Biological and Clinical Sciences Research Journal
ISSN: 2708-2261
www.bcsrj.com
DOI: https://doi.org/10.54112/bcsrj.v2022i1.88
*Biol. Clin. Sci. Res. J., Volume, **2022**: 88*
Original Research Article

EFFECTS OF *CITRULLUS COLOCYNTHIS* AND *MOMORDICA CHARANTIA* HYDRO-ETHANOL EXTRACTS ON LIPID PROFILE OF INDUCED DIABETIC ALBINO RATS

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(Received, 13th August 2021, Revised 8th March 2022, Published 21th March 2022)

Abstract: *Diabetes is a condition in which glucose levels of blood become higher and can lead to many complications and death. The recent study was designed to check the hypo-glycemic effects of the Citrullus colocynthis and Momordica charantia leaves extract on streptozotocin (STZ) induced diabetic albino rats. For this purpose, 30 albino rats were divided into five treatment groups. Three groups were treated with plant extracts and the remaining two were given only a basal diet for 21 days. At the completion of experiment, body weight and glucose level of the rats was recorded and then dissected to collect blood and organs. The blood serum was separated by centrifugation to measure various chemical compounds. The organs' weight was also recorded to check the animal performance. The recorded data was analyzed statistically by SAS and found that plants extracts separately or in combination significantly increased the body weight of rats than control groups, whereas, glucose level was decreased significantly as compared to control groups. It was observed that liver and pancreas weight were non-significantly and kidney weight was significantly decreased in treatment groups as compared to control groups. In our research, it was observed that the level of cholesterol (mg/dL), triglyceride (mg/dL) and Very low density lipoprotein (mg/dL) were non-significantly lower in treatment groups than control. However, significant increase in high density lipoprotein (mg/dL) and significant decrease in the low density lipoprotein (mg/dL) and HbA1c (%) was observed among treatment groups. It was concluded that supplementation of plant's extracts in animal's diet can put health promoting effects in diabetic rats.*

Keywords: Diabetes, *Citrullus colocynthis*, *Mamordia charantia*, cholesterol, triglyceride, Very low density lipoprotein, high density lipoprotein, low density lipoprotein and HbA1c

Introduction

Hyper-glycemia is a condition in which glucose level is increased; it is termed as diabetes. Diabetes is a condition in which glucose levels of blood become higher that can lead to illness and death. The abnormality in different body functions due to irregularity that occurs in insulin confrontation that results in damaging of beta cells of Langerhans with resulting insulin. There are two types of diabetes. Type-1 diabetes is a disorder that causes degradation of pancreatic beta cells which can react with endogenous antigen by auto reactive resistant cells (Atkinson & Eisenbarth, 2001) which leads to progressive destruction of the beta cells, decreasing the amount of insulin production usual indication for diabetes. It is very important to replace hormones which induce the healthy level of insulin to healthier the blood glucose level therefore this illness is also referred to as insulin dependent diabetes (Li et al., 2004; Atkinson, 2012). Type 2 diabetes is diabetes mellitus characterized by the destruction of beta cells which fails to secrete the insulin; this condition leads to hyper-glycemic condition. So we can say that insulin decreasing level leads to hyper-glycemic condition, by lowering the insulin level increasing the blood glucose level and this mechanism causes the weakening of signal transduction (Kasuga, 2006 and Muoio & Newgard, 2008). There are following risk factors that cause diabetes such as obesity, alcoholic lifestyle and poor eating habits (Ezuruike & Prieto, 2014). Insulin decreasing level causes the potency of beta cells to release the hormone in the body resulting in the increasing level of glucose in the body that is categorized as Type 2 diabetes (Shaw et al., 2010). Diabetes found all over the world and its prevalence increasing progressively and according to record it is the third global dangerous disease (Ogbonnia et al., 2008). Mostly chronic diabetes leads to a lot of complications and affects the different organ systems

[Citation: Saleem, S., Hayat, S., Hussain, M., Mehmood, S., Pervaiz, S, Hanif, S. (2022). Effects of *Citrullus colocynthis* and *Momordica charantia* hydro-ethanol extracts on lipid profile of induced diabetic albino rats. *Biol. Clin. Sci. Res. J.*, **2022***: 88*. doi: https://doi.org/10.54112/bcsrj.v2022i1.88]

such as, nervous system, renal failure and vascular system that cause mortality (Ballester et al., 2004). Anti-diabetic and anti-hyperlipidemic medication has been prepared worldwide by some medicinal plants. Their anti-diabetic property is recorded because these plants have the ability to secret the insulin from pancreatic beta cells and inhibit the absorption of glucose from the intestine (Malviya et al., 2010). People's interest towards traditional medicine such as herbal medicine is increasing progressively due to diverse effects of chemically anti-biotic and increasing cost of allopathic medicine (WHO, 2002). *Citrullus colocynthis* (Cucurbitaceae) contain huge quantities of phenol and flavonoids that have antioxidant accomplishments (Kumar et al., 2008). *C. colocynthis* has a useful impact on refining the glucose level in the blood without the harmful effects in Type-2 diabetic patients (Huseini et al., 2009). This fruit is called as bitter gourd and used to decrease the blood glucose level and has the valuable proteins (Raman & Lau, 1996) increase the insulin production (Shih et al., 2009). And moderate the glucose and insulin level (Celia et al., 2003), and increase the mass of beta cells in pancreas (Shett et al., 2005). *Momordica charantia* is widely used for the treatment of different chronic disorders in which diabetes is included. Once they treat the charantin compound derived from *Momordica charantia* treated orally in rabbits that decrease the blood glucose level significantly (Lotlikar & Rajarama, 1966). According to scientists, current study revealed that herbal plants used as therapy for anti-diabetic and anti-hyper-lipidemic on diabetic rats.

Material and methods

The research was undertaken at the Department of IMBB, The University of Lahore.

Collection of the plant material

The leaves of *Citrullus colocynthis* and *Momordica charantia* were collected and kept under a shadow for drying for three days.

Preparation of the extract

With the help of the electric blender, the leaves were blended into fine powder. Powder was mixed with ethanol for three days to get a fine mixture. After 72 hours, mixture was strained with the filter paper and vaporized with the help of a rotary evaporator to get extract. Then the extract was placed in the petri dishes at room temperature for 3 days to solidify the extract.

Experimental animals

For this purpose, 30 albino rats were divided into five treatment groups (A, B, C, D and E). The rats were housed at standard room temperature. Pathogenic free air conditioned environment was provided to avoid any miss assumption.

Induction of hyperglycemia

Before the induction of diabetes, rats were fasted for 24 hours. After fasting, streptozotocin (STZ) with 0.5% of normal saline was injected peritoneally at the rate of 50 mg/kg of body weight. After 24 hours glucose level of blood was checked and recorded. Up to 200mg/dL glucose level was considered as diabetic and that was able to be used in the relevant experimental trial.

Experimental design and dietary plan

30 albino rats were divided into five treatment groups (A, B, C, D and E). After induction of diabetes, three groups were treated with plant extracts at the rate of 250g/kg of the body weight and basal diet and the remaining two were given only a basal diet for 21 days. As shown in (Table 1).

Table 1: Dietary plan for the experimental and control animals

Groups	Dietary plan
A	Basal diet + *C. colocynthis* (250g/Kg Body weight)
B	Basal diet + *M. charantia* (250g/Kg Body weight)
C	Basal diet + *C. colocynthis* + *M. charantia* (250g/Kg Body weight)
D	Basal diet only (healthy control group)
E	Basal diet only (diabetic control group)

Dissection

On the 22nd day experimental rats were weighed and anesthetic using 10% chloroform. Before dissection, blood glucose levels of the rats were analyzed by using glucometer (Certeza glucometer, GL-110 Version). After that, rats were fixed on the dissecting board and dissection was done. Blood was drawn with the help of a syringe by puncturing the heart and was collected in EDTA tubes and centrifuged at 3000 rpm for 5 minutes for the separation of serum. Separated serum was collected in eppendorf and was stored at 4ºC for further analysis.

Blood chemistry analysis

At the completion of experiment, body weight and glucose level of the rats was recorded and then dissected to collect blood and organs. The blood serum was separated by centrifugation to measure various chemical compounds like, HbA1c (%), cholesterol (mg/dL), TG triglycerides (mg/dL), HDL high density lipoprotein (mg/dL), LDL low density lipoprotein (mg/dL), VLDL very low density

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lipoprotein (mg/dL) and glucose level (mg/dL). The organs' weight was also recorded to check the animal performance.

Results

This experiment was designed to see the activity of hydro-ethanol plants' extracts on the different physiological parameters in the streptozotocin-induced male albino rats. In the last day of the experiment, body weight, glucose level, HbA1c, lipid profile test and organs' weight (liver, pancreas and kidney) of the experimental groups were measured. Results of present study showed that there was non-significantly (P>0.05) increase in the body weight of treatment groups than control groups and highly significant decreased (P<0.05) in the glucose level of treated groups in relate to control groups (Table 2).There was significantly (P<0.05) decrease in the liver and pancreatic weight and highly significant (P<0.05) decrease in the kidney weight of treatment groups in comparison to control groups (Table 3). Non-significantly (P>0.05) increase in cholesterol, triglycerides, high density lipoprotein and Very low density lipoprotein level and significantly (P<0.05) decrease in the low density lipoprotein level were recorded in treated groups in comparison of the control groups (Table 4). Results of present research showed that there was a significant (P<0.05) decrease in the HbA1c (%) of treated groups than control groups (Table 5).

Table 2: Effect of supplementation of *C. colocynthis*, *M. charantia* and their combined leaves' extract on body weight (g) and glucose level (mg/dL) in STZ induced experimental (diabetic) rats

Feeding groups						
Parameters	***C. colocynthis***	***M. charantia***	***C. colocynthis* + *M. charantia***	**Diabetic control Group**	**Healthy control group**	**P-Value**
IBW	163.33 ± 4.25[a]	169.00 ± 2.00[a]	186.66 ± 11.89[a]	87.00 ± 11.00[a]	176.00 ± 5.00[a]	>0.2712
FBW	200.00 ± 18.77[a]	208.00 ± 9.00[a]	214.33 ± 54.71[a]	217.00 ± 2.00[a]	206.00 ± 5.00[a]	>0.9960
IG	265.33 ± 10.92[a]	248.00 ± 21.00[a]	273.33 ± 3.52[a]	283.00 ± 4.00[a]	89.00 ± 2.00[b]	<0.0001
FG	89.00 ± s1.52[b]	79.00 ± 3.00[bc]	89.33 ± 4.84[b]	120.00 ± 3.00[a]	73.50 ± 2.50[c]	<0.0004

Means ± Standard errors of means with different alphabets in the rows are significantly different.

IBW: Initial body weight; **FBW:** Final body weight **IG:** Initial glucose **FG**: Final glucose level in STZ induced experimental rats.

Table 3: Effect of supplementation of *C. colocynthis*, *M. charantia* and their combined leaves' extract on organs' weight (kidney, liver and pancreas) in STZ induced experimental (diabetic) rats.

Feeding groups						
Parameters	***C. colocynthis***	***M. charantia***	***C. colocynthis* + *M. charantia***	**Diabetic control Group**	**Healthy control group**	**P-Value**
Liver	7.76 ± 0.27[ab]	5.87 ± 0.08[b]	8.10 ± 1.42[ab]	9.75 ± 0.35[a]	6.70 ± 0.60[b]	<0.0242
Pancreas	0.52 ± 0.02[ab]	0.55 ± 0.02[ab]	0.43 ± 0.08[b]	0.65 ± 0.05[a]	0.40 ± 0.00[b]	<0.0458
Kidney	1.80 ± 0.05[b]	1.45 ± 0.05[b]	1.60 ± 0.20[b]	2.45 ± 0.25[a]	1.40 ± 0.10[b]	<0.0017

Means ± Standard errors of means with different alphabets in the rows are significantly different.

Table 4: Effect of supplementation of *C. colocynthis*, *M. charantia* and their combined leaves' extract on lipid profile in STZ induced experimental (diabetic) rats.

Feeding groups						
Parameters	***C. colocynthis***	***M. charantia***	***C. colocynthis* + *M. charantia***	**Diabetic control Group**	**Healthy control group**	**P-Value**
CHOL	56.33 ± 8.29[ab]	59.00 ± 2.00[ab]	62.66 ± 10.97[ab]	83.50 ± 4.50[a]	46.50 ± 0.50[b]	>0.1660

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TG	119.00 ± 9.64^{ab}	114.00 ± 3.00^{b}	123.33 ± 11.25^{ab}	151.50 ± 4.50^{a}	125.00 ± 2.00^{a}	>0.1681
HDL	23.35 ± 2.31^{a}	22.25 ± 0.85^{a}	17.95 ± 4.53^{a}	11.75 ± 0.45^{a}	78.65 ± 62.35^{a}	>0.3439
LDL	15.06 ± 1.59^{b}	18.00 ± 1.30^{b}	15.80 ± 0.93^{b}	26.30 ± 3.19^{a}	13.38 ± 0.18^{b}	<0.0080
VLDL	23.80 ± 1.92^{ab}	22.80 ± 0.60^{b}	24.66 ± 2.25^{ab}	30.30 ± 0.90^{a}	25.00 ± 0.40^{ab}	>0.1681

Means ± Standard errors of means with different alphabets in the rows are significantly different
CHOL: Cholesterol (mg/dL); **TG:** Triglycerides (mg/dL); **HDL:** High density lipoprotein (mg/dL); **LDL:** Low density lipoprotein (mg/dL) and **VLDL:** Very low density lipoprotein (mg/dL) in STZ induced experimental rats.

Table 5: Effect of supplementation of *C. colocynthis*, *M. charantia* and their combined leaves' extract on HbA1c in STZ induced experimental (diabetic) rats.

Feeding groups						
Parameters	***C. colocynthis***	***M. charantia***	***C. colocynthis + M. charantia***	**Diabetic control Group**	**Healthy control group**	**P-Value**
HbA1c	4.74 ± 0.83^{ab}	3.95 ± 0.15^{b}	7.38 ± 0.85^{a}	2.99 ± 0.89^{b}	3.98 ± 0.08^{b}	<0.0310

Means ± Standard errors of means with different alphabets in the rows are significantly different.

Discussion

This experiment was designed to see the avtivity of hydro-ethanol plants' extracts on the different physiological parameters in the streptozotocin-induced male albino rats. In the last day of the experiment, body weight, glucose level, HbA1c, lipid profile test and organs' weight (liver, pancreas and kidney) of the experimental groups were measured. In the recent study it was observed that the body weight was non-significantly differ among the supplemented group of STZ-induced diabetic rats. It was noticed that the group D (healthy control group) was higher body weight than the groups supplemented with the plant extract (Table 2). The results are similar to the early research work, according to this study they observed that the aqueous extracts of *C. colocynthis* showed increased in body weight. Another finding of (Nibras et al., 2010), they were designed a study to check out the anti-diabetic properties of *M. charantia* on diabetic rats. They were divided their experimental rats into separate groups and rats were fed with the extract of *M. charantia* seed. The results showed the remarkable increase in body weight of the rats. In contrast to present findings there was non-significantly (P>0.05) increase in the body weight of treatment groups than control groups (Table 2). The result concluded that there was outstandingly decrease in glucose level of rats treated with *C. colocynthis*. Another finding of (Al-Khateeb et al., 2009) according to this study the extract of seedless pulp of *C. colocynthis* has anti-hyper-glycemic, insulinotropic activity and healthy-hypo-glycemic on alloxan induced diabetic rats. In contrast to recent findings, result of present study showed that there was highly significant decreased (P<0.05) in the glucose level of treated groups in relate to control groups (Table 2). However it was observed that the group D (healthy control group) was higher liver weight than the groups supplemented with the plants' extract (Table 3). Another finding of (Benariba et al., 2009**)** designed a study to check the anti-hyperglycemic potential of *Citrullus colocynthis* extract in streptozotocin-induced diabetic rats. Rats were fed with the extract of *C. colocynthis*. At the end day of experiment, glucose level and organs weight (liver, pancreas and kidney) were measured. However it was observed that the group D (healthy control group) was higher pancreatic weight than the groups supplemented with the plants' extract (Table 3). Another finding of (Benariba et al., 2009) designed a study to check the anti-hyperglycemic potential of *Citrullus colocynthis* extract in streptozotocin-induced diabetic rats. The experimental rats of group C treated with combined plants' extract (*C. colocynthis* + *M. charantia*) pancreatic weight were reduced in comparison of diabetic control group. In present findings, results showed that there was significant (P<0.05) decrease in the pancreatic weight of treated groups in relate to the control groups (Table 3). In the recent research it was observed that the kidney weight significantly differs among the supplemented group of STZ-induced diabetic rats. However it was noticed that the group D (healthy control group) was higher kidney weight than the groups supplemented with the plants' extract (Table 3). Kidney weight of the healthy control group was lower in relate to diabetic control

group which is significantly high. When experimental rats of group A treated with *C. colocynthis* kidney weight was reduced than diabetic control group. The experimental rats of group B treated with *M. charantia*, kidney weight was decreased significantly in comparison of diabetic control group. The experimental rats of group C treated with combined plants' extract (*C. colocynthis* + *M. charantia*) kidney weight were decreased significantly as compared to diabetic control group. Result of present study showed that there was highly significant (P<0.05) decrease in the kidney weight of treatment groups in comparison to control groups (Table 3). Organs weight increased due to inflammation of organs and changes their morphology progressively. Present research work similar to the early finding of (Benariba et al., 2009). They designed a study to check the anti-hyperglycemic potential of *Citrullus colocynthis* extract in streptozotocin-induced diabetic rats. The experimental rats were treated with *M. charantia* triglycerides level decreased in relate to diabetic control group and when experimental rats treated with combined plant's extracts (*C. colocynthis* + *M. charantia*) triglycerides level decreased as compared to diabetic control group. In present research, result showed that there was non-significant (P>0.05) increased in the triglycerides level of treatment groups than the control groups (Table 4). In the recent study it was observed that the high density lipoprotein level was reduced in diabetic control group in relate to the control group. When the experimental rats were treated with *C. colocynthis* HDL level increased in comparison of the diabetic control group. The experimental rats were treated with *M. charantia* high density lipoprotein level increased than diabetic control group and when experimental rats treated with combined plant's extracts (*C. colocynthis* + *M. charantia*) high density lipoprotein level increased as compared to diabetic control group. The result of present study showed that there was non-significantly (P>0.05) increase in the high density lipoprotein level was recorded in treated groups in comparison of the control groups (Table 4). When all the extracts treated on the diabetic rats such as, VLDL level was increase in the diabetic rats when it treated with *C. colocynthis* as compared to control group of rats similarly when the diabetic rats treated with *M. charantia* VLDL level was significantly increased as compared to control group. When the diabetic rats was treated with combined plants extracts (*C. colocynthis* + *M. charantia*) VLDL level increased significantly as compared to control group, similarly VLDL level increased in diabetic control group than healthy control group. In present research, there was non-significantly (P>0.05) increase in the Very low density lipoprotein (mg/dL) level of treated groups was recorded in comparison of the control groups (Table 4). HbA1c of the control group was increased as compared to the diabetic (untreated) control group. When diabetic group of rats of group A treated with *C. colocynthis* its HbA1c level was increased as compared to control group that was highly significant, similarly when other diabetic rats of group B treated with *M. charantia* its HbA1c level was significantly decreased as compared to healthy control group. When the combination of both plants was treated with diabetic rats of group C its level of HbA1c was (7.38 ± 0.85%) significantly increased as compared to the healthy control group. In present findings there was significant (P<0.05) decrease in the HbA1c (%) of treated groups than control groups (Table 5).

Conclusion

In conclusion, from the results of current study as discussed above, it is clear that the plant extracts significantly modify the biochemical characteristics of serum to boost up health of diabetic rats. Thus it is recommended that these plants extracts or their products can be used in the diet of diabetic patients.

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