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Original Research Article

The Effect of *Coriandrum Sativum* Seed Extract on Hyperglycemia, Lipid Profile and Renal Function in Streptozotocin Induced Type- 2 Diabetic Swiss Albino Mice

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ABSTRACT

Background: Convectional drug treatment for diabetes mellitus carries risk that leads to many adverse effects such weight loss and hypoglycemia. Ethiopia is rich in natural resources and medicinal plants useful in the treatment of diabetes mellitus.
Aim of the study: To investigate the effect of *Coriandrum sativum* seed extracts on hyperglycemia, lipid profile and renal function in streptozotocin induced diabetic mice.
Methods: Thirty six male Swiss albino mice were kept in six different groups for 21 days. Group I served as normal controls; Group II served as diabetic control; Groups III, IV and V were given 300 mg/kg, 400 mg/kg and 500mg/kg of *Coriandrum sativum* seed extracts (70% ethanol), respectively; and Group VI received 5mg/kg glibenclamide drug. The effect of extracts on hyperglycemia, lipid profile and renal function were tested by chemistry analyzer. Results were analyzed using one way ANOVA at a 5% level of significance.
Results: The fasting blood glucose level was significantly ($p<0.05$) reduced at 400mg/kg and 500mg/kg of *Coriandrum sativum* extract in treated diabetic mice as compared to the diabetic group. It also reduced total cholesterol, triglyceride, low density lipoprotein, urea and creatinine, and improved high density lipoprotein and total protein in treated diabetic mice.
Conclusion: Reduction in the fasting blood glucose, total cholesterol, triglyceride level, low density lipoprotein, urea, creatinine, and improvement in the high density lipoprotein and total protein by *Coriandrum sativum* extract indicates that it has anti-hyperglycemic, anti-hyperlipidemia and renal failure restoration effect in streptozotocin induced diabetic mice.

Keywords: *Coriandrum sativum*; Hyperglycemia; hyperlipidemia; renal function; streptozotocin

1. INTRODUCTION

Diabetes mellitus (DM) is defined as a group of metabolic diseases manifested by hyperglycemia results from defects on insulin production or insulin action. Untreated chronic hyperglycemia can lead to

Long-term complications including microvascular and macrovascular problems that cause disturbances of carbohydrate, fat and protein metabolism, and it covers a wide range of heterogeneous diseases. [1,2]

Diabetes mellitus could be categorized into several classes but the major types are type 1 diabetes mellitus (T1DM), type 2 diabetes mellitus (T2DM) and gestational diabetes mellitus. Both T1DM and T2DM lead to hyperglycemia, excessive urine production, compensatory thirst, increased fluid intake, blurred vision, unexplained weight loss, lethargy, and changes in energy metabolism. [3]

Type -2 diabetes mellitus is caused by the failure of insulin secretion or action. The impairment of insulin actions is known as insulin resistance, presented as a suppression or retard in metabolic responses of the muscle, liver and adipose tissue to insulin action. This failure is located at the signaling pathways held after insulin binding to its specific receptor. Chronic insulin resistance leads to hyperglycemia which mainly involved in the etiology of development of diabetic complications. [4]

Currently, T2DM is managed by a combination of diet, exercise and conventional therapy. Conventional therapy is the application of drugs for T2DM treatment that normally includes sulfonylureas, biguanides, thiazolidinediones and D-phenylalanine derivatives. [5] These convectional or synthetic drugs can cause side-effects including weight gain and loss, hematological and gastrointestinal reactions, hypoglycemic coma, and disturbances in liver and kidney metabolisms. In addition, these drugs are not ideal for use during pregnancy. [6] Due to these several side effects of conventional drugs, there is a growing tendency toward finding medications with less subsidiary effects, and as a result therapeutic herbs are taking lots of attention. Plant remedies are frequently considered to be less toxic and free from side-effects than synthetic drugs, and the World Health Organization (WHO) has recommended the evaluation of traditional plant treatments for diabetes. [7] WHO has listed 21000 herbs which are used as medicines all over the world and this magnifies the importance of herbs in curing diseases. [8]

Medicinal plants play an important role in the treatment of T2DM, especially in developing countries where resources are meager. The treatment of T2DM relies heavily on dietary measures, which includes the use of traditional plant therapies. [9] Some of the reports in ethno-botany suggested that about 800 medicinal plants possess anti-diabetic potential and the bioactive compounds such as glycosides, alkaloids, terpenoids and flavonoids (phenols) are effective medications both in preclinical and clinical studies. [10] These bioactive compounds of remedial plant lower blood glucose in experimental animal models, and, currently, there is considerable interest in exploring these plant extracts for compounds that might also be useful in the clinic or might have novel effects such as stimulation of β-cell proliferation. [11] There are many reports of plants that show pancreatic islet regeneration and increase in insulin secretion in diabetic conditions. [7] Generally, anti-hyperglycemic herbs increase insulin secretion, enhance glucose uptake by adipose or muscle tissues and inhibit glucose absorption from intestine and glucose production from liver.

Coriandrum sativum is an annual herb originating from the Mediterranean and cultivated all over the world including Ethiopia. [12] Phytochemical constituents of *Coriandrum sativum* seeds have been studied; and analysis had revealed presence of polyphenols (rutin, caffeic acid derivatives, ferulic acid, galic acid, and chlorogenic acid), flavonoids (quercetin and isoquercetin) and β- carotenoids. [13]

Coriandrum sativum is among the most commonly used spices in cooking and baked food, possessing the nutritional as

well as medicinal properties. It is also used in the preparation of many household medicines to cure bed cold, nausea, seasonal fever and stomach disorders. [14] *Coriandrum sativum* has been reported to exhibit several pharmacological effects such as anti-mutagenic, [15] anthelmintic, [16] sedative-hypnotic, [17] anti-feeding, [18] anti-parasite, [19] anticancer [20] and post-coital anti-fertility activities. [21] Interestingly, *Coriandrum sativum* also possessed heavy metal detoxification properties such as lead-detoxifying potential. [22] The medicinal plants provide a useful source of oral anti-hyperglycemic bioactive compounds for the development of new pharmaceutical clues as well as a good source of dietary supplement to existing therapies. Therefore, the main aim of this study is to investigate the effects of *Coriandrum sativum* seed extracts on hyperglycemia, lipid profile and renal function in streptozotocin (STZ) induced diabetic Swiss albino mice.

2. MATERIALS AND METHODS

2.1 Instruments, Reagents and Drugs

Instruments: Whatman filter paper No.1, test tube, gel tube, volumetric flask, beakers, funnels, Erlenmeyer flasks, measuring cylinder, glass rod, spatula, magnetic stirrer, semi-automatic pipettes, gavage (oral feeding syringe), Syringe, desiccator, heater, refrigerator, digital electronic balance, pH meter, one touch basic glucometer strip, water bath, Rota vapor, 902 automated chemistry analyzer and A 25 Bio Systems Chemistry analyzer.

Reagents: Ethanol, citric acid, sodium hydroxide, tri-sodium citrate, diethyl ether, 5% glucose solution

Drugs: Glibenclamide (Sanofi Winthrop industries, France) was purchased from a local drug store. Streptozotocin was also purchased from sigma Aldrich Company, India.

2.2 Preparation and Alcoholic Extraction of *Coriandrum sativum* Seed

Coriandrum sativum seeds were purchased from the local market, Merkato, Addis Ababa, Ethiopia. It was identified and authenticated by taxonomist in national herbarium, Addis Ababa University, Ethiopia, and deposited in the Department of Plant Biology and Biodiversity Management (Voucher number; 086790/2013). The seeds were washed carefully with distilled water to remove any extraneous materials and grounded to a coarse powder using electric grinder. Three hundred gram of dried and grounded seed was extracted with ethanol (70%) in a soxhlet apparatus for 48 hour at 60 ^{o} C. After extraction, the solvent was evaporated to dry at 40 -45 ^{o}C by using a rotary evaporator and the extract left behind was stored at 4 ^{o} C.

2.3 Experimental Animals and Study Protocol

Laboratory male Swiss albino mice (26-34g), 8th week age, were obtained from the department of biomedical science, Aratkillo campus, Addis Ababa University, Ethiopia. All experimental animal procedures were in accordance with the standards set forth in guidelines for the care and use of experimental animals by Committee for Purpose and control of Supervision of Experiments on Animals, and approved by Department of Biochemistry Research and Ethics Review Committee (DRERC 07/2013). The animals were allowed to acclimatize in the laboratory environment for a week before the commencement of the experiment. The animals were housed in polypropylene plastic cages and maintained under standard laboratory conditions of temperature of 22 ± 3°C and 12 hour light/dark cycle. The mice were fed a standard commercial pellet diet and water throughout the experimental period.

2.4 Acute Toxicity Test of *Coriandrum sativum* Seed Extracts

Acute oral toxicity study was conducted according to Organization for Economic Co- operation and Development guideline 423. Six male mice were orally administered a single concentration of 2000mg/kg body weight of *Coriandrum sativum* seed extracts. Mortality and toxicity signs such as coma, anxiety, polyuria and other behavioral changes were observed and recorded after 1, 3 and 6 hours of administration of the extract for consecutive three days.

2.5 Design of Experiment

The mice were divided into six groups comprising of six mice as follows.

- Group I - Normal control and were given only 0.5ml saline daily
- Group II - STZ induced diabetic mice that served as Diabetic Control and were given 0.5ml saline only.
- Group III - STZ induced diabetic mice treated with 300 mg/kg of *Coriandrum sativum* seed extracts
- Group IV - STZ induced diabetic mice treated with 400 mg/kg of *Coriandrum sativum* seed extracts
- Group V - STZ induced diabetic mice treated with 500 mg/kg of *Coriandrum sativum* seed extracts
- Group VI - STZ induced diabetic mice treated with 5mg/kg of glibenclamide (Glb). [23]

Dose selection of the extracts was based on the safe doses of oral acute toxicity studies carried out earlier in this study. The extracts and glibenclamide were administered orally for 21 days.

2.6 Induction of Experimental Type 2 Diabetes Mellitus

Mice had developed diabetic by a single intraperitoneal injection of freshly prepared STZ at a concentration of 120 mg/kg body weight in 0.1 M citrate buffer (pH 4.5) in a volume of 20 ml/kg body weight. [24] After a week of streptozotocin induction, fasting blood glucose levels were estimated. Mice with blood glucose 200 mg/dL were considered as diabetic, and used for the experiments.

2.7 Statistical Analysis

The results of various biochemical parameters were expressed as mean ± SEM. Data analysis of the statistics were done using SPSS version 20 and Microsoft Excel. Statistical analysis was done using analysis of variance (ANOVA) at a 5% level of significance.

2.8 Biochemical Test Assay

Blood sample was collected from the tail vein of the mice, and fasting blood glucose was estimated with One Touch Basic Glucometer after 6 hour fasting on 0, 8th, 15th and 21st days. At the end of the experimental period, all groups of animals were euthanized by anesthetizing with diethyl ether and then blood was collected via direct cardiac puncture. After the blood was coagulated at room temperature for 30 minutes, it was centrifuged for 10 minutes at 3000 rpm. Serum samples were stored in deep freezer at -20 ^{o}C until further analyses of various biochemical parameters were determined. TC, TG, HDL, total protein, urea and creatinine were estimated with chemistry analyzer. LDL level was calculated using Friedwald equation. [25]

3. RESULTS

3.1 Yield

The percentage yield of dried extract was found to be 5.7% (w/w). It was dark-brown jelly and solidified when stored in a deep freezer and turn to semisolid on re-exposure to room temperature.

3.2 Acute Toxicity Test

In acute oral toxicity test, the extract revealed no mortality at 2000 mg/ kg body weight concentration in Swiss albino mice. These mice did not also show any toxic effects like changes in behavioral activities

such as anxiety, polyuria, diarrhea, seizures and coma. Thus, the extracts, 2000 mg/Kg body weight of mice were found be a good safety margin indicator. Therefore, one-fifth of the safe doses were taken by the researcher for the experiments.

3.3 The Effects of Extracts on Body Weight

The body weights were found to drop in diabetic mice as compared with control group. However, there was slight increase of the body weights in all concentrations of extract treated diabetic mice as shown below in **figure 3.1.**

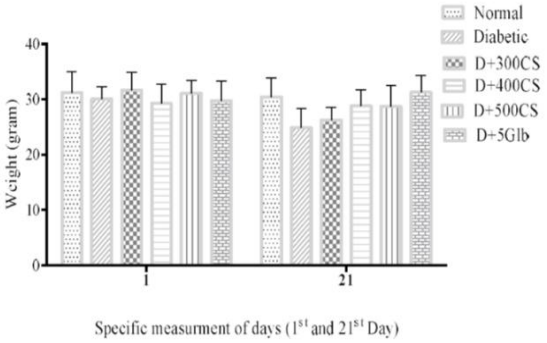

Figure 3.1: The effects of extracts on body weight

The results are expressed as mean ± SD (n =6). D-Diabetic, Glb - Glibenclamide

3.4 The Effect of Extracts on Fasting Blood Glucose

The anti-hyperglycemic effects of graded concentration of *Coriandrum sativum* extracts on the fast blood glucose (FBG) levels of STZ induced diabetic mice were presented in figure 3.2 as shown below. The FBG levels in STZ induced diabetic mice were significantly ($p<0.001$) increased as compared to normal control group throughout the study period. This increase of blood glucose was almost three-fold higher even after three weeks compared to normal mice.

However, the FBG levels were significantly ($p<0.01$) decreased in diabetic treated mice on 8th, 15th and 21st days. Similarly, treatment with glibenclamide also led to a significant ($p<0.001$) reduction of FBG levels on 8th, 15th and 21st days.

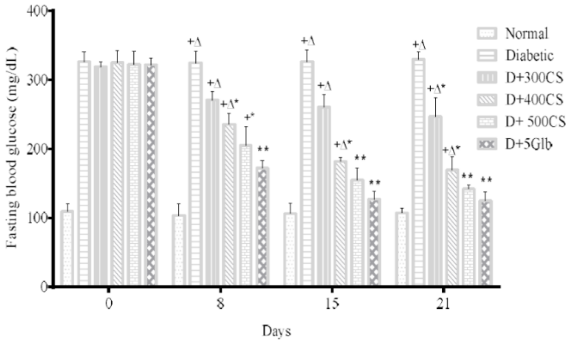

Figure 3.2: The effects of extracts on fasting blood glucose

The results are expressed as mean ± SD (n =6). * – significant at $p<0.05$ compared with diabetic control, ** - significant at $p<0.001$ compared with diabetic control, + - significant at $p<0.05$ compared with normal control, Δ - significant at $p<0.05$ compared with Glb(glibenclamide) treated group, D-Diabetic, CS- *Coriandrum sativum*

3.5 The Effects of Extracts on Serum Triglyceride

Serum TG were significantly ($P<0.01$) raised in diabetic control as compared to normal group. Oral administration of the extracts at 300mg/kg, 400mg/kg and 500mg/kg concentration reduced serum TG level as compared to diabetic mice. Treatment with 5mg/kg of glibenclamide also led to a significant ($p<0.001$) reduction on TG level as shown below in **figure 3.3.**

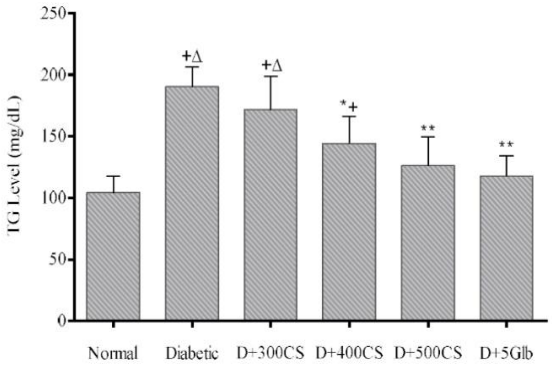

Figure 3.3: The effects of extracts on serum triglyceride

The results are expressed as mean ± SD (n =6). * – significant at $p<0.05$ compared with diabetic control, ** - significant at $p<0.001$ compared with diabetic control, +- significant at $p<0.05$ compared with normal control, Δ - significant at $p<0.05$ compared with glibenclamide treated group, D-Diabetic, CS- *Coriandrum sativum*

3.6 The Effects of Extracts on Serum Total Cholesterol

Serum TC were significantly ($p<0.001$) raised in diabetic group as compared to normal control. Administration of the extract at 300mg/kg, 400mg/kg and 500mg/kg concentration reduced serum TC as compared to diabetic mice. And, treatment with glibenclamide also led a significant ($p<0.001$) reduction of TC as shown in **figure 3.4.**

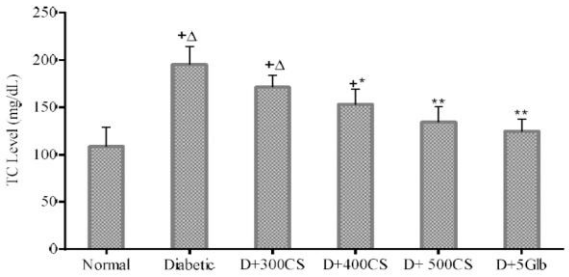

Figure 3.4: The effects of extracts on serum total cholesterol

The results are expressed as mean ± SD (n =6). * – significant at p<0.05 compared with diabetic control, ** - significant at p<0.001 compared with diabetic control, +- significant at p<0.05 compared with normal control, Δ - significant at p<0.05 compared with glibenclamide treated group, D-Diabetic, CS- *Coriandrum sativum*

3.7 The Effects of Extracts on Serum Low Density Lipoprotein

Serum LDL were significantly ($p<0.001$) raised in diabetic group as compared to normal control. Oral administration of extract at 300mg/kg, 400mg/kg and 500mg/kg concentration reduced serum, LDL levels as compared to diabetic mice. And, treatment with glibenclamide also led to a significant ($p<0.001$) reduction in LDL as shown in **figure 3.5.**

3.8 The Effects of Extracts on Serum High Density Lipoprotein

There were a significantly ($P<0.01$) decrease on serum HDL in diabetic group as compared to normal control. Administration of the extracts at the graded concentration increased the HDL levels as compared to diabetic mice. Treatment with glibenclamide also led to a significant ($p<0.001$) increase in HDL as shown below in **figure 3.6.**

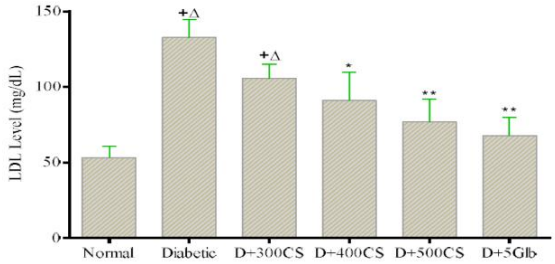

Figure 3.5: The effects of extracts on serum low density lipoprotein

The results are expressed as mean ± SD (n =6). * – significant at p<0.05 compared with diabetic control, ** - significant at p<0.001 compared with diabetic control, +- significant at p<0.05 compared with normal control, Δ - significant at p<0.05 compared with glibenclamide treated group, D-Diabetic, *CS- Coriandrum sativum*

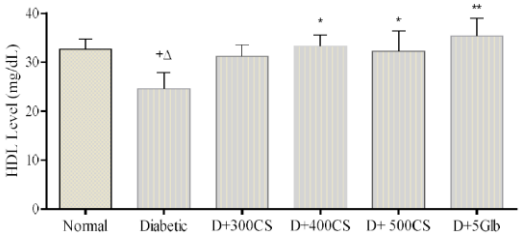

Figure 3.6: The effects of extracts on serum high density lipoprotein

The results are expressed as mean ± SD (n =6). * – significant at p<0.05 compared with diabetic control, ** - significant at p<0.001 compared with diabetic control, + - significant at p<0.05 compared with normal control, Δ - significant at p<0.05 compared with glibenclamide treated group, D-Diabetic, *CS- Coriandrum sativum*

3.10 The Effects of Extracts on Serum Creatinine

There were significant ($P<0.01$) increase in serum creatinine in diabetic group as compared to normal control. However, serum creatinine was reduced after the administration of extracts at all concentrations and 5mg/kg glibenclamide in treated diabetic mice as compared to diabetic mice as shown below in **figure 3.7.**

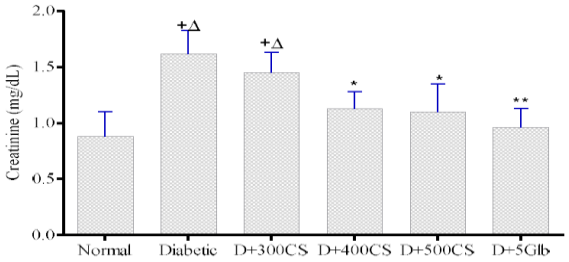

Figure 3.7: The effects of extracts on serum creatinine

The results are expressed as mean ± SD (n =6). * – significant at p<0.05 compared with diabetic control, ** - significant at p<0.001 compared with diabetic control, + - significant at p<0.05 compared with normal control, Δ - significant at p<0.05 compared with glibenclamide treated group, D-Diabetic, *CS- Coriandrum sativum*

3.11 The Effects of Extracts on Serum Urea

Serum urea was significantly increased in diabetic group as compared to normal control. However, serum urea were reduced after the administration of extracts at all concentrations and 5mg/kg glibenclamide in treated diabetic groups as compared to diabetic group (**figure 3.8)**

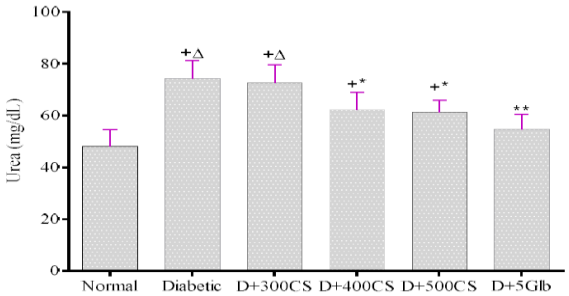

Figure 3.8: The effects of extracts on serum urea

The results are expressed as mean ± SD (n =6). * – significant at p<0.05 compared with diabetic control, ** - significant at p<0.001 compared with diabetic control, +- significant at p<0.05 compared with normal control, Δ - significant at p<0.05 compared with glibenclamide treated group, D-Diabetic, *CS- Coriandrum sativum*

3.12 The Effects of Extracts on Serum Total Protein

Total protein were significantly (p<0.001) decreased in diabetic group as compared to normal group. However, serum total protein was increased after the administration of extracts and glibenclamide in treated diabetic mice as compared to diabetic mice.

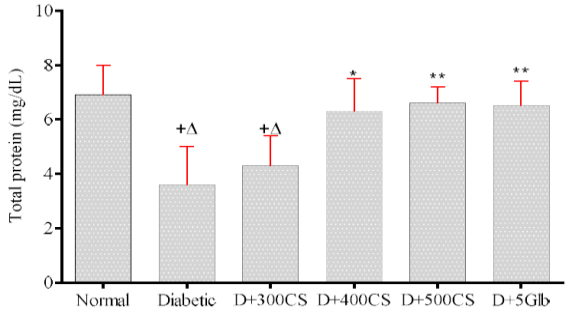

Figure 3.9: The effects of extracts on serum total protein

The results are expressed as mean ± SD (n =6). * – significant at p<0.05 compared with diabetic control, ** - significant at p<0.001 compared with diabetic control, + - significant at p<0.05 compared with normal control, Δ - significant at p<0.05 compared with glibenclamide treated group, D-Diabetic, *CS- Coriandrum sativum*

4. DISCUSSION

Diabetes mellitus is now described as a disorder of multiple etiologies with abnormalities in carbohydrate, lipid as well as protein metabolism. STZ induced animal model has been described as a useful experimental model to study the effect of anti-diabetic agent such as glibenclamide against T2DM. STZ is the well-known to induce diabetes, hyperinsulinemia, or hyperglycemia by damaging the pancreatic β cells. [26] STZ enters the β cell via GLUT-2 transporter and causes alkylation of DNA, thereby induces the activation of poly ADP ribosylation. Poly ADP-ribosylation leads to depletion of cellular NAD^+ and ATP. [27]

Management of T2DM is indeed a tough task with the convectional medicines as they may cause many side effects. Thus, as an alternative, there is an immense interest in medicinal plants for finding a cure to reduce the risk of T2DM. Scientists have started looking into the herbal extracts to observe their effective and protective role in the diabetic animal models. The present work demonstrates a significant role of *Coriandrum sativum* extracts in normalizing body weight, reducing blood glucose levels, decreasing cholesterol levels, improving cardio-protective effect and restoring renal function in STZ induced diabetic mice.

Slight body weight loss was observed in diabetic mice and almost normalized by treatment with extract. In diabetic mice, the slight loss of weight might be due to tissue protein break down and muscle wasting via unavailability of carbohydrate as an energy source and catabolism of fats. [29] However, 5mg/kg of glibenclamide treated mice gained weight (25.7%) in comparison with the normal group after 21 days of treatment.

The result of this study reveal that *Coriandrum sativum* extract treated groups did not show important body weight gain. This could support that *Coriandrum sativum*

to be an important for treatment of diabetes mellitus over glibenclamide which are mostly known to cause body weight gain. [25] The protective effect of the extract on body weight loss could be due to its ability to reduce hyperglycemia. Here, the bioactive compounds of *Coriandrum sativum* might help in suppressing the free radicals generated via hyperglycemia.

The increase in fasting blood glucose is an important characteristic feature of T2DM. In this study, there were elevations in FBG on diabetic group. However, the extract reduced FBG in treated diabetic mice. The FBG was decreased by 16.4% and 21.12% at 300mg/kg extract concentration on 8^{th} and 15^{th} days respectively, and decreased significantly ($p<0.01$) by 25.13% on 21^{st} day in treated diabetic mice as compared to diabetic group. On the other hand, administration of 400mg/kg of the extract significantly ($p<0.01$) reduced the FBG by 27.04%, 44.97% and 48.59% on 8^{th}, 15^{th} and 21^{st} days respectively as compared to diabetic group. Administration of 500mg/kg of the extract reduced the FBG significantly ($p<0.001$) by 36.49%, 53.06% and 57.0% on 8^{th}, 15^{th} and 21^{st} days respectively as compared to diabetic group. Similarly, glibenclamide (5mg/kg) led to reduction of FBG by 46.03%, 61.30% and 62.12% on 8^{th}, 15^{th} and 21^{st} days respectively as compared to diabetic group. Hence, when the concentrations of *Coriandrum sativum* extracts increased, the FBG was shown to have been decreased. The glycemic control was nearly similar between glibenclamide and 500mg/kg extract treatment. Thus, the increment of the *Coriandrum sativum* extracts concentration might further provide a similar result as the glibenclamide drug.

The present finding indicates that the extract had anti-hyperglycemic effect potential. It might be due to restoration of insulin response via the presence of "insulin-releasing" and "insulin like" activity in *Coriandrum sativum*. [31] It was also suggested that the anti-hyperglycemic effects of the extract could be caused by high level of fiber which interfere carbohydrate absorption, increased peripheral uptake of glucose, improved sensitivity of insulin receptor and regenerative effect of extracts on pancreatic tissue. [30]

Coriandrum sativum extracts were also able to alter the levels of lipid metabolites including TC, TG, HDL, and LDL in diabetic mice that suggests it had a remarkable anti-hyperlipidemic effect. The levels of serum lipids are usually raised in T2DM and such an elevation represents a risk factor for coronary heart disease. [31]

In this study, there were significant ($P<0.01$) increase in the TC, TG and the LDL levels in diabetic mice. The elevated TG might be due to the consequence of increased synthesis of triglyceride rich lipoprotein particles (VLDL) in liver and diminished catabolism. The increased levels of LDL and VLDL might also be due to over production of LDL and VLDL by the liver in turn by the stimulation of hepatic triglyceride synthesis as a result of free fatty acid influx. [32] Beside, insulin deficiency is associated with excess lipolysis and increased influx of free fatty acids to the liver. [30] Recent researches have also reported that the elevated TG level-rich lipoproteins could be a consequence of the reduction of LPL activity due to its glycation. [33]

The elevated levels of TC, TG and LDL were reduced in extract treated diabetic mice and increased HDL. Administration of 300mg/kg extract were reduced by 12.29 % in TC, 9.88 % in TG, 20.23 % in LDL, and increased by 26.34 % in HDL as compared to diabetic group. Administration of 400mg/kg extracts were also reduced significantly ($p<0.01$) by 21.52% in TC,

24.23% in TG and 31.32% in LDL, and increased by 34.82% in HDL as compared to diabetic group. Administration of 500mg/kg extracts were reduced significantly ($p<0.001$) by 31.2% in TC, 33.68% in TG and 42.04% in LDL, and increased by 30.77% in HDL as compared to diabetic group. After glibenclamide (5mg/kg) treatment of diabetic mice, there were reduction by 35.06 % in TC, 38.10 % in TG and 48.98 % in LDL, increased the HDL by 43.32% as compared to diabetic group. Thus, these result suggested that the extracts would be helpful for the prevention of diabetic complications through improving hypercholesterolemia.

The reductions of TG, TC and LDL extracts might be due to the involvement of polyphenolic part of the extract in preventing the formation of AGEs in diabetic mice. [34,35] *Coriandrum sativum* extract fiber may delay the absorption of glucose and fatty acids from the upper small intestine, thus providing less substrate for synthesis of triglycerides. [36]

Both HDL and plasma LCAT are believed to be involved in the transport of cholesterol from extra hepatic tissues to the liver for its excretion. [37] The higher levels of cholesterol associated with HDL and the increase in the activity of plasma LCAT on administration of extract might result in a higher amount of cholesterol being removed from extra hepatic tissues which may contribute to the antihypercholesterolemia observed in these mice. Hence, decreasing cholesterol levels of serum and tissues by the administration of this extract would seem to be mediated through its increased rate of degradation to bile acids and neutral sterols.

Type 2 diabetes mellitus also causes renal damage due to abnormal glucose regulation including elevated glucose and glycosylated protein tissue level, hemodynamics changes within the kidney and oxidative stress. Both negative balance of nitrogen and lowered protein synthesis leads to increased level of serum urea and creatinine that indicates progressive renal damage in diabetic mice. [38]

In this study, the level of serum urea and creatinine were raised in diabetic mice. These increased urea and creatinine production might be due to accelerated catabolism of both liver and plasma proteins. [39] Nevertheless, the extracts reduced both serum urea and creatinine in diabetic treated mice. The level of serum urea and creatinine were decreased insignificantly ($P>0.05$) by 2.02% and 10.49% at 300mg/kg extract concentration respectively as compared to diabetic group. The level of serum urea and creatinine were decreased significantly ($P<0.01$) by 16.17% and 30.25% at 400mg/kg extract respectively as compared to diabetic group. The level of serum urea and creatinine were decreased significantly ($P<0.01$) by 17.25% and 32.72% at 500mg/kg extract respectively as compared to diabetic group. Similarly, glibenclamide (5mg/kg) also significantly ($P<0.01$) reduced the serum urea and creatinine by 26.14% and 40.74% on the diabetic treated mice as compared to diabetic group respectively.

These reductions of serum urea and creatinine may show the beneficial effects of the *Coriandrum sativum* extracts on the kidney function of diabetic mice. Thus, this renephroprotective function could be mediated via antioxidant and/or free radical scavenging activities as they possess high concentration of flavonoids and alkaloids. [40,41]

Protein metabolism is impaired in T2DM as a result of insulin resistance that led to a defect in amino acid metabolism and suppression of protein synthesis. Insulin resistance of protein metabolism could be impaired as one of the causes of protein malnutrition. [28] In this study, it was found

that serum total protein was decreased significantly ($p<0.01$) in diabetic group. However, it was improved in extract treated diabetic mice. Total protein was raised by 20.95% at 300mg/kg extract as compared to diabetic group. On the other hand, there were a significant ($P<0.01$) increase by 74.56% and 83.79% of serum total protein after a 400mg/kg and 500mg/kg extract treatment respectively as compared to diabetic group. Similarly, there were also significant ($P<0.01$) improvement of total protein (81.56%) in treated diabetic mice with glibenclamide (5mg/kg) as compared to diabetic group. Here, the extracts might be attributed to an improvement in glycemic control and insulin secretion that in turn leads to increase protein synthesis or decrease in protein degradation.

5. CONCLUSION

Generally, *Coriandrum sativum* extract has anti-hyperglycemic, anti-dyslipidemia effect and restoring the function of kidney in STZ induced diabetic Swiss albino mice. Thus, the extract could be helpful in preventing future damages caused by T2DM and its complications such as cardiovascular diseases. There were also a gradual improvement of hyperglycemia, dyslipidemia and renal failure within the graded concentration. Hence, the 500mg/kg concentration of the extract has a better anti-diabetic capacity, and almost equipotent with glibenclamide drug.

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