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Potential health effects of tomato (*lycopersicon esculentum*) juice and hypoglycemic amelioration in the atherogenic indices between diabetic animal models

Nazeha KHALIL[1], Nora Abdullah ALFARIS[2], Jozaa Zaidan ALTAMIMI[2*]

Abstract

This study aimed firstly to evaluate the antioxidants levels (Lycopene & Beta-carotene) within fresh tomato juice (FTJ) and its health effects on atherogenic indices in association to lipid profiles and kidney functions between diabetic animal models. Rats (thirty-two; 180 ± 5 g) were randomly divided to groups; control negative (G1; non-diabetic), control positive (G2; fed standard basil diet), and three diabetic groups induced by single dose of streptozotocin (STZ; 65 mg/kg body weight). Groups of diabetic G3 & G4 (given FTJ by gavages at 2 and 4 mL/day respectively). Glucose, lipid profile (Cholesterol, Triglyceride, LDL.c, HDL.c and VLDL.c), kidney functions with atherogenic indices; the activity of glutathione peroxidase (GSH.Px), glutathione reduced (GSH.Rd) and superoxide dismutase (SOD) were evaluated. Results expressed data indicated that fresh tomato juice antioxidant activities presented at 72.83 ± 2.62 while Lycopene and β-carotene levels were 10.37 ± 1.36 and 3.91 ± 0.22 mg/100 mL respectively. Also, FTJ administration at 4 mL/day was the best effective dose; glucose, cholesterol, triglyceride and LDL.c. However, an elevation in the HDL.c, GSH.Px, GSH.Rd, and SOD were seen compared to G2. In conclusion, fresh tomato juice had hypoglycemic and positive atherogenic indices/effects that enhanced the model lipid profile to nearly the normal levels between diabetic rats especially at 4 mL/day.

Keywords: lycopene; lipid profile; streptozotocin; glutathione peroxidase; superoxide dismutase.

Practical Application: Control of hyperglycemic and anti-atherogenic actions between diabetic via encouraging them to consume fresh tomato juice.

1 Introduction

Dietary natural antioxidants are a diverse group of chemicals found in plants in order to support the human body system due to their numerous healthy beneficial effects. They are mainly controlling the occurrence of oxidative stress that known as imbalance between antioxidants and oxidants and may affect physiological functions (Dini, 2021). Such imbalanced between the oxidants and the antioxidants is causing damage and interruption in molecular of redox cell signaling. Furthermore, oxidative stress causes numerous phenotypic changes in vascular smooth muscle cells (Jiang et al., 2021). Also, previous researchers shown that oxidative damage causes various chronic diseases, including Cancer, Alzheimer, Diabetes mellitus (DM) and Cardiovascular diseases (CVD) (Forman & Zhang, 2021). Indeed, chronic oxidative stress was key factors for insulin resistance, metabolic dysfunction, DM, and CVD due to disrupting signaling and metabolism. This may be because DM and dyslipidemia usually coincided as lipid disturbances observed in 60-70% of diabetic patients, in addition to hyperglycemia hastening due to atheroma development in the situation of diabetic dyslipidemia (Mohammed et al., 2020). Both DM and CVD are frequency have a strong connection as DM increases CVD risk. Indeed, a previous study showed that CVD risk increased by two-three folds and three-five folds in diabetic males and females respectively compared to their non-diabetic counterparts (Standl et al., 2009). Diabetes mellitus is considered as a prevalent heterogeneous metabolic disorder leading causes of death and disease by its significant morbidity and mortality rates worldwide. It was known and characterized by chronic hyperglycemia and disruptions in the metabolism of carbohydrates, lipids and protein in males and females of all ages. Additionally, that causes oxidative stress by producing reactive free radicals, resulting in an imbalance and the cell's antioxidant defense mechanism (Jouki et al., 2020). Also, oxidative stress induced by hyperglycemia, causes endothelial dysfunction and has a key role in CVD development was observed by lipid peroxide levels and micro/macro-vascular damage associated with DM (Khalil et al., 2021). Such indicator of dyslipidemia and associated diseases were measured by the atherogenic index of plasma (AIP) that is composed of triglycerides and high-density lipoprotein cholesterol (Zhu et al., 2018). Several mechanisms contribute to the evolution and exacerbation of oxidative stress due to impaired metabolism related to DM. For instance, secondary diabetic sequelae such as nephropathy, retinopathy, neuropathy, and macro/micro-vascular damage can be caused by glucose autoxidation and protein glycation (World Health Organization, 2016). It can boost the expression of pro-

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[1]*Nutrition and Food Sciences Department, Faculty of Home Economics, Menoufia University, Menoufia Government, Shibin El-Kom City, Egypt*
[2]*Department of Physical Sports Sciences, College of Education, Princess Nourah Bint Abdulrahman University, Riyadh, Saudi Arabia*
*Corresponding author: jzAltamimi@pnu.edu.sa

inflammatory and pro-coagulant factors, promote apoptosis, in addition to decrease the nitric oxide production (Dini, 2021).

One main reason for such health problems is consuming unhealthy dietary patterns that low in their antioxidants concentrations causing oxidative stress that has been correlated with different metabolic disorders (Dini, 2021). The antioxidants concentrations are diverse between the food sources so it is important to know each chemical class of antioxidants with its potential preventive therapeutic effect mainly its full advantage of actions in the body (Jiang et al., 2021). On the other hand, having healthy diets as shown with many previous evidences; eating fruits and vegetables lowers the risk of oxidative damage due to their great levels of the natural antioxidants (Ojetola et al., 2021). So it is quite important to consume healthy diets and/or consume dietary food supplements containing antioxidant molecules in order to regulate oxidative stress (Xie et al., 2022) and help to maintain cell and tissue homeostasis in addition to prevent inflammation and chronic metabolic diseases (Dini, 2021). Again, the potential main role for the antioxidants within the human body is the defense from free radicals; stopping and/or decreasing free radicals development by different enzyme activities (Xie et al., 2022) such as glutathione peroxidase (GSH. Px), reduced glutathione (GSH.Rd) and Superoxide dismutase (SOD) in co-operation with metal cofactors such as Manganese (Mn), Copper (Cu), Selenium (Se) and Zinc (Zn) (Dini & Laneri, 2019). The glutathione (GSH) universally is found to have important roles in the body as component of the antioxidant system by providing many antioxidant functions but it easily can be useless by the oxidative stress and such depletes GSH stores may cause hypertension and CVD (Ojetola et al., 2021).

One of the most important dietary antioxidants; due to its powerful antioxidant especially lycopene and β–carotene is the Tomato [*Lycopersicon esculentum*; Rodrigues et al. (2022)]. It is not only a staple component of the Mediterranean diet but it is broadly consumed at global level because of its diversified use, whether raw or after various processing methods (El-Beltagy et al., 2015). Additionally, tomato has different bioactive compounds that may have anti-hyperglycemic effects, such as vitamins C and E (Jouki et al., 2020) in addition to carotenoids; lycopene, β–carotene, ascorbic acid and much more phenolic compound (Periago et al., 2009). Lycopene is a carotenoid naturally occurring in tomatoes and tomato derivatives (El-Beltagy et al., 2015). Again, tomato has a strong antioxidant activity with free radicals scavenging ability higher than β-carotene (two folds) and α-tocopherol (ten folds) (Cefali et al., 2015). Thus it can help diabetic endothelium dysfunction by lowering oxidative stress (Zhu et al., 2011). Indeed, fresh or cooked tomatoes consumption have been reported by their high nutritive value especially their beneficial to DM complications (Rodrigues et al., 2022) and that due to a reduction in the oxidative stress biomarkers, inflammation, accelerated atherosclerosis, and tissue damage (Banihani, 2018). Also, diabetes as high glucose levels cause kidney damage and impairment in renal function, resulting in rise in the concentrations of urea, creatinine and uric acid which is considered indicators of renal dysfunction (Xie et al., 2022). Furthermore, tomatoes showed high lipid metabolism levels that have been induced by genes over expression; the one that has been involved in more efficient fatty acid oxidation (Mohammed et al., 2020). However, the best to our knowledge no published data has yet examined the association between fresh tomato juice consumptions and hypoglycemic due to its atherogenic index in association to lipid profile and kidney functions within any diabetic model. Consequently, the current study aimed to measure the levels of Lycopene, β-carotene and antioxidant activity of fresh Tomato juice (FTJ) and then evaluating its hypoglycemic properties on diabetic rats' health states; their potential amelioration of the atherogenic indices and kidney functions.

2 Materials and methods

2.1 Tomato juice collection and preparation

Fresh tomatoes were acquired from the domestic marketplace of Egypt (Menoufia Government- Shibin El-Kom City). Washed 250 g with running water has been cut into small pieces and finally blended for 10 minutes with 25 mL distilled water in a Braun blender (Model No 4979, Germany) at maximum speed. The prepared fresh tomato juice (FTJ) was used daily at two different concentrations (2 & 4 mL/day) for feeding the used animal models.

2.2 Chemical collection and analysis

All used kits have been purchased from a local medical company in the city of Cairo, Egypt. Streptozotocin (STZ) was obtained from Sigma-Aldrich Inc. (St.Louis, Mo, USA).

2.3 Lycopene, beta-carotene and antioxidant activity of fresh tomato juice

Lycopene and β-carotene were estimated in fresh prepared tomatoes juice according to Nagata & Yamashita (1992) while the antioxidant activity of fresh tomatoes juice was determined according to the methods described by Yang et al. (2006); 2.2 diphenyl -picrylhydrazyl (DPPH).

2.4 Induction of diabetes between experimental rats

A single dose of Streptozotocin (STZ; 65 mg/kg body weight) was used for Diabetes mellitus induction between normal healthy male rats by intraperitoneal injection after being dissolved in a freshly prepared 0.01M citrate buffer (PH 4.5) as described by Yanardag et al. (2003). The animal experimental has been carried out in accordance with the faculty of Home Economics, department of nutrition and food sciences guidelines following the properly scientific procedures within their laboratory rules. Fasting blood glucose levels later of STZ injection were measured to ensure diabetes mellitus induction and rats with levels of more than 130 mg/dL considered diabetic and have been used as described within the following section of the experimental and study design (Khalil et al., 2021).

2.5 Experimental and study design

Thirty-two albino male rats were housed separately in the faculty animal house and fed standard basil diet (SBD) according to AIN -93 guidelines (Reeves et al., 1993) for seven

days as an adaptation period (Khalil et al., 2021). Experimental rats were assigned randomly to one of two groups. A control negative group (G1; n = 8) that fed only a standard basil diet and the rest of the rats (n = 24) were induced to DM condition as previously described and were split randomly into three equal subgroups. The first subgroup (diabetic positive control; G2) was supplemented with only normal basil diet and water while the remaining two diabetic subgroups (G3 & G4) were given normal basil diet with orally fresh tomatoes juice (FTJ) supplementations at 2 and 4 mL/day respectively for 42 days. All Animal's body weight was recorded at the start, during and by the end of the study duration. All experimental animals at the end of running the experimental were anaesthetized with diethyl-ether after fasting for 12 h then their blood samples were collected. Experimental and study design between used animal models fed fresh tomato juice (Figure 1).

2.6 Sample preparation for biochemical analysis

All collected blood samples were centrifuged to obtain their serum that then kept in frozen conditions for further biological analysis.

2.7 Biochemical analysis

Collected serum samples were used to measure glucose levels at 0 h, 14, 28 and 42 days according to Rojas et al. (1999). Also, serum total cholesterol (TC), triglyceride (TG) and High-density lipoprotein cholesterol (HDL.c) levels were determined as described by Allain et al. (1974); Burstein et al. (1970) and Fossati & Prencipe (1982). Additionally, Low-density lipoprotein cholesterol (LDL.c) and very low density lipoprotein cholesterol (VLDL.c) concentrations were determined using the methods of Lee & Nieman (1996) as follows: LDL.c = Total cholesterol - (HDL.c + VLDL.c) while VLDL.c = TG/5. Additionally, the atherogenic ratios were also computed by the methods of Bhardwaj et al. (2013). The atherogenic fraction (AF) was obtained from the difference between TC and HDL.C as described by Aguilar et al. (2011). Also, kidney functions by serum creatinine, urea and uric acid levels were determined as described by Jendrassik & Grof (1983), while the Malonaldehyde (MDA) level was determined according to Jentzsch et al. (1996). Finally, different enzyme activities GSH.Px, GSH.Rd and SOD were assayed as described by van Doorn et al. (1978); Beutler et al. (1963) and Misra & Fridovich (1972), respectively.

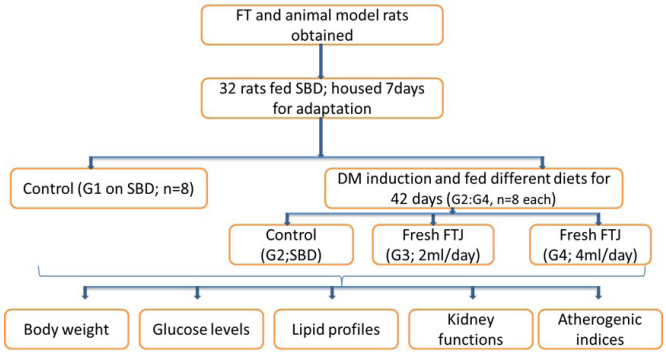

Figure 1. Experimental and study design between used animal models fed fresh tomato juice.

2.8 Statistical analysis

All measured collected data were presented as means and stander deviation (SD) using one-way analysis of variance (ANOVA) and it is extension that was used to analyze multiple variable comparisons data. Duncan's test was used as a post hoc test to compare significance between groups, according to the statistical package program (Khalil et al., 2021).

3 Results and discussion

All the measured parameters described within the previous material and method section have been presented as mean ± SD; n = 8 in each group. All the collected data were significantly studied by SPSS program; ANOVA and its extensions.

3.1 Antioxidants levels (lycopene & beta-carotene) measurements

Lycopene, beta-carotene and antioxidant activity of fresh tomato juice

Tomatoes are a rich source of antioxidants in the usual diet, have high antioxidant capacity and contain relatively high bioactive components, especially lycopene and β–carotene (Samaniego-Sánchez et al., 2014). Lycopene, β-carotene and antioxidant activity of fresh TJ are recorded in Table 1.

The data collected indicated that used fresh TJ had 10.37 mg/100 mL lycopene, 3.91 mg/100 mL β-carotene and 72.83% antioxidant activity. Similar results have been reported by Shabana (2016) and Youssef & El-Din (2015), who found that lycopene, β-carotene and antioxidant activity of TJ were 9.84 mg/100 mL, 3.72 mg/100 mL and 73.1%, respectively. However, it is all a pit higher than data obtained herein and that could be related to the difference of the original used tomato or to the variation of the laboratory hands and/or methods used. Also, the antioxidant activity is nearly the same as it is primarily driven by its lycopene content as described before by Harms-Ringdahl et al. (2012).

3.2 Effect of tomato juice on blood glucose levels

Table 2 shows the effect of TJ on serum blood glucose within the diabetic rat used models. Blood glucose level was significantly higher at $P \leq 0.05$ in diabetic rats than in the normal control during all the experimental period. Indeed, previous published studies such as Wei et al. (2003) found that Streptozotocin (STZ)

Table 1. Lycopene, β-carotene and antioxidant activity of used fresh tomato juice.

Parameters	Fresh used tomatoes juice
Lycopene (mg/100 mL)	10.37 ± 1.36
β-carotene (mg/100 mL)	3.91 ± 0.22
Antioxidant activity %	72.83 ± 2.62

Each value in the table is the mean ± SD (n = 3).

exhibited a high capacity for connecting the glucose receptors on pancreatic β-cells, and its administration had a cytotoxic effect on these cells, causing cell death or malfunction. Consequently, insulin level and blood glucose concentration are influenced. The body works to compensate for normal glucose homeostasis by secreting more insulin during hyperglycemia, resulting in pancreatic β-cell malfunction, decreased β-cell mass, and insulin insufficiency (Nichols & Remedi, 2012).

It can be notice from Table 2 that, the blood glucose level was not affected along the experimental total period for the normal negative and the positive control rats significantly, which fed on the stander basal diet (G1 & G2; data within the same row). Also, the started time point (0 h; at the beginning of the experimental period) shows no significant difference in the measured blood glucose levels between all the diabetic rat groups (within the same column); the positive control rats (G2) and diabetic rats administrated with TJ (G3 & G4). On the other hand, the blood glucose level of diabetic rats administrated with FTJ was significantly (G3 & G4) decreased by increasing the experimental time period (in the same row) and again as well as by increasing FTJ consumed levels (the same column). E.g. samples measured at days 14^{th}, 28^{th} and 42^{nd} of the experimental period was observed with significant ($P \leq 0.05$) declined blood glucose level between diabetic rats administrated with TJ at 4 mL/day compared to the positive control rats by the period increased ($190^{Bc} \pm 2.16$, $152.75^{Cc} \pm 12.69$, $123.75^{Dc} \pm 2.84$ *VS.* $233.25^{Aa} \pm 4.99$, $235.25^{Aa} \pm 6.85$, $238.5^{Aa} \pm 3.87$ mg/dL respectively; Table 2). This hypoglycemic effect of FTJ could be attributed to its content of lycopene and β-carotene as shown previously. For instance, Banihani (2018) showed that tomatoes or its bioactive components have anti-hyperglycemic properties. Similarly, Ali & Agha (2009) discovered that supplemented oral intake of tomato extract lycopene (90 mg/kg body weight) to diabetic rats led to a lower fasting serum glucose level. This result is consistent with the findings of Al-Numair et al. (2015), who observed that feeding diabetic rat with kaempferol; as an antioxidant flavonoid present in tomatoes, restored normal plasma glucose levels. Moreover, lycopene administration might be able to help humans lessen the negative impacts of diabetes by including oxidative damage, decreasing plasma insulin concentration, and blood glucose levels (Celik & Aydin, 2012). Lycopene's hypoglycemic effect shown to be attributed to a number of processes, including increased insulin production, increased repair and proliferation of β–cells, enhanced insulin and adrenaline effects, and increased ant oxidative capabilities (Ali & Agha, 2009). Thus increasing the tomato juice as a Lycopene source by time or levels consumed could be attributed to decrease the blood glucose levels as seen within the current results especially at 42^{nd} days and 4 mL/day.

3.3 Effect of tomato juice on lipid profiles

Data are seen in Table 3 reflect the effect of TJ on serum lipid profile (TC, TG, LDL.c, VLDL.c and HDL.c) between used rat models fed two different TJ concentrations (2 & 4 mL/day) for 42 days.

Diabetic overall rats (G2:G4) had higher significant ($P \leq 0.05$) TC, TG, LDL.c, VLDL.c and HDL.c levels than normal control rats (G1) as it can be seen in Table 3. These findings confirmed the results obtained previously by Aly et al. (2015), who found that the levels of serum and plasma cholesterol, TG, LDL.c and VLDL.c increased between diabetic rats. Additionally, it can be noticed that no significant differences were found in the level of TG and VLDL.c in diabetic rats (G3; $142.35^{a} \pm 2.77$ and $28.47^{a} \pm 0.56$ mg/dL) administrated with 2 mL/day TJ and the positive control rats (G2; $138.91^{a} \pm 2.26$ and $27.78^{a} \pm 0.45$ mg/dL), whereas administration diabetic rats with TJ (either 2 and/or 4 mL/day) improved the level of cholesterol and LDL.c ($223.03^{a} \pm 1.73$, $125.53^{c} \pm 3.19$ and $142.73^{a} \pm 1.1$, $39.7^{d} \pm 4.62$ mg/dL respectively).

Table 2. Effect of tomato juice on serum blood glucose levels between used animal models.

Groups	Glucose levels (mg/dL)				
	0 h	14^{th} Day	28^{th} Day	42^{nd} Day	Differences (42-0 days)
G1; negative non-diabetic control	$99^{Ab} \pm 2.58$	$98.75^{Ad} \pm 1.71$	$97^{Ad} \pm 2.58$	$95.25^{Ad} \pm 2.63$	-3.75
G2; positive diabetic control	$233.5^{Aa} \pm 4.51$	$233.25^{Aa} \pm 4.99$	$235.25^{A\,a} \pm 6.85$	$238.5^{Aa} \pm 3.87$	5
G3; diabetic fed 2% FTJ	$234.25^{Aa} \pm 7.5$	$208^{Bb} \pm 5.72$	$176.25^{Cb} \pm 2.99$	$164.75^{Db} \pm 2.5$	-69.5
G4; diabetic fed 4% FTJ	$232.25^{Aa} \pm 4.86$	$190^{Bc} \pm 2.16$	$152.75^{Cc} \pm 12.69$	$123.75^{Dc} \pm 2.84$	108.5-

Values in the table were expressed as means ± SD (n = 8). Small letters (in the same column) referred to statistical differences among groups, while CAPITAL letters (in the same row) referrer to statistical differences among experimental time periods. Different letters are significantly different at $P \leq 0.05$. h means started time point while FTJ means fresh tomatoes juice.

Table 3. Effect of tomato juice on serum lipid profile levels between used animal models.

Parameters (mg/dL)	G1; negative non-diabetic control	Diabetic rat groups			
		G2; control	G3; fed 2% FTJ	G4; fed 4% FTJ	Differences of 4% FTJ from G2
Cholesterol	$129.38^{c} \pm 1.39$	$190.47^{b} \pm 3.12$	$223.03^{a} \pm 1.73$	$125.53^{c} \pm 3.19$	-64.94
Triglyceride	$123.13^{b} \pm 2.59$	$138.91^{a} \pm 2.26$	$142.35^{a} \pm 2.77$	$109.77^{c} \pm 2.16$	-29.14
HDL.c	$58.7^{b} \pm 1.51$	$51.03^{c} \pm 1.96$	$46.33^{d} \pm 0.87$	$63.89^{a} \pm 2.63$	12.86
VLDL.c	$24.63^{b} \pm 0.52$	$27.78^{a} \pm 0.45$	$28.47^{a} \pm 0.56$	$21.95^{c} \pm 0.43$	-5.83
LDL.c	$46.05^{c} \pm 2.57$	$111.68^{b} \pm 2.77$	$142.73^{a} \pm 1.1$	$39.7^{d} \pm 4.62$	-71.98

Values in the table were expressed as means ± SD (n = 8). Different letters in the same row are significantly different ($P \leq 0.05$). FTJ: fresh tomatoes juice; HDL.c: high density lipoprotein cholesterol; VLDL.c: very low density lipoprotein cholesterol; LDL.c: low density lipoprotein cholesterol.

Regarding the HDL.c, Table 3 showed a significant increase within the 4 mL/day administration (63.89^{a} ± 2.63 mg/dL) compared with the positive control rats (G2; 51.03^{c} ± 1.96 mg/dL). Interestingly, consumed FTJ at 4 mL/day show differences from the control diabetic group (G2) by reduction levels of LDL.c, Cholesterol, Triglyceride and VLDL.c by -71.98, -64.94, -29.14 and -5.83 mg/dL respectively) while HDL.c increased by 12.86 mg/dL. Again, the positive effect of FTJ additions mainly at 4 mL/day may be due to its high lycopene content. The same trend was obtained by Ferreira-Santos et al. (2020), who reported that lycopene significantly depresses cholesterol and triglycerides in rats that fed on a high fructose diet. The absorption of cholesterol is greatly diminished and delayed by these phytochemicals. They can also enhance bile acid-binding, resulting in insoluble complexes and increased fecal excretion, leading to lower plasma cholesterol concentrations (Siasos et al., 2013). Such collected data could be due to the presented lycopene levels within high TJ consumption and that can suppress cholesterol production (Palozza et al., 2011). Indeed, the natural antioxidants availability is to donate the hydrogen radicals that are able to pair with other available free radicals which in turn can inhibit the propagation reaction throughout the lipid oxidation process (Jouki et al., 2020).

Lycopene possesses lipid-lowering effects that inhibit the oxidation of TC, TG, and LDL.c and the formation of dysfunctional HDL.c (Mozos et al., 2018). Thus diabetic rats administrated 4 mL/day FTJ and had the highest reduction in the concentrations of cholesterol, TG, LDL.c and VLDL.c with an elevation HDL.c levels again did not differ from normal control rats (G1). These findings also are concomitant with Li et al. (2014), who found that lycopene reduces cholesterol, TG and LDL.c levels and increases HDL.c in diabetic rats.

3.4 Effect of tomato juice on atherogenic indices

The effects of used FTJ on atherogenic indices between the experimental rats are presented in Table 4 with the measured parameters of Atherogenic Index of plasma (AIP), Cardiac risk ratio (CRR %), Castelli's Risk Index (CRI), Atherogenic fraction (AF) and Atherogenic coefficient (AC).

Table 4 illustrated that a significant increase ($P \leq 0.05$) in AIP, CRR, CRI, AF and AC were reported in greater levels between diabetic rats group (G2) compared to normal control group (G1). On the other hand, administration of FTJ to diabetic rats (2 and 4 mL/day) caused a significant drop in levels of AIP, CRR, CRI, AF and AC compared to positive control rats. However, the best effected used FTJ in reducing AI, CRR, CRI, AF and AC levels was seen with the 4 mL/day supplementation (G4) comparing to the diabetic positive group (G2) and the 2 mL/day supplementations (G3). AIP, CRR, CRI, AF and AC were 0.96^{d} ± 0.1, 1.97^{d} ± 0.1, 0.62^{d} ± 0.09, 61.65^{d} ± 4.39 and 0.97^{d} ± 0.1 mg/dL *vs.* 2.73^{b} ± 0.13, 3.74^{b} ± 0.13, 2.19^{b} ± 0.11, 138.24^{b} ± 4.34 and 2.73^{b} ± 0.13 for G2 and 3.69a ± 0.08, 4.81^{a} ± 0.09, 3.08^{a} ± 0.06, 176.7^{a} ± 1.6 and 3.81^{a} ± 0.08 mg/dL respectively. These findings could be explained by the associated high serum levels of TC, TG, LDL.c and VLDL.c and lower levels of HDL.c, which was seen within diabetic rat groups. The current results were consistent with those of Tripathi (2003) that showed DM is linked to impaired lipid metabolism and an elevation in the atherogenic index which are significant predictors of CVD risk; the greater of the atherogenic indices value, the greater of the CVD risk occurrence (Chigozie & Chidinma, 2013). Additionally, these findings are consistent with Choi et al. (2013), who stated that tomato consumption reduced CVD incidence that may be due to its antioxidant activities and lycopene levels. Indeed, Story et al. (2010) found that consuming more lycopene lowers CVD risks additionally to early results within *in vitro* investigations that indicated lycopene molecules have anti-atherogenic properties (Hung et al., 2008). Thus, 4 mL/day tomato juice shows the best treated levels that could be the recommended for diabetic models.

3.5 Effect of tomato juice on kidney function

Regarding the effect of TJ on kidney function within the used animal rats, Table 5 shows urea, creatinine and uric acid levels within the collected serum samples. They were all used as biochemical markers to evaluate renal injury as it could affected by high glucose levels; an important reason for kidney damage and impairment in renal function which is considered indicators of renal dysfunction (Mohammed et al., 2020).

It can be observed from the following table (Table 5) that serum urea, creatinine and uric acid levels were significantly higher in the positive control rats (G2; 45.6^{b} ± 3.08, 1.31^{a} ± 0.04 and 2.52^{a} ± 0.14 mg/dL respectively) than in the normal control rats (G1; 34.1^{c} ± 2.57, 0.83^{b} ± 0.05 and 2.12^{b} ± 0.13 mg/dL respectively). This elevation in serum markers of kidney function was an indicator of a decrease in glomerular filtration rate and tissue injury due to the diabetic conditions presented within G2. Such collected result is compatible with Dhananjayan et al. (2017), who concluded that an elevation in the kidney markers such as urea, creatinine and uric acid occurs within diabetic rat models.

Table 4. Effect of tomato juice on atherogenic indices between used animal models.

Parameters (mg/dL)	G1; negative non-diabetic control	Diabetic rat groups			
		G2; control	G3; fed 2% FTJ	G4; fed 4% FTJ	Differences of 4% FTJ from G2
AIP	1.27^{c} ± 0.11	2.73^{b} ± 0.13	3.69^{a} ± 0.08	0.96^{d} ± 0.1	-1.77
CRR	2.21^{c} ± 0.08	3.74^{b} ± 0.13	4.81^{a} ± 0.09	1.97^{d} ± 0.1	-1.77
CRI	0.85^{c} ± 0.09	2.19^{b} ± 0.11	3.08^{a} ± 0.06	0.62^{d} ± 0.09	-1.57
AF	70.67^{c} ± 2.62	138.24^{b} ± 4.34	176.7^{a} ± 1.6	61.65^{d} ± 4.39	-76.59
AC	1.21^{c} ± 0.08	2.73^{b} ± 0.13	3.81^{a} ± 0.08	0.97^{d} ± 0.1	1.76

Values in the table were expressed as means ± SD (n = 8). Different letters in the same row are significantly different ($P \leq 0.05$). FTJ: fresh tomatoes juice; AIP: atherogenic index of plasma; CRR: cardiac risk ratio; CRI: Castelli's risk index; AF: atherogenic fraction; AC: atherogenic coefficient.

Again, the same data in Table 5 showed no significant differences in creatinine and uric acid concentrations that were reported among the positive control rats (G2) and diabetic rats administrated with 2 mL/day FTJ (G3). Administration of 2 mL/day FTJ for diabetic rats caused a significant decrease in urea concentrations. However, serum urea, creatinine and uric acid concentrations were significantly ($P \leq 0.05$) declined in diabetic rats consumed 4 mL/day of FTJ by -19.55, -0.77 and -0.64 mg/dL comparing to the positive diabetic control rats (G2) respectively. This improvement of kidney function in rats administrated with FTJ may be due to a high amount of lycopene presented within FTJ in addition to its the antioxidant effects in order to help keeping the kidney functioning regularly and prevent renal failures. The results shown herein are consistent with those found by Daniel et al. (1989), who revealed that lycopene prevents kidneys impairment caused by DM through increasing system anti-oxidative defense and improving renal function in diabetic models. Furthermore, lycopene previously reduced creatinine in diabetic rats significantly which inhibit the formation of diabetic nephropathy in addition to improved kidney function in rats with DM (Mucyn et al., 2009).

3.6 Effect of tomato juice on antioxidant status

Data recorded in Table 6 show the effect of FTJ on antioxidant status between used animal models. Measured MDA, GSH.Px, GSH.Rd and SOD were recorded.

Results showed that diabetes mellitus caused a significantly ($P \leq 0.05$) elevation in the concentration of MDA ($27.12^{b} \pm 1.04$) and reduction in the activities of GSH.Px, GSH.Rd and SOD ($15.42^{c} \pm 0.44$, $8.26^{c} \pm 0.58$ and $30.89^{c} \pm 1.01$ respectively) as compared with normal control rats ($20.64^{c} \pm 1.58$, $20.29^{b} \pm 1.05$, $10.31^{b} \pm 0.49$ and $39.66^{b} \pm 1.14$ respectively; Table 6). Such findings in agreement with those found by Bastos et al. (2016) and who observed that alteration in oxidative metabolism and accelerated lipid peroxidation were linked to DM and dyslipidemia. Also, the significant rise in oxidative stress coupled with decreased antioxidant activity (Negre-Salvayre et al., 2008). Indeed, there was an association between free radical-induced lipid peroxidation and decreased antioxidant enzymes activity, linked to elevated oxidative stress in DM, a key factor for diabetic complications. Also, alteration in the endogenous free radicals quenching defense mechanisms may cause insufficient scavenging, leading to oxidative damage and tissue injury (Xie et al., 2022). Additionally, Eliza et al. (2009) showed that STZ elevate the lipid peroxides level and reduce the antioxidant enzymes activity of diabetic rats. The autoxidation of glucose and glycosylation of proteins produce an overabundance of free radicals (Al-Faris et al., 2010). Morover, the data collected again in the same Table 6 illustrated there is no significant differences in the activity of GSH.Px among the positive control rats (G2) and diabetic rats (G3) consumed 2 mL/day FTJ ($15.42^{c} \pm 0.44$ and $14.02^{c} \pm 0.98$ nmol/mL respectively). However, feeding diabetic rats (G4) with 4 and 4 mL/day FTJ resulted in the highest reduction in MDA levels significantly ($18.06^{c} \pm 0.91$ that was about 9 nmol/mL reduction) comparing to the control positive group rats (G2; Table 6). On the other hand, all of GSH.Px, GSH.Rd and SOD had an opposite trend that were increased by 8.51, 4.16 and 13.89 unite differences respectively from the control positive diabetic rats (G2; Table 6). These results could be due to the considerable medicinal benefits of tomato lycopene as an antioxidant that is a strong antioxidant effectively scavenges free radicals and affects the composition of antioxidant enzymes like SOD and CAT (Pereira et al., 2017). On the other hand, Celik & Aydin (2012) and Palozza et al. (2012) reported lycopene additions improved the oxidative damage related to DM which appears to work as an *in vivo* redox agent, protecting tissues from ROS high levels with its therapeutic effect reducing cells oxidative and DNA damage in addition to the effect of β-carotene consumption in order to reducing oxidative stress that has been reported by

Table 5. Effect of tomato juice on kidney functions between used animal models.

Parameters (mg/dL)	G1; negative non-diabetic control	Diabetic rat groups			
		G2; control	G3; on 2% FTJ	G4; on 4% FTJ	Differences of 4% FTJ from G2
Urea	$34.1^{c} \pm 2.57$	$45.6^{b} \pm 3.08$	$56.52^{a} \pm 2.76$	$26.05^{d} \pm 0.91$	-19.55
Creatinine	$0.83^{b} \pm 0.05$	$1.31^{a} \pm 0.04$	$1.36^{a} \pm 0.02$	$0.54^{c} \pm 0.03$	-0.77
Uric acid	$2.12^{b} \pm 0.13$	$2.52^{a} \pm 0.14$	$2.61^{a} \pm 0.36$	$1.88^{c} \pm 0.29$	-0.64

Values in the table were expressed as means ± SD (n = 8). Different letters in the same row are significantly different ($P \leq 0.05$). FTJ: fresh tomatoes juice.

Table 6. Effect of tomato juice on antioxidant status between used animal models.

Parameters	G1; negative non-diabetic control	Diabetic rat groups			
		G2; control	G3; on 2% FTJ	G4; on 4% FTJ	Differences of 4% FTJ from G2
MDA (nmol/mL)	$20.64^{c} \pm 1.58$	$27.12^{b} \pm 1.04$	$32.64^{a} \pm 2.61$	$18.06^{c} \pm 0.91$	-9.06
GSH.Px (nmol/mL)	$20.29^{b} \pm 1.05$	$15.42^{c} \pm 0.44$	$14.02^{c} \pm 0.98$	$23.93^{a} \pm 1.02$	8.51
GSH.Rd (mg/dL)	$10.31^{b} \pm 0.49$	$8.26^{c} \pm 0.58$	$6.29^{d} \pm 0.51$	$12.42^{a} \pm 0.51$	4.16
SOD (U/g Hb)	$39.66^{b} \pm 1.14$	$30.89^{c} \pm 1.01$	$26.23^{d} \pm 0.69$	$44.78^{a} \pm 1.001$	13.89

Values in the table were expressed as means ± SD (n = 8). Different letters in the same row are significantly different ($P \leq 0.05$). FTJ: fresh tomatoes juice; MDA: malondialdehyde; GSH.Px: glutathione peroxidas; GSH.Rd: reduced glutathione; SOD: superoxide dismutase.

Table 7. Effect of tomato juice on body weight gain between used animal models.

Parameters	G1; negative non-diabetic control	Diabetic rat groups			
weight (g)		G2; control	G3; on 2% FTJ	G4; on 4% FTJ	Differences of 4% FTJ from G2
Initial	$183.5^{a} \pm 1.29$	$183^{a} \pm 0.82$	$182.5^{a} \pm 0.58$	$183.75^{a} \pm 0.96$	0.75
Final	$194.25^{b} \pm 0.96$	$189.25^{c} \pm 0.96$	$172.75^{d} \pm 0.96$	$203.5^{a} \pm 1.29$	14.25
Relative change %	$5.86^{b} \pm 0.55$	$3.42^{c} \pm 0.28$	$-5.65^{d} \pm 0.58$	$10.75^{a} \pm 0.53$	7.33

Values in the table were expressed as means ± SD (n = 8). Different letters in the same row are significantly different ($P \leq 0.05$). FTJ: fresh tomatoes juice.

Subhash et al. (2007). So FTJ at 4 mL/day show the best affect due to its antioxidant status by lycopene and β-carotene levels.

3.7 Effect of tomato juice on body weight

The following table (Table 7) indicates the effect of used fresh TJ on body weight gain within all the used animal models. Initial and final body weight were recorded and the relative changes were calculated after running the experimental between all the rat groups.

It can be seen from the table that there was no significant difference ($P \leq 0.05$) in initial weight between diabetic groups and negative control group especially was no differences from G4 and G2 (0.75 g). However, the final body weigh was significantly reduced between the diabetic control groups (G2; $189.25^{c} \pm 0.96$) comparing to the non-diabetic control group (G1; $194.25^{b} \pm 0.96$). Such collected results agree with Coskun & Bolkent (2014), who reported that the body weight declined significantly in diabetic rats compared to control rats. On the other hand, the relative body weight gain elevated in diabetic rats administrated with 4 ml of TJ ($203.5^{a} \pm 1.29$ g significantly; $P \leq 0.05$) comparing to the positive control group (G2; $189.25^{c} \pm 0.96$) with differences of about 14 g. Again it was increased at the end of running the experimental by about 11 g within the same group (relative change % by $10.75^{a} \pm 0.53$ g). Thus, the more effective group with significant ($P \leq 0.05$) increase relative body weight gain was with group fed 4 mL/day of FTJ. Indeed previous collected data by Yossef et al. (2016) concluded that giving diabetic rats 3 and 6 mL of cherry TJ increased the relative body weight compared to positive control group that may be due to the ingestion of lycopene that leads to a significant elevation in body weight within diabetic rats (Zhu et al., 2011). Again 4 mL/day fresh tomato juice administration presented the best effective treatment for body weight gain levels.

4 Conclusion

To conclude up, fresh used tomato juice consumptions show hypoglycemic effects and anti-atherogenic actions between diabetic used animal models comparing to either positive and negative diabetic rat models; they can ameliorate the efficiency of the antioxidant defense system in STZ-induced diabetic rats. This effect of FTJ may be due to its high content of bioactive components especially measured lycopene and β-carotene sue to their antioxidant properties. Thus the 4 mL/day FTJ is recommended for daily consumption between diabetic models; however, more human studies are needed in order to conduct more effective oxidation pathways inside the cell.

Conflict of interest

There is no conflict of interest that I should disclose, having read the above statement.

Availability of data and material

The data used to support the findings of this study are included within the article.

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