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RESEARCH PAPER

Effect of a different forms of ketogenic diets on some biochemical variables in male type II DM rats model

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A B S T R A C T:

Ketogenic diets (KD) have been used in recent years for the treatment of many metabolic disorders. This study aimed to modify the KD to improve hyperglycemia. Forty-eight male albino rats weighing 250–350 g were divided into two groups. Control (n = 8) and type II diabetic groups (n = 40) were injected with a single low dose of streptozotocin (25 mg/kg) intraperitoneally after they fed on a high-fat high-fructose (HFHF) diet for 8 weeks, and then divided into six subgroups. The first subgroup was a diabetic control and fed on a basic diet, while subgroup 2, was fed on a saturated KD, subgroup 3, was fed on an unsaturated KD, subgroup 4, was fed on a saturated KD combined with orlistat drug, subgroup 5, was fed on a saturated KD combined with vinegar, and the final subgroup was fed on a saturated KD combined with orlistat and vinegar for 8 weeks. After comparing the results with controls, it was indicated that rats injected with STZ had significantly ($P \leq 0.05$) higher blood glucose levels. In comparison to the control positive group, the treated rats' liver and renal functions improved when KD was combined with butter, olive oil, orlistat, and vinegar. In conclusion, feeding an HFHF diet with a single low-dose streptozotocin injection, induced a stable type 2 diabetes mellitus (T2DM) model also the KD and when combined, both have shown to be potentially beneficial diets for diabetic disease. However, orlistat and vinegar, when combined with KD, hurt rats' livers and kidneys.

KEY WORDS: Ketogenic diet, Type II diabetes, Olive oil, Orlistat and Ketoacidosis
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1. INTRODUCTION:

Ketogenic diet fat contents were typically 60% to 85%, protein, 15% to 30%, and 5% to 10% carbohydrate. This causes the synthesis of high quantities of ketogenic bodies via fat metabolism, which makes all cells use fat as their primary source of energy (Boison, 2017).There are several variations of the KDs, but they all have a similar result. The four primary types are cyclic KD (CKD), high protein KD (HPKD), standard KD (SKD) and target KD (TKD) respectively. A fore mentioned different KDs are usually comparable in a lot of ways, notably in terms of how low in carbohydrates and high in dietary fat they are (D'Andrea Meira et al., 2019). The liver produces the ketone bodies 3-hydroxybutyrate (3HB), acetone, and acetoacetate (AcAc), which are utilized by peripheral tissues as an energy source when glucose becomes unavailable or decreases to a low concentration (Puchalska and Crawford, 2017).

Glucagon and insulin control the synthesis and metabolism of ketone bodies (Weber et al., 2020). The complicated process of ketone body generation (Ketogenesis), which takes place in the mitochondria of the liver cell, requires three enzymes: mitochondrial acetoacetyl-CoA thiolase, mitochondrial 3-hydroxy-3-methylglutaryl-CoA (HMG-CoA) synthase and mitochondrial HMG-CoA lyase (Jensen et al., 2020). The additional cellular cells in the liver simply pick up the AcAc and 3HB, which are soluble in blood circulation. Due to incomplete enzymatic decarboxylation, some AcAc may convert to acetate, which is a volatile ketone that can be detected in the breath (Trimboli et al., 2020).

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Ketolysis is the term for the oxidation of ketone bodies that occurs in the majority of cells to provide energy. The elimination of ketone molecules from blood is mostly accomplished by the plasma membrane protein known as monocarboxylate transporter 1 (MCT1). A specific enzyme changes the ketone body AcAc or 3HB to produce Acetyl-CoA, which enters the TCA cycle to produce ATP (Shafqat et al., 2013).

Recently, ketogenic diets have been employed as a method for treating obesity and several disorders. These diets may help people with T2DM and improve their clinical conditions, such as glycemic management, cholesterol levels, normal blood electrolytes, and weight loss (Buehler et al., 2021). Although KD was used to treat epilepsy by mimicking the effects of fasting, it had the advantage of being able to be maintained for a long time. According to a research, KD may decrease fatty liver by reducing insulin levels and increasing fat oxidation (Schugar and Crawford, 2012).

Consuming KD combined with orlistat (lipase inhibitor) is used for increased weight reduction and improved dyslipidemia (Aaseth et al., 2021). The use of apple cider vinegar has been linked to changes in several metabolic pathways, including those involved in the production and storage of glucose (delayed gastric emptying and enteral absorption, increased glucose utilization, decreased hepatic glucose formation, flow-mediated vasodilatation, increased lipolysis, and decreased lipogenesis) (Kausar et al., 2019).

The ketogenic diet application in people with a normal lipid profile causes a considerable drop in blood triglycerides, a minor rise in total and LDL cholesterol, and a moderate increase in HDL cholesterol. Another study found that HDL cholesterol raised by 0.009 for every kilogram lost while triglycerides dropped by 0.015 mmol/L for every kilogram lost (Dashti et al., 2006). It has been suggested that low-CHO diets may prevent the production of hepatic cholesterol through reducing insulin levels (Kirkpatrick et al., 2019).

The hepatic response to excess body fat, known as nonalcoholic fatty liver diseases (NAFLD), has been associated with insulin resistance, elevated oxidative stress, inflammation, and severe fibrosis. Application of KDs leaded to lowering insulin levels due to their extremely low carbohydrate content, which then reduces lipogenesis and increases FA oxidation rate (Paoli et al., 2013). Other research also suggests that such a sharp reduction in dietary carbs triggers a change in the gut flora, which in turn triggers the creation of folate, which improves lipid metabolism and lowers inflammation and oxidative stress that cause to decrease NAFLD and inhanced the (Mardinoglu et al., 2018).

The other research found statistically and physiologically significant improvements in hepatic and renal health, including alanine aminotransferase, alkaline phosphatase, γ-Glutamyl transferase, creatinine, estimated glomerular filtration rate (eGFR), and urea. Changes in liver enzymes revealed an improvement in hepatic steatosis as well as biochemical markers associated with renal and hepatic disease (Rolland et al., 2013).

The aims of this study are to improve and modify the ketogenic diet on type II diabetic rats. Explore the possible role of low-carb diets in clinical conditions, such as blood PH, glycemic management, cholesterol levels and vital organs function. Role of ketogenic diet on dyslipidemia and fatty liver.

2. MATERIALS AND METHODS

2.1 Chemical substances

In this study, distilled water, (70%) Ethanol, fructose, Supplement foods, Streptozotocin, Citric acid, Sodium citrate, Orlistat, Apple cider vinegar, Ketamine 10% and Xylazine 2% are used.

2.2 Animals

In all studied groups, 48 adult male albino rats (12-16 weeks, 250-350g) were recruited. They were bought from Cihan University in Erbil and kept in well-ventilated cages with a temperature of 25 °C, a humidity of about 50 percent, and a light and dark cycle of about 12:12 hours. Through the whole time of adaptation and treatment, all rats had access to standard rat food pellets table 1, and water ad libitum (Olfert et al., 1993).

Table 1: High-fat and regular diet components:

High-fat diet	g/100	Basic diet	g/100
Soya bean	6.5	**Soya bean**	20
Casein	11.0	**Whole wheat**	20
Mountain flour	0.6	**Mountain flour**	12
Butter	23	**Butter**	5.0
Sodium chloride	0.2	**Sodium chloride**	0.2
Refined wheat	40	**Refined wheat**	18.8
Calcium bicarbonate	1.0	**Calcium bicarbonate**	1.0
Fructose	15.7	**Corn starch**	21
Vitamin and minerals	2.0	**Vitamin and minerals**	2.0

2.3 Experiment design

The forty-eight rats were separated into two groups after two weeks of acclimation as follows: first group (n=8) was retained as a healthy control and fed on a standard diet, while the second group (Diabetic group) n=40 was subdivided into five groups, one of the five subgroups was considered as positive control n=8 that fed a normal diet. The remaining four subgroups are treated with KD (T2DM) which is prepared to meet the nutritional requirements of adult rats as presented in table 2 and mentioned by the American Institute of Nutrition (AIN-93M). The first subgroup was treated with KD which contains saturated fat (butter) named (keto 1). The second subgroup was treated with KD containing unsaturated fat olive oil (keto 2). The third subgroup was treated with KD containing saturated fat and combined with orlistat, 30 mg/kg (Caroline et al., 2021) (keto 3). The fourth subgroup was treated with KD containing saturated fat and combined with vinegar, 2 ml/kg (Ousaaid et al., 2020) (keto 4). The fifth subgroup was treated with KD combined with orlistat and vinegar (keto 5).

2.4 Induction of T2DM animal model:

By consuming a high-fat, high-fructose diet (HFHF diet; table 1) for 8 weeks, followed by an intraperitoneal injection of 25 mg/kg streptozotocin(STZ) dissolved in 0.1 mol/l citrate buffer (pH 4.5), diabetes was induced. Testing blood glucose levels a few days later revealed that any reading above 250 mg/dl considering diabetes (Guo et al., 2018).

Table 2: Macronutrient components and their quantity for each treatment subgroup:

Component	keto 1	Keto 2	keto 3	keto 4	keto 5
Protein (Casein) (20%) g/kg	170	170	170	170	170
Carbohydrate (Wheat) (5%) g/kg	7	7	7	7	7
Saturated Fat (Butter) (75%) g/kg	710	-	710	710	710
Unsaturated Fat (75%) ml/L	-	710	-	-	-
Orlistat tab mg/kg	-	-	30	-	30
Apple acid vinegar ml/L	-	-	-	2	2
Ca2(PO4) g/kg	35	35	28	35	25
Vitamin (V.C.X.L) g/kg	13	13	10	11	10
Choline chloride g/kg	2.5	2.5	2.5	2.5	2.5
Trace element g/kg	2.5	2.5	2.5	2.5	2.5
Methionine g/kg	15	15	7.5	15	7.5
Lysine g/kg	15	15	7.5	15	7.5
NaCl g/kg	15	15	15	15	15
Sand g/kg	15	15	10	15	11
TOTAL	1000	1000	1000	1000	1000

2.5 Blood collection

After 8 weeks of treatment, all rats were injected intraperitoneally with ketamine-xylazine (K, 100 mg/kg; X, 10 mg/kg) to induce a profound coma. Over 30 minutes, the depth of anaesthesia was achieved by both anaesthetic combinations. However, KD administration resulted in a 20% drop in heart rate, a 33% decrease in respiratory rate, and 20% decrease in PaO2 (Wellington et al.,

2013). The blood was collected from the hearts by using a syringe of 10 ml and then dispensed into 2.5 ml heparinized microfuge tubes and the remaining blood was inserted into a gel tube, both tubes were ice kept until centrifugation. During centrifugation, blood samples were spun at 2500 rpm for 9 min to separate the plasma and serum from the other blood components. Plasma was used for the estimation of pH by pH probe device while serum samples were used for the determination of glucose by accu- chek device, Lipid profile, blood urea, creatinine and liver enzymes by Fuji film (Dri-Chem NX500, Japan) Spectrophotometer device.

2.6 Data Analysis, Statistical Analysis:

The results were expressed as Mean ± Mean Standard Error (MSE) and analyzed statistically using one-way analysis of variance ANOVA. The results were considered significant at $P \leq 0.05$ and highly significant at $P \leq 0.001$. Calculations were done by Graph Pad Prism software version 9. Tukey test was used for comparing the mean groups, asteroid and Hash represent the significant change between KD groups that compared with positive control.

3. RESULTS

3.1 pH concentration

The pH value was affected by diabetes and KDs. Table 3, illustrates the effect of different types of KDs on these values in nondiabetic and diabetic groups.

Table 3: The effect of a keto diet on hydrogen ion concentration in diabetic rats.

Rats groups	Plasma pH (Mean ± S.E)
control	8.283 ± 0.14
Diabetic rat (control)	8.017 ± 0.047
Keto1 (KD+ Saturated fat)	6.867 ± 0.25 **
Keto2(KD+Unsaturated fat)	5.933 ± 0.10 **** #
Keto3 (KD+ Saturated fat+ Orlistat)	6.200 ± 0.14 ****
Keto4 (KD+ Saturated fat+ vinegar)	5.700 ± 0.23 **** ###
Keto5 (KD+ Saturated fat+ vinegar+ Orlistat)	6.967 ± 0.05 **

Values were expressed as mean ± SE. asteroid represents the significant change between all the groups compared with positive control. Hash represents the significant change between all groups compared with keto 1.

The plasma pH level showed a non-significant change in the diabetic group when compared with the control group. However, in comparison with keto groups, they decreased highly significantly ($P<0.0001$) except keto 5, which showed a significant ($P<0.0038$) decrease. The keto 1 group showed non-significant changes with keto 5 and 3 but with the keto 4 group, it decreased significantly ($P<0.0010$). In comparison with the keto 1 and 2 groups, the change was significant ($P<0.0139$) but between keto 1 and control was decreased ($P<0.0012$) significantly.

3.2 Lipid profile

The results of the current study indicated that serum lipid profiles were affected by diabetic treatments and keto diets. Table 4 illustrated the effect of different studied keto diet types on lipid profiles in nondiabetic and diabetic groups.

Table 4: The effect of a keto diet on lipid profile in diabetic and nondiabetic rats.

Rats groups	HDL (mg/dl) Mean ± S.E	TG (mg/dl) Mean ± S.E	TCHO (mg/dl) Mean ± S.E	LDL (mg/dl) Mean ± S.E
control	23.50 ± 3.77 ****	89.83 ± 4.33 ****	83.50 ± 2.60 ****	89.83 ± 4.33 ****
Diabetic rat (control)	7.17 ± 0.84	221.0 ± 9.57	158.2 ± 7.70	221.0 ± 9.57
Keto 1 (KD+ Saturated fat)	13.00 ± 1.23	98.33 ± 9.18 ****	74.83 ± 4.93 ****	98.33 ± 9.18 ****
Keto 2 (KD+ Unsaturated fat)	13.83 ± 1.2	38.43 ± 3.1 **** ####	57.67 ± 3.9 ****	38.43 ± 3.2 **** ####
Keto 3 (KD+ Saturated fat+ Orlistat)	11.83 ± 2.2	27.5 ± 1.7 **** ####	57.83 ± 7.3 ****	27.50 ± 1.7 **** ####
Keto 4 (KD+ Saturated fat+ vinegar)	12.33 ± 0.88	44.83 ± 3.6 **** ####	58.35 ± 2.6 ****	44.83 ± 3.6 **** ####
Keto 5 (KD+ Saturated fat+ vinegar+ Orlistat)	9.33 ± 1.2	34.50 ± 0.4 **** ####	37.33 ± 0.66 **** ###	34.50 ± 0.42 **** ####

The differences in the studied HDL levels showed a highly significant (P<0.0001) decrease in diabetic rats without treatment when compared with control, while there were no significant changes between all studied keto diet groups as depicted in table above. The LDL levels increased highly significantly (P<0.0001) in the diabetic group in comparison to the control, and there was a highly significant (P<0.0001) decrease between the diabetic group and all other studied KDs groups. The TG levels increased highly significantly (P<0.0001) in diabetic rats in comparison to the control, and the differences were a highly significant (P<0.0001) decrease between diabetic group and all other studied KDs groups. The TCHO showed a highly significant increase (P<0.0001) in diabetic rats compared to control, while there was highly significant decrease (P<0.0001) between diabetic group and all other keto groups also there was a non-significant change between keto 1 with keto 2, 3 and 4, but with keto 5 was decreased significantly (P<0.0002).

3.3 Fasting blood sugar concentration (FBS)

The concentration of glucose was affected by diabetes and KD. Table 5 illustrated the effect of different types of KD on the concentration of blood sugar in nondiabetic and diabetic groups.

Table 5. The effect of KDs on blood sugar concentration in diabetic rats.

Rat groups	Fasting blood sugar (mg/dl) (Mean ± MSE)
control	100.0 ± 3.109 ****
Diabetic rat (control)	488.0 ± 12.020
Keto 1 (KD+ Saturated fat)	140.5 ± 2.742 ****
Keto 2 (KD+ Unsaturated fat)	128.2 ± 4.468 ****
Keto 3 (KD+ Saturated fat+ Orlistat)	126.8 ± 6.074 ****
Keto 4 (KD+ Saturated fat+ vinegar)	134.7 ± 4.216 ****
Keto 5 (KD+ Saturated fat+ vinegar+ Orlistat)	136.3 ± 1.430 ****

The concentration of serum sugar was increased a highly significantly (P<0.0001) in the diabetic group when compared with the control group. However, all diabetic keto groups showed a highly significant decrease (P<0.0001) when compared with diabetic groups but in comparison with each other groups, it didn't show any significant change.

3.4 Liver enzymes

The liver enzymes (AST and ALT) are affected by diabetes and KD. Table 6 illustrates the effect of different types of KD on these enzymes in nondiabetic and diabetic groups.

Table 6. The effect of KD on liver function enzymes in diabetic rats.

Rats groups	AST (U/L) Mean ± MSE	ALT (U/L) Mean ± MSE
Control	117.5 ± 1. 041 ****	93.00 ± 0.85 ****
Diabetic rats (Positive Control T2DM)	152.3 ± 1.25	110.0 ± 0.73 ****
Keto 1 (KD+ Saturated fat)	124 ± 2.90 ****	98 ± 0.31 ****
Keto 2 (KD+ Unsaturated fat)	121.4 ± 1.94 ****	97.85 ± 1.62 ****
Keto 3 (KD+ Saturated fat+ Orlistat)	128.5 ± 1.20 ****	95.8 ± 1.98 ****
Keto 4 (KD+ Saturated fat+ vinegar)	122 ± 1.70 ****	95.8 ± 0.98 ****
Keto 5 (KD+ Saturated fat+ vinegar+ Orlistat)	269.8 ± 2.05 **** ####	198.5 ± 1.32 **** ####

The activity of serum AST was increased highly significantly (P<0.0001) in the diabetic group when compared with the consistent value of the control (nondiabetic) group. The activity of this enzyme in diabetic groups that were treated by KD and with their supplements decreased highly significantly (P<0.0001) in comparison with the control group. However, there was non-significant change between keto 1 with keto 2 and keto 4 but the keto 5 groups increased highly significantly (P<0.0001) when compared with keto 1 and diabetic groups.

The activity of the ALT enzyme increased highly significantly (P<0.0001) in the diabetic group compared to the consistent value of the control group. The activity of this enzyme in diabetic groups that were treated by KD decreased highly significantly (P<0.0001) when compared with diabetic groups without treatment. However, there were non-significant changes between keto 1, keto 2 and keto 4 but the keto 5 groups increased highly significantly (P<0.0001) in comparison with keto 1 and diabetic groups.

3.5 Kidney function

The urea and creatinine are affected by diabetes and KDs. Table 7, illustrated the effect of different types of KD on these products in nondiabetic and diabetic groups.

Table 7. The effect of KD on kidney function in diabetic rats.

Rat groups	Creatinine (mg/dl) Mean ± S.E	Urea (mg/dl) Mean ± S.E
control	0.40 ±0.0070 ***	39.50 ± 0.7139 ****
Diabetic rat (control)	0.90 ± 0.014	65.05 ± 1.721
Keto 1 (KD+ Saturated fat)	0.36 ± 0.025 ***	37.98 ± 0.8483 ****
Keto 2 (KD+ Unsaturated fat)	0.53 ± 0.021 *	43.65 ± 1.817 ****
Keto 3 (KD+ Saturated fat+ Orlistat)	0.62 ± 0.020 *	56.95 ± 2.581 **##
Keto 4 (KD+ Saturated fat+ vinegar)	0.75 ± 0.040 *	43.53 ± 1.796 ****
Keto 5 (KD+ Saturated fat+ vinegar+ Orlistat)	1.34 ± 0.15 ** ####	53.47 ± 2.343 ** ##

The activity of serum urea was increased highly significantly (P<0.0001) in the diabetic group compared with the control, however, the levels were decreased highly significantly (P<0.0001) between diabetic group (control) and keto 1, 2, and 4 but they decreased significantly (P<0.0030) with keto 3 and 5. There was a non-significant change between keto 1, 2, 3 and 4, but keto 5 increased significantly (P<0.0049) with keto 1. The activity of the creatinine in serum showed a highly significant increase (P<0.0001) in diabetic group when compared with the control group. However, keto 1 showed a significant (P<0.0002) decrease in comparison with the control, and also the groups (keto 2, 3 and 4) showed a significant (P<0.0366) decrease. But with keto 5, it increased significantly (P<0.0012) compared to control, but it increased highly significantly (P<0.0001) with keto 1. Other groups didn't show any significant change between them.

4. DISCUSSION

The ketogenic diets are being a highly effective treatment for metabolic syndrome and DM (Gupta et al., 2017). It is an effective way to manage DM and lose Body weight. (Merra et al., 2016). To regulate blood glucose levels and other aberrant metabolic parameters, the American Diabetes Society (ADA) advised physical activity, food management, medicinal intake, and other techniques should be used concurrently. Patients with T2DM who followed a ketogenic diet reported several health improvements (McKenzie et al., 2017). Numerous studies have shown the effectiveness of KD in promoting weight reduction and suggest that it may have positive benefits on diabetes patients' glycemic control, TG levels, and HDL levels (Dashti et al., 2007).

The current study findings concerning hydrogen ion concentration were confirmed and improved by (Arsyad et al., 2020), who showed that treating with KD in 60 days cause the formation and accumulation of a high amount of ketone body in the blood and this substance reduce plasma pH and this called ketoacidosis. In a further study done by (Alessandro et al., 2015) they found that consuming ketogenic diet for 20 days significantly reduced carbon dioxide deposits in the body, which may find clinical benefit in patients with increased PaCO2 due to respiratory failure. Furthermore, the carbon dioxide pressure, oxygen pressure, total carbon dioxide, or haemoglobin oxygen saturation did not significantly alter in conjunction with the drop in blood pH. Even though the blood bicarbonate levels of the KDs did not change much (Arsyad et al., 2020).

The findings of the present study concerning TCHO, TG & LDL and HDL, were also confirmed by a study done on diabetic rats by Merra and his team in 2017, who investigated that fluctuations occurred due to high fat high fructose feeding, that in turn induced T2DM (Merra et al., 2017), and also in agreement with those of (Castellana et al., 2020), who done study on rat and determined that after treating rats to KD, the levels of TCHO, TG & LDL were improved. Furthermore, these results were compatible with those of (Gardner, 2010), who found that Orlistat improved blood lipid profile after being added with KD. Regarding adding cider vinegar, the current study findings were confirmed by (Shishehbor et al., 2008), who determined that cider vinegar able to enhance lipid profile and blood glucose by the active component (acetic acid) which is present in vinegar and reduced serum cholesterol through the inhibition of hepatic

lipogenesis and the promotion of fecal bile acid excretion (Omar et al., 2016).

Furthermore, the present study findings showed that Serum glucose was increased in diabetic rats, while after treating the diabetic rats with KD, the blood glucose was reduced significantly due to low consumption of carbohydrate that causes the body shifting to fat source for energy and these findings were compatible with those of (H Negm, 2020), who revealed that after treating the diabetic rats with KD, either enriched with oil or no, the glucose level was reduced significantly. In a further study done by (Choudhury et al., 2018), they found that rats after feeding KDs, blood glucose levels reduced significantly, this might be due to persisting and continuing insulin production by pancreas β- cells that enhanced glycogen synthesis as confirmed by (Gupta et al., 2017), who did a study on mice that fed on KD, have shown that KD may prevent hyperglycemia by reducing glucagon synthesis and this led to less gluconeogenesis.

Concerning the liver enzymes of the present study were matched with those of (Veech, 2004) besides (Kosinski and Jornayvaz, 2017), who revealed the same result. Furthermore, these results were in agreement with those of (Patni et al., 2018), who have suggested that due to chemical substance side effects on the liver organs that cause hepatotoxicity that occurred after being combined with orlistat, the mechanism that injured the liver remained unknown.

Haghighatdoost et al., (2016) and (Johansson et al., 2019) in an observational study on rats, have examined the effects of low carbohydrate diets (LCDs) on nonalcoholic fatty liver disease (NAFLD), they found that KD improved metabolic abnormalities of NAFLD in just a few days, and this clarifies the improvement effect of KD (Haghighatdoost et al., 2016) and (Johansson et al., 2019).

Serum creatinine and urea results are compatible with those of (Mircescu et al., 2007), who demonstrated in experimental models of CKD, that a high protein diet worsened renal damage and increased proteinuria, hypertension, and mortality. In contrast, a long-term LPD can slow the rate of progression of renal failure, attenuating the impact of hemodynamic and metabolic factors.

Moreover, olive oil combined with KD , has improved both kidney and liver functions, and these findings were compatible with those of (Santangelo et al., 2016), who demonstrated that olive oil consumption were not only reduced fasting plasma glucose (FG) or fasting glucose (FG) significantly but also preserved hepatic and renal tissue from damage in diabetic rats. However, the treated diabetic rats with KD combined with orlistat and cider vinegar showed a highly significant increase in both creatinine and urea, and this may be due to consuming high amounts of chemical substances with KD that cause kidney tissue injury.

5. CONCLUSIONS

The KD significantly decreased blood glucose levels and made excellent glycemic control. The classic KD with very low carbohydrates, is considered a more effective diet for most metabolic disorders than others. Using unsaturated fat olive oil in KD was more reliable for most metabolic disorders than other fat types. Fat absorption inhibitor orlistat was more efficient for lipid profile improvement than cider vinegar. A combination of orlistat and cider vinegar with KD reduce the activity of kidney and liver organs.

Conflict of Interest (1)

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