemicals like flavonoids, phenolics, and tannins in the test plants which are responsible for antioxidant actions and inhibiting the progression of oxidative stress in STZ induced diabetic rats. Hence, these plants can be used in the management of diabetes and diabetic complications.

ACKNOWLEDGEMENT: Nil

CONFLICT OF INTEREST: The author declares that there is no conflict of interest.

REFERENCES:

1. Uchimura K, Nagasaka A and Hayashi R: Changes in superoxide dismutase activities and concentrations and myeloperoxidase activities in leukocytes from patients with diabetes mellitus. *J Diabetes Complications* 1999; 13(5-6): 264-270.
2. Makimattila S, Liu ML and Vakkilainen J: Impaired endothelium-dependent vasodilation in type 2 diabetes. *Diabetes Care* 1999; 22: 973-981.
3. Kesavulu MM, Giri R, Kameswara Rao B and Apparao C: Lipid peroxidation and antioxidant enzyme levels in type 2 diabetics with microvascular complications. *Diab Metab* 2000; 26(5): 387-392.
4. Matough FA, Budin SB, Hamid ZA, Alwahaibi N and Mohamed J: The role of oxidative stress and antioxidants in diabetic complications. *Sultan Qaboos Univ Med J* 2012; 12(1): 5-18.
5. Birben E, Sahiner UM, Sackesen C, Erzurum S and Kalayci O: Oxidative stress and antioxidant defense. *World Allergy Organ J* 2012; 5(1): 9-19.
6. Phaniendra A, Jestadi DB and Periyasamy L: Free radicals: Properties, sources, targets, and their implication in various diseases. *Indian J Clin Biochem* 2015; 30(1): 11-26.
7. Kasote DM, Katyare SS, Hegde MV and Bae H: Significance of antioxidant potential of plants and its relevance to therapeutic applications. *Int J Biol Sci* 2015; 11(8): 982-991.
8. Doss A, Pugalenti M, Rajendrakumar D and Vadivel V: Phenols, flavonoids and antioxidant activity of underutilized legume seeds. *Asian J Exp Biol Sci* 2010; 1: 700-705.
9. Zhou X, Seto SW, Chang D, Kiat H, Razmovski-Naumovski V, Chan K and Bensoussan A: Synergistic effects of Chinese Herbal Medicine: A comprehensive review of methodology and current research. *Front Pharmacol* 2016; 7: 1-16.
10. Parasuraman S, Thing GS and Dhanaraj SA: Polyherbal formulation: Concept of Ayurveda. *Pharmacogn Rev* 2014; 8(16): 73-80.
11. Kavitha R: Antidiabetic and enzymatic antioxidant potential from ethanolic extracts of leaf and fruit of *Trichosanthes dioica* and leaf of *Clitoria ternatea* on diabetic rats induced by streptozotocin. *Asian J Pharm Clin Res* 2018; 11(5): 233-239.
12. Haines HH: The botany of Bihar and Orissa reprinted, Edition Botanical Survey and India, Calcutta, Vol. II, 1961: 406.
13. Hooker JD: Flora of British India. Reprinted edition, Periodical experts, Delhi, Vol. II, 1973: 609.
14. Kanjilal VN: Flora of Assam. Reprinted edition, Vol. II, 1997: 329.
15. Kavitha R and Premalakshmi V: Synergetic effect of *Trichosanthes dioica* and *Clitoria ternatea* leaf extract on the streptozotocin-induced diabetic rats. *Int J Res Pharm and Biomed Sci* 2012; 3(3): 1056-1064.
16. Kavitha R: Evaluation of the hypoglycemic effect of ethanolic extracts of leaf and fruit of *T. dioica* and leaf of *C. ternatea* in streptozotocin-induced diabetic rats. *Int J Pharm Bio Sci* 2014; 5(3): 1061-1068.
17. Parrotta JA: Healing Plants of Peninsular India. CABI Publisher, New York 2001: 382-383.

18. Prajapati ND, Purohit SS, Sharma AK and Kumar T: A Handbook of Medicinal Plants: A complete source book. Agrobios Publisher, Jodhpur, India 2003: 154-155.
19. Khare CP: Encyclopedia of Indian Medicinal Plants. Springer Berlin, Heidelberg, New York 2004: 153-154.
20. Kapoor LD: Handbook of Ayurvedic Medicinal Plants. Boca Raton, FL, USA, CRC Press 2005: 126-127.
21. Kavitha R: Effect of ethanolic extracts of leaf and fruit of *Trichosanthes dioica* and leaf of *Clitoria ternatea* on serum lipids in streptozotocin-induced diabetic rats. Int J Pharm Bio Sci 2015; 6(4): 430-439.
22. Devi BR, Boominathan R and Mandal SC: Anti-inflammatory, analgesic and antipyretic properties of *Clitoria ternatea* root. Fitoterapia 2003; 74: 345-349.
23. Nirmal SA, Bhalke RD, Jadhav RS and Tambe VD: Antihelminthic activity of *Clitoria ternatea*. Pharmacol 2008; 1: 114-119.
24. Lachman J, Hamouz K, Orsak M and Pivec V: Potato tubers as a significant source of human antioxidant nutrition. Rostl Vyr 2000; 46: 231-236.
25. Zhishen J, Mengcheng T and Jianming W: The determination of flavonoid contents in mulberry and their scavenging effects on superoxide radicals. Food Chem 1999; 64: 555-559.
26. Sun B, Richardo-de-silvia JM and Sparger L: Critical factors of vanillin assay for catechins a proanthocyanidins. J Agric Food Chem 1998; 46: 4267-4274.
27. Obadani BO and Ochuko PO: Phytochemical studies and comparative efficacy of the crude extracts of some homeostatic plants in Edo and Delta States of Nigeria. Global J Pure Appl Sci 2001; 8: 203-208.
28. Harborne JB: Phytochemical methods. London Chapman and Hall Ltd., 1973: 49-188.
29. Yen GC and Chen HY: Antioxidant activity of various tea extracts about their antimutagenicity. J Agric Food Chem 1995; 43: 27-32.
30. Ellman GL: Tissue sulfhydryl groups. Arch Biochem Biophys 1959; 82: 70-77.
31. Baker H, Frank O, Angelis B and Feingold S: Plasma tocopherol in man at various times after ingesting free or acetylated tocopherol. Nutr Rep Int 1951; 21: 531-536.
32. Nino HV and Shah W: Vitamins. In: Tietz NW. Editor. Fundamentals of clinical chemistry, WB Saunders, Philadelphia, USA, Edition 2nd, 1986: 547-550.
33. Neeld JB and Pearson WN: Macro-and micro-methods for the determination of serum vitamin A using trifluoroacetic acid. J Nutr 1963; 79: 454-462.
34. Allen RG: Oxygen-reactive species and antioxidant responses during development: the metabolic paradox by cellular differentiation. Proc Soc Exp Biol Med 1991; 196: 117-129.
35. Wadood A, Ghufran M, Jamal SB, Naeem M, Khan A, Ghaffar R and Asnad: Phytochemical analysis of medicinal plants occurring in the local area of Mardan. Biochem Anal Biochem 2013; 2(4): 2-4.
36. Choudhury H, Pandey M and Hua CK: An update on natural compounds in the remedy of diabetes mellitus: A systematic review. J Traditional and Complementary Medicine 2018; 8: 361-376.
37. Uddin G, Sattar S and Rauf A: Preliminary phytochemical. *In-vitro* pharmacological study of *Bauhinia alba* and *Bauhinia variegata* flowers. Middle-East J Medicinal Plants Res 2012; 1(4): 75-79.
38. Alagammal M, Agnel RA and Mohan VR: Antidiabetic and antihyperlipidaemic effect of *Polygala javana* DC on alloxan induced diabetic rats. Int Res J Pharm 2012; 3: 231-234.
39. Mohan S and Nandhakumar L: Role of various flavonoids: Hypotheses on novel approach to treat diabetes. J Medical Hypotheses and Ideas 2014; 8: 1-6.
40. Lin D, Xiao M and Zhao J: An overview of plant phenolic compounds and their importance in human nutrition and management of type 2 diabetes. Molecules 2016; 21: 1-19.
41. Grosso G, Stepaniak U, Micek A, Kozela M, Stefler D, Bobak M and Pajak A: Dietary polyphenol intake and risk of type 2 diabetes in the Polish arm of the Health, Alcohol and Psychosocial factors in Eastern Europe (HAPIEE) study. Br J Nutr 2017; 118(1): 60-68.
42. Zujko ME, Waśkiewicz A, Witkowska AM: Dietary total antioxidant capacity and dietary polyphenol intake and prevalence of metabolic syndrome in polish adults: A nationwide study. Oxidative Medicine and Cellular Longevity 2018; 1-11.
43. Zujko ME, Waśkiewicz A, Witkowska AM: Dietary total antioxidant capacity and dietary polyphenol intake and prevalence of metabolic syndrome in polish adults: A nationwide study. Oxidative Medicine and Cellular Longevity 2018; 1-10.
44. Jo SH, Cho CY, Lee JY, Ha KS, Kwon YI and Apostolidis E: *In-vitro* and *in-vivo* reduction of post-prandial blood glucose levels by ethyl alcohol and water *Zingiber mioga* extracts through the inhibition of carbohydrate hydrolyzing enzymes. BMC Complement Altern Med 2016; 16(111): 1-7.
45. Agarwal P and Gupta R: Alpha-amylase inhibition can treat diabetes mellitus. Research and Reviews Journal of Medical and Health Sciences 2016; 5(4): 1-8.
46. Mojzer EB, Hrnčič MK, Škerget M, Knez Z and Bren U: Polyphenols: Extraction methods, antioxidative action, bioavailability and anticarcinogenic effects. Molecules 2016; 21: 2-38.
47. Kumari M and Jain S: Tannins: An antinutrient with positive effect to manage diabetes. Res J Rec Sci 2012; 1(12): 1-8.
48. Afrisham R, Aberomand M, Ghaffari MA, Siahpoosh A and Jamal M: Inhibitory effect of *H. persicum* and *Z. jujuba* on activity of α -amylase. J Bot 2015; 2015: 1-8.
49. Jesch ED and Carr TP: Food ingredients that inhibit cholesterol absorption. Prev Nutr Food Sci 2017; 22(2): 67-80.
50. Zhang YJ, Gan RY, Li S, Zhou Y, Li AN, Xu DP and Li HB: Antioxidant phytochemicals for the prevention and treatment of chronic diseases. Molecules 2015; 20: 21138-21156.
51. Kurutas EB: The importance of antioxidants which play the role in cellular response against oxidative/nitrosative stress: current state. Nutr J 2016; 15: 71.
52. Sathiya Jeeva J, Sunitha J, Ananthalakshmi R, Rajkumari S, Ramesh M and Krishnan R: Enzymatic antioxidants and its role in oral diseases. J Pharm Bioallied Sci 2015; 7(2): S331-S333.
53. Hea L, Hea T, Farrarb S, Jia L, Liua T and Maa,c X: Antioxidants maintain cellular redox homeostasis by elimination of reactive oxygen species. Cell Physiol Biochem 2017; 44: 532-553.
54. Garg MC, Ojha S and Bansal DD: Antioxidant status in streptozotocin diabetic rats. Int J Exp Biol 1996; 34: 264-266.
55. Jain SK: Glutathione and glucose-6-phosphate dehydrogenase deficiency can increase protein glycation. Free Radic Biol Med 1998; 24: 197-201.
56. De Mattia G, Laurenti O, Bravi C, Ghiselli A, Iuliano L and Balsano F: Effect of aldose reductase inhibition on

- glutathione redox status in erythrocytes of diabetic patients. *Metabolism* 1994; 43: 965-968.
57. Santhakumari P, Prakasam A and Pugalendi KV: Modulation of oxidative stress parameters by treatment with *Piper betle* leaf in streptozotocin-induced diabetic rats. *Indian J Pharmacol* 2003; 35: 373-378.
 58. Konig GM, Wright AD and Keller WJ: Hypoglycaemic activity of an HMG-containing flavonoid glucoside, chamaemeloside, from *Chamaemelum nobile*. *Planta Med* 1998; 64(7): 612-614.
 59. Jouad H, Eddouks M, Lacaille-Dubois MA and Lyoussi B: Hypoglycaemic effect of *Spergularia purpurea* in normal and streptozotocin-induced diabetic rats. *J Ethnopharmacol* 2000; 71: 169-177.
 60. Jain SK, Mc Vie R and Jaramillo JJ: Effect of Modest Vitamin E supplementation on blood glycated hemoglobin and triglyceride levels and red cell indices in type 1 diabetic patients. *J Am Coll Nutr* 1996; 15: 458-461.
 61. Jain SK, Mc Vie R and Smith T: Vitamin supplementation restores glutathione and malondialdehyde to normal concentrations in erythrocytes of type 1 diabetic children. *Diab Care* 2000; 23(9): 1389-1394.
 62. Hunt JV: Ascorbic acid and diabetes mellitus. *Subcell Biochem* 1996; 25: 369-405.
 63. Senthilkumar K and Jeyaprakash K: Antioxidant and cytotoxic efficacy of chitosan on bladder cancer. *Asian Pacific J Tropical Disease* 2012; S769-S773.
 64. Kartha VNR and Krishnamurthy S: Effect of Vitamins antioxidants and sulfhydryl compounds on *in-vitro* rat brain lipid peroxidation. *Int J Vit Nut Res* 1978; 48: 38-43.
 65. Suzuki K, Ito Y and Nakamura S: Relationship between serum carotenoids and hyperglycemia: a population-based cross-sectional study. *J Epidemiol* 2002; 12: 357-366.
 66. Wang N, Wang Li P and Peng W: Hepatoprotective effect of *Hypricum japonicum* extract and its function. *J Ethnopharmacol* 2008; 116: 1-6.

How to cite this article:

Kavitha R: Effect of ethanolic extracts of Indian medicinal plants on the non-enzymatic antioxidant system in streptozotocin induced diabetic rats in comparison with Glibenclamide. *Int J Pharm Sci & Res* 2019; 10(1): 418-30. doi: 10.13040/IJPSR.0975-8232.10(1).418-30.

All © 2013 are reserved by International Journal of Pharmaceutical Sciences and Research. This Journal licensed under a Creative Commons Attribution-NonCommercial-ShareAlike 3.0 Unported License.

This article can be downloaded to **ANDROID OS** based mobile. Scan QR Code using Code/Bar Scanner from your mobile. (Scanners are available on Google Playstore)