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ORIGINAL ARTICLE

Medicine Science International Medical Journal

Medicine Science 2023;12(1):167-74

Importance of curcumin effect and asprosin level on glucose metabolism in diabetic rats

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Received 29 December 2022; Accepted 27 January 2023
Available online 24.02.2023 with doi: 10.5455/medscience.2022.12.281

Abstract

Asprosin is a new hormone secreted mainly from white adipose tissue. It may be associated with the pathogenesis of obesity, diabetes and some metabolic diseases. The changes in plasma asprosin levels of experimental diabetic rats and the relation of these changes with liver glucose metabolism and some diabetes parameters were investigated, and the effects of metformin, gliclazide or curcumin treatment on plasma asprosin levels were tried. The study was designed as an animal model in diabetic rats The albino rats were divided into five groups. To induce diabetes, a single dose of STZ was injected intraperitoneally. Diabetics rats were treated intragastrically with metformin (D+Metformin group), gliclazide (D+Giliclazide group) or 20 curcumin (D+Curcumin group) for eight weeks. Fasting blood glucose, insulin levels and other parameters were measured. Plasma asporsin levels of untreated diabetic rats increased significantly (P<.001). Although the plasma asprosin levels of diabetic rats treated with the rugs were significantly lower (P<.001). Fasting blood glucose levels of diabetic rats treated with the drugs were found to be remarkably lower than the diabetic control values (P<.001, respectively). There was no significant difference in the insulin levels and HOMA-IR between these three groups. Curcumin treatment provides significant improvements in plasma asprosin level and diabetes parameters. The increase in plasma asprosin level in diabetic rats may be one of the main reasons that facilitate the development of the disease or is responsible for its pathogenesis. Our findings support the idea that curcumin may be an important treatment option for diabetes.

Keywords: Streptozotocin, Metformin, Gliclazide, Curcumin, Rat

Introduction

Diabetes mellitus (DM) is a very important metabolic and chronic disease affecting all organs and systems. Micro and macrovascular complications occur, especially in uncontrolled patients [1]. It is interesting that complications may develop in some patients despite being under medical control. Therefore, alternative appropriate treatment methods should be developed to treat the disease and prevent complications [2]. Oxidative stress has been noted in the pathogenesis of diabetes, since some complications cannot be prevented despite treatment with insulin or antihyperglycemic drugs. Based on this, it has been suggested to add various antioxidants to the treatment protocol in recent years [3].

The mechanisms involved in the pathogenesis of diabetes have

CITATION
Gokdemir GS, Gokdemir MT, Tasdemir E, et al. Importance of curcumin effect and asprosin level on glucose metabolism in diabetic rats. Med Science. 2023;12:167-74.

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DOI: 10.5455/medscience.2022.12.281

not yet been fully clarified. In recent years, some hormones defined as adipokines/adipocytokines secreted from adipose tissues have been associated with the pathogenesis of diabetes. Asprosin, which is encoded by the Fibrillin 1 gene in white adipose tissue, is a new hormone discovered in 2016. The main source of asprosin in the blood is white adipose tissue [4]. Asprosin, secreted between meals to maintain the energy level, stimulates the release of glucose from the liver into the bloodstream [5]. As a glucogenic hormone, it stimulates the appetite center in the hypothalamus while increasing the release of glucose from the liver to maintain glucose homeostasis [6]. It is thought to be associated with the pathogenesis of diabetes, as it directly stimulates hepatic glucose secretion and appetite. However, our current literature on the effects of asprosin on glucose metabolism and its relationship with diabetes parameters is not yet sufficient.

In this study, possible changes in plasma asprosin levels of diabetic rats induced by streptozocin(STZ) and the relationship of this change with glucose metabolism, insulin resistance and other diabetes parameters were investigated. Moreover, the effects of metformin, gliclazide and curcumin, which is claimed to be an antidiabetic phytochemical agent, on plasma asprosin levels and liver enzymes related to glucose metabolism were evaluated comparatively.

Key Points

• Asprosin uses various intracellular signals and prepares the ground for insulin resistance through disruption of glucose metabolism.

• Changes in plasma asprosin levels are associated with some diabetes parameters and have a positive effect on plasma asprosin levels after clinical improvement with antidiabetic treatment.

• Treatment of diabetic rats with curcumin resulted in improvements in fasting blood glucose, asprosin levels, and insulin resistance. These results suggest that curcumin, which is known to have no known side effects, may gain a more important place among antidiabetic drugs in the future.

Material and Methods

Experimental methods

Our project was approved by Dicle University Animal Experiments Local Ethics Committee with protocol number 2019/07/4 and date 28/03/2019. In this study, thirty-five Wistar albino adult male rats (224-295 g.) were used. Subjects were divided into one control and four diabetic groups, each with 7 rats. To induce diabetes, STZ solution (single dose, 60 mg/kg) prepared in phosphate-citrate buffer (pH: 4.5) was injected in the same way 15 minutes after nicotinamide (110 mg/kg) was administered intraperitoneally. Two days later, fasting blood glucose was measured in blood samples taken from the tail vein with a glucometer (Plusmedfast test, Tyson Bioresearch Inc., Taiwan). Those with a blood glucose level of 14 mmol/dl=250 mg/dl and above were included in the diabetic groups. All groups were fed in stainless steel cages with 12 hours light, 12 hours dark and 22±2 °C with normal pellet feed and tap water for 8 weeks without any restriction. Healthy rats and non-medicated diabetic rats were fed a normal diet, and no drugs were administered. Only placebo (tap water) was given by gastric gavage. Other diabetic rats were treated with 150 mg/kg/day metformin (D+Metformin group), 10 mg/kg/day gliclazide (D+Gliclazide group), or 200 mg/kg/day curcumin extract (D+Curcumin group) by gastric gavage for 8 weeks. Weekly decrease or increase in body weight and fasting blood glucose measurements of all groups were determined. At the end of the eight-week experimental period, rats were sacrificed by cardiac puncture under mild ketamine anesthesia after 12 hours of fasting. After the abdomen was opened and the liver samples taken were homogenized, hexokinase (HK),pyruvatekinase (PK), glucose-6-phosphatase (G6P-az) and glucose-6-phosphate dehydrogenase (G6PD) activities related to glucose metabolism were measured using appropriate kits and methods.

Chemicals and application methods

To induce diabetes, nicotinamide (Sigma Chemical, St. Louis, MO., USA) dissolved in saline was administered intraperitoneally at a dose of 110 mg/kg after 12 hours of fasting. After 15 minutes, a single dose of 60 mg/kg STZ (Sigma Chemical, St. Louis, MO., USA)] dissolved in 0.1 M phosphate-citrate buffer (pH: 4.5) was injected intraperitoneally. Eight hours after STZ injection, 15% glucose solution given to prevent hypoglycemia.

Preparation of Samples

Blood samples taken by cardiac puncture were centrifuged at 3000 rpm for 10 minutes (Heraeus Biofuge Stratos; Kendo Laboratory Products, Osterode-Germany), and their sera were separated. To obtain plasma samples, blood samples were placed in EDTA tubes. Serum and plasma samples placed in Eppendorf tubes were stored at -80°C until analysis.

After the liver tissues were rapidly homogenized, the supernatants were stored at -80°C until the enzyme activities were measured by ELISA.

Measurement methods

Insulin Level

Serum insulin concentration was measured spectrophotometrically with a rat insulin ELISA kit from Sun Red (Catalog no: 201-11-0708) Biochrom in an ANTHOS-ZENYTH200 Microplate reader.

Plasma Asprosin Level

A rat asprosin ELISA kit (Sun Red, catalog no: 201-11-2025) was used to measure plasma asprosin levels. After the absorbances were determined spectrophotometrically in a microplate reader (Biochrom®ANTHOS-ZENYTH200), the results were expressed as pg/mL.

DOI: 10.5455/medscience.2022.12.281

Other Biochemical Parameters

Fasting blood glucose, TG, TC, VLDL-C, LDL-C and HDL-C levels were measured on the Abbott Architect C16000 Photometric Autoanalyzer device using Abbott Diagnostics original kits (Abbott Laboratories, Abbott Park, IL, USA). The HOMA-IR (homeostatic model assessment-insulin resistance) formula was used to determine HOMA-IR.

HOMA-IR was calculated using the formula below after measuring fasting blood insulin and glucose levels. HOMA-IR=Fasting Glucose (mg/dL) X Fasting insulin (uIU/mL)/405. In addition, parameters related to lipid metabolism, including serum triglyceride(TG), total cholesterol (TC), High-density lipoprotein-cholesterol (HDL-C),Low-density lipoprotein-cholesterol (LDL-C) and Very Low-Density Lipoprotein Cholesterol (VLDL-C) levels, were determined.

Liver enzymes

Nine milliliters of phosphate buffer solution was added to one gram of liver tissue and homogenized in a Bandelin-UW 2070 brand tissue homogenizer at 15000 rpm for 60 seconds. The homogenates were centrifuged at 5000 rpm for 10 minutes at 4°C. Supernatants were transferred to Eppendorf tubes, and liver enzymes were measured spectrophotometrically in the Biochrom ®ANTHOS-ZENYTH200 Microplate reader with HK, PK, G6P-az and G6PD Sun Red brand ELISA kits on the same day.

Statistical Evaluation

SPSS 25 version statistical program was used in computer environment for data analysis. Student's t test was used for comparisons between binary variable groups, and analysis of variance (ANOVA) was used for more than 2 comparisons. Tukey's test was used for multiple comparisons within groups. Positive or negative relationships among the data were determined with Spearman's correlation test. The results are expressed as the arithmetic mean±standard deviation, and $p < 0.05$ was considered significant for one-way ANOVA, Tukey's test, and Spearman's correlation tests.

Results

Body weight changes of the rats

The weekly feed and water consumption and body weight changes of all groups are shown in Table 1. The feed and water consumption of all groups, except the D+ metformin group, increased significantly over the weeks. However, diabetic rats consumed more feed and water than healthy controls. While the body weights of healthy rats increased over time, the body mass of diabetic patients who consumed excessive feed and water decreased significantly.

Plasma asprosin levels

After the experimental period, the fasting plasma asprosin levels of all groups are shown in Table 2. Plasma asporsin levels of untreated diabetic rats increased significantly (P<.001). Although the plasma asprosin levels of diabetic rats treated with metformin, gliclazide or curcumin were significantly lower (P<.001), they did not fully return to normal healthy values. When the effects of these three antidiabetic agents on blood asprosin levels were compared, no significant difference was found between them (Figure 1).

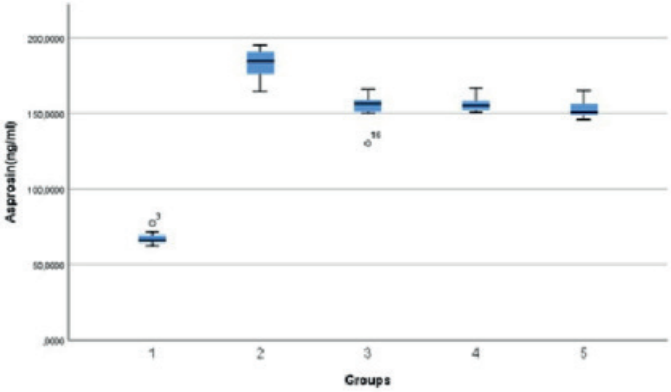

Figure 1. Plasma asprosin levels of healthy controls and diabetic rats treated with metformin, gliclazide and curcumin

Fasting blood glucose, insulin levels and HOMA-IR

As seen in Table 3, fasting blood glucose levels of diabetic rats treated with metformin, gliclazide or curcumin were found to be remarkably lower than the diabetic control values (P<.001, respectively). However, it was determined that the antidiabetics used could not provide a complete improvement in fasting blood glucose level and were effective at a rate of 18%, 27% and 19%, respectively. Although antidiabetic treatment with metformin, gliclazide or curcumin increased insulin levels in diabetic rats, this increase was not statistically significant. In addition, the insulin levels of these three groups were quite close to each other, and there was no significant difference between them (Figure 2). Thus, the effects of metformin, gliclazide and curcumin on HOMA-IR in diabetic rats were also quite similar. Antidiabetic treatments improved insulin resistance by 9%, 20%, and 13%, respectively.

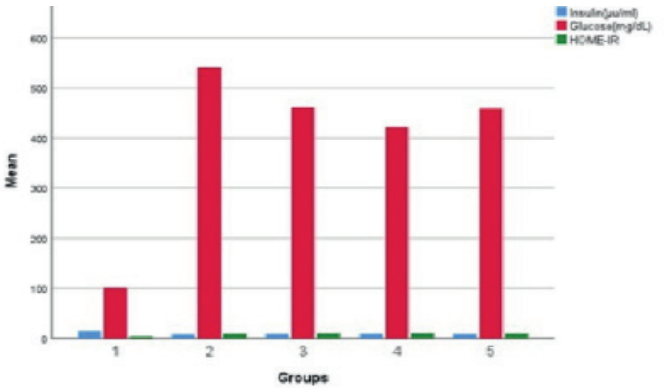

Figure 2. The effects of curcumin on insulin level, glucose level and insulin resistance in diabetic rats and comparison with the effects of metformin and gliclazide

DOI: 10.5455/medscience.2022.12.281

Table 1. Change in body weight (g) at the end of the 1st and 8th weeks of all groups

Weeks	Groups				
	Control Mean(SD)	**Diabetic (DM)** Mean(SD)	**DM+Metformin** Mean(SD)	**DM+Gliclazide** Mean(SD)	**DM+CurCumin** Mean(SD)
Week 1	450.3(44.1)$^{p=.971}$	496.4(24.6)$^{p<.001*}$	448.3(21.9)$^{p<.001*}$	451.3(38.3)$^{p=.003*}$	443.9(19.9)$^{p<.001*}$
Week 8	449.6 (26.4)	299.6(2.6)	345.4(36.1)	341.8(63.7)	364.6(28.5)

P: Pairwise group comparisons for continuous variable *: P<.05 was considered statistically significant (Student's t test) SD: Standard deviation

Table 2. Comparison of Asprosin level between rat groups

Parameters	Groups				
	Control Mean(SD)	**Diabetic (DM)** Mean(SD)	**DM+Metformin** Mean(SD)	**DM+Gliclazide** Mean(SD)	**DM+CurCumin** Mean(SD)
Asprosin	67.5(5.2)$^{\beta}$	182.3(11.1)^{a}	153.1(11.4)^{a,b}	156.0(5.6)^{a,b}	^{1}52.9(7.1)^{a,b}

All data were calculated using the Tukey test for p Multiple Comparisons (Mean difference is significant at the p<.05 level). P^{a}<.001 compared with the control group, P^{b}<.001 compared with the diabetic group

Table 3. Comparison of Insulin, Glucose and HOMA-IR between rat groups

Parameters	Groups				
	Control Mean(SD)	**Diabetic (DM)** Mean(SD)	**DM+Metformin** Mean(SD)	**DM+Gliclazide** Mean(SD)	**DM+CurCumin** Mean(SD)
Glucose (mg/dl)	100.3(9.3) $^{\beta}$	541.3(21.3)^{a}	460.7(47.4)^{a,b}	421.3(10.6) ^{a,b}	458.4(19.7)^{a,b}
Insulin (µU/ml)	14.8(0.7) $^{\beta}$	7.7(0.6)^{a}	8.5(0.9)^{a}	8.6(0.8)^{a}	8.2(0.7)^{a}
HOMA-IR	3.7(0.4) $^{\beta}$	8.9(0.8)^{a}	9.6(1.2)^{a}	10.2(0.6)^{a,b}	9.3(0.7)^{a}

All data were calculated using the Tukey test for p Multiple Comparisons (Mean difference is significant at the p <.05 level).The HOMA-IR was calculated as shown in the formula: HOMA-IR=[fasting insulin (µU/l)×fasting glucose (nmol/l)]/405; P^{a}<.05 compared with the control group, Pb<.001 compared with the diabetic group. P$^{\beta}$: one-way Anova test, P$^{\beta}$<.001

Table 4. Comparison of Liver Enzyme values

Parameters	Groups				
	Control Mean(SD)	**Diabetic (DM)** Mean(SD)	**DM+Metformin** Mean(SD)	**DM+Gliclazide** Mean(SD)	**DM+CurCumin** Mean(SD)
HK(µmol/mg tissue)	262.1(7.8)$^{\beta}$	130.9(8.1)^{a}	255.1(6.2)^{b}	246.7(3.3)^{a,b}	227.7(9.5)^{a,b,c,d}
G6P(µmol/mg tissue)	1064.4(3.2)$^{\beta}$	2103.9(1.7)^{a}	1804.7(0.7)^{a,b}	1865.1(8.4)^{a,b,c}	1821.1(16.4)^{a,b,c,d}
G6PD(µmol/mg tissue)	514.8(2.7)$^{\beta}$	260.7(1.7)^{a}	409.1(0.4)^{a,b}	427.3(1.1)^{a,b,c}	416.1(1.2)^{a,b,c,d}
PK(µmol/mg tissue)	207.1(1.9)$^{\beta}$	98.2(0.9)^{a}	156.3(1.4)^{a,b}	155.6(3.1)^{a,b}	152.9(1.5)^{a,b,c}
A LP(U/L)	189.3(7.5)$^{\beta}$	771.4(104.1)a	691.0(7.4) ^{a,b}	657.3(40.5)^{a,b,c}	674.6(52.1)^{a,b,c,d}
A LT(U/L)	44.7(4.8)$^{\beta}$	95.3(9.2)^{a}	87.4(5.6)^{a}	90.3(6.9)^{a}	90.3(10.8)^{a}
A ST(U/L)	89.1(6.6)$^{\beta}$	138.6(11.4)^{a}	131.4(8.1)^{a}	132.3(10.1)^{a}	133.1(5.9)^{a}
GGT (U/L)	6.6(1.5)$^{\beta}$	17.3(0.8)^{a}	15.3(0.5)^{a,b}	15.1(09.7)^{a,b}	15.4(0.5)^{a,b}

All data were calculated using the Tukey test for p Multiple Comparisons (Mean difference is significant at the p<.05 level). P^{a}<.001 compared with the control group, P^{B}<.001 compared with the diabetic group, p^{c}<.05 compared with DM+Metformin group p^{d}<.05 compared with DM+Gliclazide group. P$^{\beta}$:one-way Anova test, P$^{\beta}$<.001

HK: Hexokinase, G6P: Glucose 6 Phosphate, G6PDH: Glucose 6 Phosphate Dehydrogenase, PK: Pyruvate Kinase, ALP: alkaline phosphatase, ALT: alanine aminotransferase, AST: Aspartate Aminotransferase

DOI: 10.5455/medscience.2022.12.281

Table 5. Comparison of Serum Lipid values

Parameters	Groups				
	Control Mean(SD)	**Diabetic (DM)** Mean(SD)	**DM+Metformin** Mean(SD)	**DM+Gliclazide** Mean(SD)	**DM+CurCumin** Mean(SD)
TC (mg/dL)	77.3(6.1)$^{\beta}$	95.1(4.9)^{a}	80.1(1.9)^{b}	79.0(1.3)^{b}	82.1(2.4)^{b}
HDL (mg/dL)	33.6(1.9)$^{\beta}$	23.2(2.6)^{a}	26.2(1.3)^{a,b}	28.3(1.1)^{a,b}	26.3(2.1)^{a,b}
TG (mg/dL)	78.0(8.3)$^{\beta}$	100.4(11.2)^{a}	87.9(6.7)^{b}	84.9(5.4)^{b}	85.7(6.1)^{b}
VLDL(mg/dL)	15.6(1.7) $^{\beta}$	20.1(2.6)^{a}	17.6(1.3)^{b}	16.9(1.1)^{b}	17.1(1.2)^{b}
LDL-C(mg/dL)	28.1(6.6)	51.9(4.5)^{a}	36.4(1.7)^{a,b}	33.8(1.6)^{b}	38.7(2.9)^{a,b}

All data were calculated using the Tukey test for p Multiple Comparisons (Mean difference is significant at the P <.05 level). P^{a}<.05 compared with the control group, P^{b}<,05 compared with the diabetic group. P$^{\beta}$:One-way Anova test, P$^{\beta}$<.001
TC: Total Cholesterol TG: Triglyceride, HDL: High Density Lipoprotein Cholesterol, LDL: Low Density Lipoprotein Cholesterol, VLDL: Very Low Density Lipoprotein

Liver enzymes

Liver enzymes related to glucose metabolism in healthy and diabetic rats are presented in Table 4. HK, G6PD and PK activities were significantly decreased in diabetic rats, while G6P-ase activity increased. These changes in diabetes-related liver enzyme activity were significantly improved with metformin, gliclazide or curcumin treatment and were very close to healthy control values.

Enzymes related to the assessment of liver injury, alanine amino transferase (ALT), aspartate amino transferase (AST), alkaline phosphatase (ALP), and gamma glutamyl transferase (GGT) activity were significantly elevated in diabetic rats (Figure 3). This negative effect of diabetes on the liver decreased significantly with metformin, gliclazide, or curcumin treatment (Table 4).

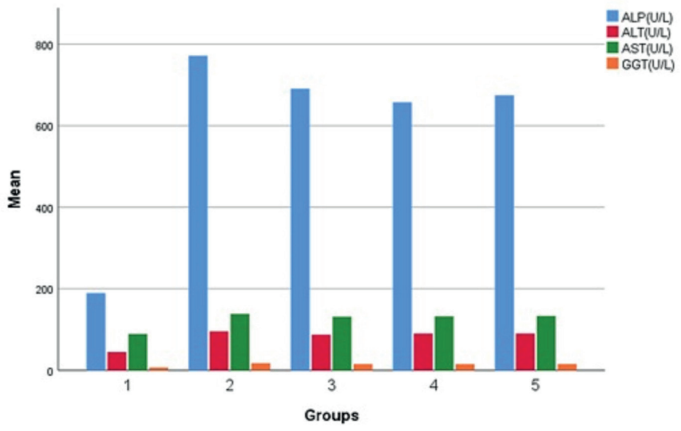

Figure 3. The comparison of liver enzymes levels related to glucose metabolism of healthy and diabetic rats

Serum lipid levels

The serum lipid parameters of all groups are shown in Table 5. Serum TG, TC, VLDL-C and LDL-C levels of diabetic control rats increased significantly compared to normal values, while HDL-C levels decreased. Metformin, gliclazide, or curcumin treatment produced significant improvements in serum lipid parameters of diabetic rats, close to healthy control values.

Correlation tests

In this study, the correlations with Asprosin and other variables are shown in Table 6. We determined that plasma asprosin levels were positively correlated with fasting blood glucose and insulin resistance but negatively correlated with insulin levels (R=.976, P<.001, R=.874, P<.001, R=-.936, P<.001, respectively). When the relations of asprosin with glucose metabolism were examined, it was observed that there was a positive correlation between plasma asprosin level and liver enzymes, G6P, and GGT (R=.965, P< .001 and R=.981, P< .001), although there was a negative correlation with G6P-ase activity (R= -.829, P<.001). In addition, our results showed that there is a negative correlation between plasma asprosin levels and liver health status. Likewise, asprosin was also found to be associated with lipid metabolism. While there were positive correlations between plasma asprosin concentration and serum lipid parameters CHOL, TG and LDL-C (R=.558, P<.001; R=.594, P<.001 and R=.696, P<.001, respectively), plasma asprosin level and serum HDL-C amount were found to be negatively correlated (R= -.826 P<.001).

DOI: 10.5455/medscience.2022.12.281

Table 6. Correlation of Asprosin Level with Insulin HOMA-IR, Blood Glucose, Liver Enzymes, and Blood Lipid and Cholesterol

Parameters	Asprosin (R,P)
Insulin (µU/ml)	(R=-.936, P< .001)
HOME-IR	(R=.874, P< .001)
Glucose (mg/dl)	(R=.976, P< .001)
HK(µmol/mg tissue)	(R=-.611, P< .001)
G6PD(µmol/mg tissue)	(R=-.829, P< .001)
PK(µmol/mg tissue)	(R=-.897, P< .001)
A LP(U/L)	(R=.958, P< .001)
A LT(U/L)	(R=.900, P< .001)
A ST(U/L)	(R=.862, P< .001)
TC(mg/dL)	(R=.558, P< .001)
HDL (mg/dL)	(R=-.826, P< .001)
TG (mg/dL)	(R=.594, P< .001)
LDL-C(mg/dL)	(R=.696, P< .001)
G6P(µmol/mg tissue)	(R=.981, P< .001)
GGT(U/L)	(R=.965, P< .001)

*p<0.05 was considered statistically significant
Abbreviations: WBC:white blood cells; RDW=:red blood cell distribution width; MPV=mean platelet volume (MPV); NLR=Neutrophil to lymphocyte ratio; PLR= Platelet to lymphocyte ratio; SII= systemic immune inflammation index

Discussion

Asprosin shows complex important effects in carbohydrate and lipid metabolism and metabolic diseases. It plays a role in glucose metabolism and insulin resistance by using many intracellular signaling pathways [7]. It has been shown in vitro to cause inflammation, apoptosis, a decrease in insulin production and cellular dysfunction in pancreatic β cells [8]. Plasma asprosin levels were found to be higher in people with high insulin resistance, Type 2 diabetic patients and mice than in healthy controls [7-10]. Some researchers have documented an independent positive correlation between plasma asprosin levels and insulin resistance [11-14]. In addition, serum asprosin levels were recently found to be higher in the umbilical cord of pregnant women with diabetes and their babies [15].

Considering these results, asprosin seems to be a major component in glucose homeostasis. Indeed, Romere et al. showed that a single subcutaneous injection of recombinant asprosin into mice causes hyperinsulinemia after hyperglycemia, and specific asprosin antibodies ameliorate insulin resistance by normalizing blood glucose and insulin levels [11]. Considering these data, it was suggested that plasma asprosin levels can be used as a biomarker for the early diagnosis of diabetes and monitoring its prognosis.

In our study, as in many previous similar studies, plasma asprosin levels in STZ-induced diabetic rats were significantly elevated. In addition, we found positive correlations between plasma asprosin levels and fasting blood glucose, insulin levels and insulin resistance. Our findings support the majority of available literature [9,12-14]. However, it is necessary to consider the results of studies that do not confirm a positive correlation between plasma asprosin level and insulin resistance or, on the contrary, show a negative relationship [15].

Treatment of diabetic rats with curcumin or conventional antidiabetic drugs, metformin or gliclazide resulted in improvements in fasting blood glucose, asprosin levels, and insulin resistance. When the effects of these three antidiabetic agents were compared, it was seen that there was no significant difference between them. Considering the increase in plasma asprosin levels and partial recovery after antidiabetic treatment in diabetic rats, the idea that asprosin may increase insulin resistance by negatively affecting fasting blood sugar and insulin levels should be considered.

In our study, hepatic enzymes related to glucose metabolism, HK, G6PD and PK levels of diabetic rats increased significantly, while G6P-ase activity decreased. Increased glycolysis on the one hand and increased gluconeogenesis on the other, this imbalance between liver enzymes contributed significantly to the elevation of blood glucose levels in untreated diabetic rats. Metformin, gliclazide or curcumin treatment significantly reduced this diabetes-related imbalance in glucose metabolism. Moreover, the three antidiabetic agents we used in this study showed a rather similar curative effect on biomarkers of liver injury and serum ALP, ALT, AST and GGT levels in diabetic rats.

Dyslipidemia is frequently encountered in diabetic patients, especially those with Type 2 diabetes. Generally, patients have an increase in serum triglyceride, VLDL-C and LDL-C levels, while a decrease in HDL-C levels is observed [16,17]. Serum triglyceride, VLDL-C and LDL-C levels increased, while HDL-C levels decreased. The therapeutic effects of curcumin, metformin, and gliclazide on the plasma lipid profile in STZ-induced diabetic rats were quite similar, but curcumin increased HDL-C levels more than the others.

In our study, the effects of curcumin were compared with those of other antidiabetic drugs, metformin and gliclazide. Curcumin has a potential role in both the treatment and prevention of various diseases due to its antibacterial, anti-diabetic, anti-viral and anticancer effects [18-20]. It has been reported to improve pathological events, blood glucose, lipid profiles, hepatic antioxidant levels, and biomarkers of liver and kidney damage in type 2 diabetic patients through different mechanisms and multiple molecular targets [21-24]. Curcumin treatment with yogurt for one month showed antihyperglycemic and antihyperlipidemic effects in STZ-induced diabetic rats.25The same researchers observed that supplementation of 50 or 100 mg/kg/day curcumin to the diet of diabetic rats reduced hyperglycemia and vascular

DOI: 10.5455/medscience.2022.12.281

inflammation [26]. Current information and the results of this study indicate that curcumin may be an alternative antidiabetic in the treatment of diabetes.

Our study was done as an experimental rat model and there are some limitations. Since our study was an animal experiment, a limited number of rats were included. Results such as serum glucose, liver enzymes, insulin resistance and cholesterol in rats may differ from humans. Another limiting factor is the inability to study the pancreatic pathology of rats.

Conclusion

Some proinflammatory adipocytokines secreted from white adipose tissue have been associated with diabetes pathogenesis or prognosis. New adipokines are being discovered every day, and the number of cytokines associated with diabetes pathogenesis is increasing. Although the pathogenesis of diabetes is not completely clear, we can say that there is a clear relationship between asprosin and the development of diabetes. If its negative effects on glucose metabolism can be controlled, asprosin may be a new target for the prevention and alternative treatment of diabetes. The available information is not yet sufficient to establish a causality between high plasma asprosin levels and diabetes. Whether the increase in plasma asprosin levels is a protective feedback mechanism for diabetes or a result of metabolic disorders has not yet been fully proven. In any case, the results of this study and many similar studies support the idea that plasma asprosin levels may be an important biomarker for the diagnosis and prognosis of diabetes.

As in many similar studies, our findings confirm that curcumin is an antidiabetic compound and show that it has similar effects on glucose metabolism as the classical antidiabetics metformin or gliclazide. Curcumin may be an alternative option in the treatment of diabetes, as it has been reported that it has no significant side effects or its anti-inflammatory and other positive effects.

Conflict of interests

As the authors, we declare that there is no conflict of interest between us.

Financial Disclosure

The authors declare that they have received no financial support for the study.

Ethical approval

Our project was approved by Dicle University Animal Experiments Local Ethics Committee with protocol number 2019/07/4 on 28/03/2019.

Acknowledgments

I would like to thank the staff of Dicle University Health Sciences Application and Research Center for their contribution to the feeding and preparation of animals.

References

1. Karagoz ZK, Sahin I,Kurt F, Cil BO. Evaluation of the effect of metformin treatment on markers of bone formation and resorption in patients newly diagnosed with Type 2 diabetes. Medicine Science 2022;11:1715-9
2. Alshabi AM, Shaikh IA. Antidiabetic and antioxidant potential of Gardenia latifolia in type-2 diabetic rats fed with high-fat diet plus low-dose streptozotocin. Saudi Med J. 2022;43:881-90
3. Darenskaya MA, Kolesnikova LI, Kolesnikov SI. Oxidative Stress: Pathogenetic Role in Diabetes Mellitus and Its Complications and Therapeutic Approaches to Correction. Bull Exp Biol Med. 2021;171:179-89.
4. Jiang WY, Huo JY, Wang SC, et al. Trimethylamine N-oxide facilitates the progression of atrial fibrillation in rats with type 2 diabetes by aggravating cardiac inflammation and connexin remodeling. J Physiol Biochem 2022; 78:855-67.
5. Mazur-Bialy AI. Asprosin-A Fasting-Induced, Glucogenic, and Orexigenic Adipokine as a New Promising Player. Will It Be a New Factor in the Treatment of Obesity, Diabetes, or Infertility? A Review of the Literature. Nutrients. 2021;13:620.
6. Hu Y, Xu Y, Zheng Y, et al. Increased plasma asprosin levels in patients with drug-naive anorexia nervosa. Eat Weight Disord. 2021;26:313-21.
7. Hoffmann JG, Xie W, Chopra AR. Energy Regulation Mechanism and Therapeutic Potential of Asprosin. Diabetes. 2020;69:559–66
8. Lee T, Yun. S, Jeong JH, Jung TW. Asprosin impairs insulin secretion in response to glucose and viability through TLR4/JNK-mediated inflammation. MolCell Endocrinol. 2019;486:96–104.
9. Roh KH, Abdellrahim AA, Abo Elwafa RAH, Moawad MG. Study of the Relationship between Serum Asprosin, Endothelial Dysfunction and Insulin Resistance. Clin Diabetol. 2022;11:73–79
10. He F, Huang Y, Song Z, et al. Mitophagy-mediated adipose inflammation contributes to type 2 diabetes with hepatic insulin resistance. J Exp Med. 2021;218:e20201416.
11. Romero C, Duerrschmid C, Bournat J, et al. Asprosin, a fasting-induced glucogenic protein hormone. Cell. 2016;165:566–79
12. Li X,Liao M, Shen R, et al. Plasma asprosin levels are associated with glucose metabolism, lipid, and sex hormone profiles in females with metabolic-related diseases. Mediators of Inflammation. 2018; 6;2018:737529412.
13. Zhang X, Jiang H, Ma X, Wu H. Increased serum level and impaired response to glucose fluctuation of asprosin is associated with type 2 diabetes mellitus. J Diabetes Investig. 2020;11:349-55.
14. Goodarzi G,Setayesh L,Fadaei R, et al. Circulating levels of asprosin and its association with insulin resistance and renal function in patients with type 2 diabetes mellitus and diabetic nephropathy. Mol Biol Rep.2021;48:5443-50
15. Baykus Y, Yavuzkir S, Ustebay S, et al. Asprosin in umbilical cord of newborns and maternal blood of gestational diabetes, preeclampsia, severe preeclampsia, intrauterine growth retardation and macrosemic fetus. Peptides.2019;120:1–5.
16. Zhang X, Xing L, Jia X, et al. Comparative Lipid-Lowering/Increasing Efficacy of 7 Statins in Patients with Dyslipidemia, Cardiovascular Diseases, or Diabetes Mellitus: Systematic Review and Network Meta-Analyses of 50 Randomized Controlled Trials. Cardiovasc Ther. 2020;23:3987065.
17. Kane JP, Pullinger CR, Goldfine ID, Malloy MJ. Dyslipidemia and diabetes mellitus: Role of lipoprotein species and interrelated pathways of lipid metabolism in diabetes mellitus. Curr Opin Pharmacol. 2021;61:21-7.
18. Marton LT, Pescinini-E-Salzedas LM, Camargo MEC, et al. The Effects of Curcumin on Diabetes Mellitus: A Systematic Review. Front Endocrinol (Lausanne). 2021;12:669448.
19. Peng Y, Ao M, Dong B, et al. Anti-Inflammatory Effects of Curcumin in the Inflammatory Diseases: Status, Limitations and Countermeasures. Drug Des Devel Ther. 2021;15:4503-25
20. Giordano A, Tommonaro G.Curcumin and Cancer. Nutrients. 2019;11:2376.

DOI: 10.5455/medscience.2022.12.281

21. Seo KI, Choi MS, Jung UJ, et al. Efect of curcumin supplementation on blood glucose, plasma insulin, and glucose homeostasis related enzyme activities in diabetic db/db mice. Mole. Nutr. Food Res. 2008;52:995–04.

22. Jiménez-Flores LM, López-Briones S,Macías-Cervantes MH, et al. A PPAR, NF-_B and AMPK-Dependent mechanism may be involved in the beneficial e_ects of curcumin in the diabetic db/db mice liver. Molecules. 2014;19:8289–302.

23. Gutierres VO, Assis RP, Arcaro CA, et al. Curcumin improves the effect of a reduced insulin dose on glycemic control and oxidative stress in streptozotocin-diabetic rats. Phytotherapy Research. 2019;33:976–88.

24. Pivari F, Alessandra Mingione A, Brasacchio C, Laura Soldati L. Curcumin and Type 2 Diabetes Mellitus: Prevention and Treatment. Nutrients. 2019;11:1837

25. Gutierres VO, Pinheiro CM, Assis RP, et al. Curcumin supplemented yoghurt improves physiological and biochemical markers of experimental diabetes. Br J Nutr. 2012;108:440-8.

26. Jain SK, Rains J,Croad J,et al. Curcumin Supplementation Lowers TNF-_, IL-6, IL-8, and MCP-1 Secretion in High Glucose-Treated Cultured Monocytes and Blood Levels of TNF, IL-6, MCP-1, Glucose, and Glycosylated Hemoglobin in Diabetic Rats. Antioxid. Redox Signal. 2008;11:241–9.