IJP (2017), Vol. 4, Issue 10 **(Research Article)**

Received on 21 May 2017; received in revised form, 22 August 2017; accepted, 17 September 2017; published 01 October 2017

PROTECTIVE PROFILE OF *CITRULLUS COLOCYNTHIS* ROOT EXTRACTS ON LIPID PROFILE STATUS IN STZ CHALLENGED RATS

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Keywords:

Anti-hyperlipidemic activity, *Citrullus colocynthis*, Cardiovascular diseases, Streptozotocin

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ABSTRACT: Diabetes mellitus is one of the widespread and severe metabolic disorders in humans all over the world. It is initially characterized by a loss of glucose homeostasis resulting from defects in insulin secretion, insulin action or both resulting in impaired glucose metabolism and other energy-yielding fuels such as lipids and proteins. The association of hyperglycemia with altered lipid parameters presents a major risk for all cardiovascular diseases. In recent years, there has been an increased inclination towards herbal drugs due to the trend towards the natural sources and healthy lifestyle. The present study was designed to evaluate the potential antihyperlipidemic efficacy of *Citrullus colocynthis* roots in streptozotocin (STZ) induced diabetic rats. Diabetes was induced by giving streptozotocin (35-50mg/kg) intraperitoneally. The aqueous and ethanolic root extracts of *Citrullus colocynthis* (AECC and EECC) were administered at a dose of 100, 200, 300 mg/kg orally. Metformin was given as a standard drug at a dose of 50mg/kg orally. The fasting and postprandial blood glucose levels were estimated by the glucose oxidase method. Serum insulin levels were measured and found a distinguish raise in the insulin levels in extract treated groups. The plasma levels of cholesterol (CH), triglycerides (TG), low-density lipoproteins (LDL) and very low-density lipoproteins (VLDL) were estimated and found to be significantly ($p<0.0001$) lowered in extract treated diabetic rats. The results showed that the present study provided a rationale for the use of *Citrullus colocynthis* root extracts as antidiabetic and antihyperlipidemic agent.

INTRODUCTION: Diabetes mellitus is a chronic disease caused by inherited and acquired deficiency in production of insulin by the pancreas and by the ineffectiveness of the insulin produced.

QUICK RESPONSE CODE

DOI: 10.13040/IJPSR.0975-8232.IJP.4(10).338-44

The article can be accessed online on www.ijpjournal.com

DOI link: http://dx.doi.org/10.13040/IJPSR.0975-8232.IJP.4(10).338-44

Such a deficiency results in increased plasma glucose, which in turn damages many of the body's systems, in particular, the blood vessels and nerves. Besides hyperglycemia, the levels of plasma lipids are usually raised in diabetes mellitus causing a risk factor for coronary heart disease [1]. Hypertriglyceridemia is also related to insulin resistance and glucose intolerance [2]. It is characterized by increased levels of cholesterol (CH), triglycerides (TG), low-density lipoproteins (LDL) and very low-density lipoproteins (VLDL) [3]. NDDM has also been associated with an increased

risk of premature arteriosclerosis with an increase in triglycerides and low-density lipoprotein levels. About 70-80% of deaths in diabetic patients are due to vascular disease [4]. Treatment for diabetic hyperlipidemia includes glycemic control, exercise and lipid-lowering diet and drugs [5]. Currently, the available therapy of diabetes includes insulin and various oral antidiabetic agents such as sulfonylureas, thiazolidinediones, α- glucosidase inhibitors, etc. These drugs are used as monotherapy or in combination to achieve better glycemic control. Each of the above oral antidiabetic agents is associated with several serious adverse effects [6]. An ideal treatment for diabetes would be a drug that not only controls the glycemic level but also prevent the development of arteriosclerosis and other complications of disease [7].

Despite the remarkable progress in the management of diabetes mellitus by synthetic drugs, there has been renewed interest in the medical plants attributed to therapeutic virtues. The use of herbal medicines for the treatment of diabetes has gained importance throughout the world. Hence there is an increased demand to use natural products which shows effects on lowering hyperglycemia along with hypercholesterolemia and hyper-triglyceridemia.

The plants which show significant pharmacological activity and low toxicity need extensive screening. *Citrullus collicynthis* belonging to the family of Cucurbitaceae is one of the ancient plants in the world, which is used in the traditional system for various ailments. It is a tree found in Mediterranean Basin and Asia, is distributed among the west coast of Northern Africa eastwards through Sahara until India. It is commonly known as bitter apple, bitter cucumber. It is an annual or perennial plant in Indian arid zones and has a great survival rate under extreme xeric conditions. The whole plant has many medicinal properties as an anti-inflammatory, anti-candidial and bacterial, anti-oxidant and free radical scavenging activity, *etc*.

The plant subjected to the current research work had been used traditionally as anti-diabetic, the fruit is scientifically proved as antidiabetic; therefore, it was thought interested to evaluate the antidiabetic profile of the selected plant part (root) in streptozotocin challenged rats which have not yet been scientifically undertaken.

MATERIALS AND METHODS:

Collection of Plant Material: The plant material (root) was collected from Tirumala hills, Tirupathi, A. P., India bearing a voucher specimen no. 1487. The plant material was identified and authenticated taxonomically by botanist, Department of Botany, S.V University, Tirupathi.

Preparation of Extracts: The shade dried plant materials were crushed, powdered and exhaustively defatted by petroleum ether (60 °C - 80 °C) and then successively extracted with ethanol and water. All the extracts were filtered, pooled and concentrated under reduced pressure using rotavapor (Buchi, USA).

Preliminary Phytochemical Analysis: The preliminary phytochemical screening of extract of *Citrullus colocynthis* gave positive tests for carbohydrates, resins, saponin, anthraquinone, steroids, and alkaloids [8].

Animals: Animal protocol was approved by IAEC (Institutional Animal Ethical Committee) of CPCSEA (Committee for the purpose of Control and Supervision of Experimentation on Animals) through its reference no: IAEC/SVCP/2011/008, dated: 26/7/11. Male Wistar rats, weighing (180-250gms) were obtained from NIN (National Institute of Nutrition), Hyderabad. The animals were housed with free access to food and water for at least one week in an air-conditioned room (25 °C) under a 12 h, light: dark cycle before the experiment. They were fed with a standard diet (Hindustan Lever) and water *ad libitum*.

Anti-diabetic Activity:

Induction of Experimental Diabetes: Diabetes was induced by a single intraperitoneal injection of a freshly prepared Streptozotocin (STZ) solution (Sisco Research laboratories Pvt Ltd. Mumbai - 93, India. Batch No: T-835796) (Dose: 30-50mg/kg) in citrate buffer 0.1 M, pH 4.5 to overnight fasted rats. Diabetes was identified by polydipsia, polyuria and by measuring blood glucose levels 48 h after injection of STZ. Animals that did not develop more than 250 mg/100 ml of blood glucose levels were rejected [9].

Experimental Groups: The animals were divided into fifteen groups of 6 animals each.

- **Group I:** Normal untreated rats (Control).
- **Group II:** Diabetic control (STZ).
- **Group III:** Diabetic rats given with metformin (50 mg/kg) (o).
- **Group IV:** Normal rats given with aqueous root extract (AECC) (100 mg/kg) (o).
- **Group V:** Normal rats given with aqueous root extract (AECC) (200 mg/kg) (o).
- **Group VI:** Normal rats given with aqueous root extract (AECC) (300 mg/kg) (o).
- **Group VII:** Normal rats given with ethanolic root extract (EECC) (100 mg/kg) (o).
- **Group VIII:** Normal rats given with ethanolic root extract (EECC) (200 mg/kg) (o).
- **Group IX:** Normal rats given with ethanolic root extract (EECC) (300 mg/kg) (o).
- **Group X:** Diabetic rats given with aqueous root extract (AECC) (100 mg/kg) (o).
- **Group XI:** Diabetic rats given with aqueous root extract (AECC) (200 mg/kg) (o).
- **Group XII:** Diabetic rats given with aqueous root extract (AECC) (300 mg/kg) (o).
- **Group XIII:** Diabetic rats given with ethanolic root extract (EECC) (100 mg/kg) (o).
- **Group XIV:** Diabetic rats given with ethanolic root extract (EECC) (200 mg/kg) (o).
- **Group XV:** Diabetic rats given with ethanolic root extract (EECC) (300 mg/kg) (o).

Animals of group I were given with 0.9% saline and served as control and groups II served as diabetic control, group III served as standard, groups IV, V, VI, VII, VIII, IX are normal rats treated with aqueous root extract of *Citrullus colocynthis* (AECC) and ethanolic root extract of *Citrullus colocynthis* at the doses of 100 mg/kg, 200mg/kg, 300mg/kg respectively. Groups X, XI, XII are diabetic rats treated with aqueous root extract of *Citrullus colocynthis* (AECC), groups XIII, XIV, XV are diabetic rats treated with ethanolic root extract of *Citrullus colocynthis* (EECC) at the doses of 100 mg/kg, 200 mg/kg, 300 mg/kg respectively for a period of 15 days.

On the 16th day, blood was collected by retro-orbital sinus puncture. Blood withdrawn was centrifuged, and serum was separated for biochemical study. Serum lipid profile (total cholesterol, triglycerides, HDL cholesterol, LDL cholesterol, and VLDL-cholesterol) was measured by using ERBA reagents and ERBA kit in Semi-Auto Analyzer. The Fasting blood glucose (FBS) and Post-Prandial glucose (PLBS) levels were estimated by Glucose-oxidase method [10].

Oral Glucose Tolerance Test (OGTT): Diabetes was induced by an intraperitoneal injection of freshly prepared STZ (30-50mg/kg) in rats. 15 groups of six animals in each group were used. The OGTT was performed in overnight fasted (18 h) animals. After overnight fasting a 0 min blood sample (0.2 ml) was taken from each rat in the different groups. Test drugs were administered orally in 0.25% carboxymethyl cellulose, and standard drug metformin was also administered orally in diabetic rats. Glucose solution (2g/kg) was administered orally 30 min after the administration of extracts. Blood samples were taken at 0 minutes, 30 min, 60 min, 90 min and 120 min after glucose administration. All the blood samples were collected with potassium and sodium fluoride solution for the estimation of blood glucose [11].

Statistical Analysis: The results of the estimation were reported as Mean ± SEM. Student's t-test was applied when two groups amongst were compared. The values were considered significant when $p<0.05$, $p<0.001$, $p<0.0001$. Statistical calculations were done using Graph Pad Prism.

RESULTS: In rats, diabetes was induced by using STZ at a dose of (30-50mg/kg), where blood glucose levels were > 250mg/dl that indicated the induction of diabetes and the results were evaluated. The acute oral toxicity study of *Citrullus colocynthis* showed no mortality rate up to 2000 mg/kg.

OGTT was performed in all the rats from the group I to group XV (n = 6). **Table 1** shows the results of an oral glucose tolerance test. All the drug-treated (AECC and EECC) groups at 100 mg/kg, 200 mg/kg and 300 mg/kg doses in diabetic rats showed a significant reduction in blood glucose values at 60, 90 and 120 min ($p<0.0001$) respectively when compared to the diabetic control group.

TABLE 1: EFFECT OF *CITRULLUS COLOCYNTHIS* ROOT EXTRACT ON OGTT IN NORMAL AND DIABETIC RATS

Groups	Treatment	0 min	30 min	60 min	90 min	120 min
I	Normal	81.0±0.763	102.6±2.036	96.51±1.46	91.6±1.46	80.71±1.59
II	Diabetic Control	^{b}296.83±4.43	^{b}273.40±2.98	^{b}296.7±3.35	^{b}294.35±2.04	^{b}270.08±1.54
III	Metformin + D	^{b}283.91±2.36	^{b}262.63±2.30	^{b}245.34±3.23	^{b}171.76±2.53	^{b}129.41±2.72
IV	N+AECC 100mg/ml	79.10±0.85	84.86±1.82	83.23±1.00	80.67±0.69	79.51±1.69
V	N+AECC 200mg/ml	89.80±1.32	81.64±1.408	82.68±1.24	79.36±2.030	77.94±1.308
VI	N+AECC 300mg/ml	85.96±1.52	83.41±1.505	81.67±1.77	80.74±0.683	77.09±1.501
VII	N+EECC 100mg/ml	81.15±2.57	79.97±0.871	78.26±1.801	77.94±1.221	78.33±1.51
VIII	N+EECC 200mg/ml	82.98±0.846	80.54±0.55	82.68±0.68	78.44±0.933	71.47±0.801
IX	N+EECC 300mg/ml	82.03±0.424	81.70±0.368	77.87±1.55	77.98±0.39	74.56±0.62
X	D+AECC 100mg/ml	^{NS}297.54±4.035	^{NS}272.83±2.47	^{b}257.15±2.72	^{b}179.10±1.93	^{b}160.82±1.720
XI	D+AECC 200mg/ml	^{NS}288.07±1.48	^{NS}269.42±2.205	^{b}188.74±2.09	^{b}172.44±2.08	^{b}149.26±1.640
XII	D+AECC 300mg/ml	^{NS}293.47±2.36	^{NS}271.76±1.83	^{b}184.37±1.23	^{b}159.08±0.936	^{b}139.76±0.841
XIII	D+EECC 100mg/ml	^{NS}290.06±2.72	^{NS}276.59±1.168	^{b}267.43±1.55	^{b}182.62±2.05	^{b}167.76±1.109
XIV	D+EECC 200mg/ml	^{NS}283.16±0.95	^{NS}277.73±3.36	^{b}199.78±2.69	^{b}177.66±2.38	^{b}157.78±1.437
XV	D+EECC 300mg/ml	^{NS}287.08±2.60	^{NS}270.69±4.83	^{b}181.18±1.54	^{b}161.27±1.92	^{b}140.82±1.33

Values were reported as Mean ± SEM. Diabetic control compared with Normal $^{b}p < 0.0001$; Diabetic + Metformin compared to diabetic control group, $^{b}p < 0.0001$; Diabetic + AECC and Diabetic + EECC compared to diabetic control, $^{b}p<0.0001$, $^{a}p<0.001$.

Table 2 shows the levels of blood glucose levels, *i.e.*, FBS and PLBS in control and experimental animals. Diabetic rats showed a significant increase in blood glucose compared to corresponding control rats. Following the oral administration of aqueous and ethanolic extracts of *Citrullus colocynthis* (200 mg/kg, 300 mg/kg) PLBS levels significantly decreased ($p<0.0001$) in the diabetic treated group when compared to the diabetic control group. In the present study, metformin was used as a standard oral hypoglycemic agent, which showed a significant reduction in postprandial blood glucose as compared to diabetic rats.

TABLE 2: EFFECT OF *CITRULLUS COLOCYNTHIS* ON BLOOD GLUCOSE LEVELS IN CONTROL AND EXPERIMENTAL RATS

Groups	Treatment	FBS mg/dl	PLBS mg/dl
I	Normal	95.6 ± 2.32	135.5 ± 2.56
II	Diabetic Control	^{b}299.04 ± 3.61	292.3 ± 3.16
III	Metformin+D	^{NS}290.41 ± 4.64	155.16 ± 1.310
IV	N+AECC 100mg/ml	^{NS}88.5 ± 2.35	90.14 ± 2.62
V	N+AECC 200mg/ml	^{NS}86.32 ± 1.05	92.45 ± 3.80
VI	N+AECC 300mg/ml	^{NS}90.15 ± 1.40	94.82 ± 0.892
VII	N+EECC 100mg/ml	^{NS}90.32 ± 3.21	25.61 ± 0.642
VIII	N+EECC 200mg/ml	^{NS}89.62 ± 2.51	96.32 ± 0.182
IX	N+EECC 300mg/ml	^{NS}91.41 ± 0.93	92.15 ± 0.143
X	D+AECC 100mg/ml	^{NS}280.83 ± 1.61	185.41 ± 1.82
XI	D+AECC 200mg/ml	^{NS}282.0 ± 2.32	175.69 ± 2.08
XII	D+AECC 300mg/ml	^{NS}279.0 ± 0.65	165.83 ± 1.81
XIII	D+EECC 100mg/ml	^{NS}275 ± 1.60	189.32 ± 1.23
XIV	D+EECC 200mg/ml	^{NS}278 ± 2.34	177.52 ± 2.42
XV	D+EECC 300mg/ml	^{NS}281.0 ± 1.82	165.0 ± 0.89

Values were reported as Mean ± SEM. Diabetic control compared with Normal $^{b}p<0.0001$; Normal (control) group compared to all extract treated normal groups, NS-Not significant; Diabetic + Metformin compared to diabetic control group, $^{b}p < 0.0001$; Diabetic + AECC and Diabetic + EECC compared to diabetic control, $^{b}p<0.0001$, $^{a}p<0.001$.

TABLE 3: EFFECT OF *CITRULLUS COLOCYNTHIS* ON SERUM INSULIN LEVELS IN CONTROL AND DIABETIC RATS

Groups	Treatment	Dose (mg/kg)	Insulin levels
I	Normal	-	7.82±0.82
II	Diabetic Control	-	^{b}3.50±0.21
III	Metformin+D	50mg/kg	^{b}10.32±1.02
IV	N+AECC	100 mg/kg	^{NS}8.02±1.06
V	N+AECC	200 mg/kg	^{NS}8.50±3.02
VI	N+AECC	300mg/kg	^{NS}8.00±2.10
VII	N+EECC	100 mg/kg	^{NS}7.35±1.34
VIII	N+EECC	200mg/kg	^{NS}7.62±2.62
IX	N+EECC	300 mg/kg	^{NS}7.92±0.83
X	D+AECC	100 mg/kg	7.15±0.73
XI	D+AECC	200 mg/kg	^{b}7.80±0.50
XII	D+AECC	300 mg/kg	^{b}8.00±0.23
XIII	D+EECC	100 mg/kg	^{b}7.86±0.28
XIV	D+EECC	200 mg/kg	^{b}8.00±0.30
XV	D+EECC	300 mg/kg	^{b}8.31±0.21

Values were reported as Mean ± SEM. Diabetic control compared with Normal $^{b}p<0.0001$; Normal (control) group compared to all extract treated normal groups, NS-Not significant; Diabetic + Metformin compared to diabetic control group, $^{b}p<0.0001$; Diabetic + AECC and Diabetic + EECC compared to diabetic control, $^{b}p<0.0001$, $^{a}p<0.001$.

The anti-hyperlipidemic activity was evaluated by the results obtained. **Table 3** shows the increased levels of serum cholesterol, triglycerides, LDL, VLDL and decrease in HDL levels found in diabetic rats. Administration of (AECC) aqueous extract of *Citrullus colocynthis* (200 mg/kg, 300 mg/kg) showed a significant reduction ($p<0.0001$) in the level of serum cholesterol, TG's, LDL and VLDL. It was also observed that HDL levels increased significantly and the values were almost near to the values of normal rats. Similarly administration of (EECC) ethanolic extract of *Citrullus colocynthis* (200 mg/kg, 300 mg/kg) also showed a significant reduction ($p<0.0001$) in the level of cholesterol, triglycerides, LDL and VLDL as well as raise in HDL simultaneously when compared to the corresponding diabetic rats.

The insulin levels were also monitored in the extract treated groups. In the group that received aqueous extract (200 mg/kg and 300 mg/kg) have shown a significant increase in insulin levels when compared to that of diabetic control. Similarly, there was an increase in insulin levels significantly ($p < 0.0001$) in the groups treated with ethanolic extract of *Citrullus colocynthis* (200mg/kg, 300mg/kg). **Table 4** depicts the insulin levels in drug-treated groups.

TABLE 4: EFFECT OF *CITRULLUS COLOCYNTHIS* ON LIPID PROFILE IN CONTROL AND DIABETIC RATS

Groups	Treatment	CH	TG	HDL	LDL	VLDL
I	Normal	131.58±3.51	76.125±3.43	49.48±2.72	84.69±3.90	14.4±0.92
II	Diabetic Control	^{b}200.06±1.90	^{b}150.60±1.83	^{b}21.20±1.28	^{b}130±1.24	^{b}30.50±2.00
III	Metformin + D	^{b}141.01±1.42	^{b}144.57±1.89	^{b}41.35±1.63	^{b}73.80±1.60	^{b}27.41±1.24
IV	N+AECC 100mg/ml	^{NS}137.25±1.54	^{NS}61.06±1.175	^{NS}52.21±1.90	^{NS}86.77±1.80	^{NS}11.35±0.247
V	N+AECC 200mg/ml	^{NS}137.66±2.44	^{NS}58.59±2.83	^{NS}48.52±1.17	^{NS}89.19±1.96	^{NS}11.31±0.41
VI	N+AECC 300mg/ml	^{NS}156.17±2.00	^{NS}79.00±1.55	^{NS}57.47±1.58	^{NS}91.20±0.99	^{NS}15.96±0.260
VII	N+EECC 100mg/ml	^{NS}149.98±2.77	^{NS}77.6±1.76	^{NS}50.69±1.99	^{NS}91.15±1.52	^{NS}11.75±0.45
VIII	N+EECC 200mg/ml	^{NS}145.82±1.42	^{NS}75.10±0.28	^{NS}52.62±3.42	^{NS}89.18±1.32	^{NS}12.62±2.12
IX	N+EECC 300mg/ml	^{NS}140.00±2.03	^{NS}78.60±1.23	^{NS}56.42±1.02	^{NS}85.10±2.02	^{NS}12.00±1.62
X	D+AECC 100mg/ml	^{NS}203.60±2.00	^{NS}149.17±2.61	^{b}37.54±2.47	^{NS}135.59±3.4	^{NS}32.23±0.78
XI	D+AECC 200mg/ml	^{b}166.22±1.44	^{a}142.60±1.33	^{b}39.11±0.473	^{b}101.01±1.58	^{NS}26.07±0.82
XII	D+AECC 300mg/ml	^{b}153.45±1.66	^{b}124.18±1.19	^{b}42.94±2.34	^{b}86.22±1.05	^{b}19.69±0.77
XIII	D+EECC 100mg/ml	^{NS}199.75±0.87	^{NS}145.62±1.53	^{b}31.62±1.066	^{NS}131.88±0.96	^{NS}33.14±0.72
XIV	D+EECC 200mg/ml	^{b}164.96±1.60	^{b}142.48±1.405	^{b}134.50±1.31	^{b}94.07±1.14	^{b}18.11±0.78
XV	D+EECC 300mg/ml	^{b}156.32±1.30	^{b}122.29±1.32	^{b}43.94±1.22	^{b}77.77±0.64	^{b}16.78±0.86

Values were reported as Mean ± SEM. Diabetic control compared with Normal $^{b}p < 0.0001$; Normal (control) group compared to all extract treated normal groups, NS-Not significant; Diabetic + Metformin compared to diabetic control group, $^{b}p < 0.0001$; Diabetic + AECC and Diabetic + EECC compared to diabetic control, $^{b}p < 0.0001$, $^{a}p < 0.001$.

DISCUSSION: In the present study the hypoglycaemic and antihyperlipidemic activities of the aqueous and ethanolic root extract of *Citrullus colocynthis* was evaluated in streptozotocin-induced diabetic rats. Continuous treatment of *Citrullus colocynthis* root extracts for 15 days caused a significant reduction in blood glucose levels in diabetic rats indicating that the *Citrullus colocynthis* root extracts may be useful in the management of diabetes. Both the extracts (AECC and EECC) also caused an increase in the insulin levels of diabetic rats. This finding supports the previous reports of the effectiveness of the plant in the treatment of diabetes.

Streptozotocin (STZ) (2-deoxy-2-(3-methyl-3-nitrosuuredio)-D-glucopyranose) is commonly used for experimental induction of type-I diabetes mellitus, which causes selective pancreatic islet β-cell cytotoxicity mediated through the release of nitric oxide (NO). This results in a rapid reduction in pancreatic islet pyridine nucleotide concentration and subsequent β -cell necrosis. The action of STZ on mitochondria generates SOD anions, which leads to diabetic complications [12]. Based on the above perspectives, in the present study, the antidiabetic activity has been assessed in rats made diabetic by STZ. Diabetes affects both glucose and lipid metabolism [13].

The preliminary phytochemical screening of the extract revealed the presence of glycosides (saponin glycoside), alkaloids, flavonoids, and resins. The administration of AECC and EECC showed a significant lowering of postprandial blood glucose levels in diabetic drug-treated groups. Both the extracts have also shown raise in insulin levels in diabetic extract treated groups significantly. This signifies that *Citrullus colocynthis* root extracts are lowering the blood glucose by not only increasing the glucose uptake by the cells but also significantly raising the insulin levels which is, therefore, sensitizing the cells for insulinotropic action.

Insulin deficiency depletes the activity level of lipoprotein lipase, thus leading to deranged lipoprotein metabolism during diabetes [14]. The lipoprotein levels in the STZ induced diabetic rats of the present study reveal a significant alter in lipoprotein metabolism. Since insulin has a potent inhibitory effect on lipolysis in adipocytes, insulin deficiency is associated with excess lipolysis and increased influx of free fatty acids to the liver [15, 16]. The increased levels of low-density lipoprotein (LDL) and very low-density lipoprotein (VLDL) in the diabetic animals might be due to overproduction of LDL and VLDL by the liver due to the stimulation of hepatic triglyceride synthesis as a result of the free fatty acid influx. The high-density lipoprotein (HDL) was significantly reduced in the diabetic rats which indicate a positive risk factor for atherosclerosis [17]. Supplementations of *Citrullus colocynthis* to treated diabetic groups restored the lipid profile. The rise in the insulin levels may contribute to its strong inhibitory action on lipolysis. When the root extracts of *Citrullus colocynthis* were given, there was significant reduction CH, TG'S, LDL, VLDL and increase in HDL in extract treated diabetic rats ($p<0.0001$).

In diabetic condition, there is an increase in insulin resistance and a decrease in glucose uptake by the peripheral tissues. Moreover, due to deficiency of insulin, there is altered lipid metabolism which raises the lipid levels. Both the root extracts of the plant *Citrullus colocynthis* have shown a significant lowering of blood glucose levels, and an increase in insulin levels signifies the increased glucose uptake due to reduced insulin resistance. Increase in insulin levels is also responsible for the lowering of CH, TG'S, LDL, VLDL and raise in HDL levels.

CONCLUSION: Our study had shown that the AECC and EECC of *Citrullus colocynthis* root possess blood glucose, cholesterol and triglycerides lowering effect in streptozotocin-induced hyperglycaemic rats. In conclusion, the anti-oxidants present in plants such as glycosides, flavonoids, saponins are known to reduce hyper-lipidaemia in diabetes. Preliminary phytochemical screening revealed the presence of saponins, resins, flavonoids in the extracts. Thus, the phytochemical constituents present in *Citrullus colocynthis* root extract may be responsible, in part, for the hypoglycaemic effect. The hypoglycaemic effect of the extract may be implicated as the major reason for the observed antihyperlipidaemic effect of the extract. The work showed that *Citrullus colocynthis* root extract may be used for the control and management of diabetes.

ACKNOWLEDGEMENT: Nil

CONFLICT OF INTEREST: Nil

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How to cite this article:
Kalva S and Ragunandan N: Protective profile of *Citrullus colocynthis* root extracts on lipid profile status in STZ challenged rats. Int J Pharmacognosy 2017; 4(10): 338-44. doi link: http://dx.doi.org/10.13040/IJPSR.0975-8232.IJP.4(10).338-44.