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Research Article
Chemical Composition and Ameliorative Effect of Tomato on Isoproterenol-induced Myocardial Infarction in Rats

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Abstract
Background and Objective: Tomatoes are rich in active components, such as polyphenols and carotenoids. This study investigated the chemical composition of tomato fruit and the ability of fruits and their pomace (peel, pulp and seeds) to protect against isoproterenol-induced myocardial infarction in rats. **Materials and Methods:** The proximate chemical composition and the concentrations of some minerals (Ca, Fe, Zn and K), vitamins (C, A, B1, B2 and B6) and antioxidants (β-carotene, lycopene and total phenolic compounds) were estimated in tomato fruits. About 40 rats were injected subcutaneously with isoproterenol dissolved in normal saline at the dose of 100 mg kg^{-1} daily for 3 consecutive days to induce acute myocardial infarction. Then, rats were classified into the untreated group (positive control) and four treated groups (tomato peel, seed, pulp and whole fruit). **Results:** The tomato fruits were rich in carbohydrate, protein and fiber but contained little lipid. Phenolic compounds, vitamin C, lycopene, vitamin A and calcium were detected. Compared to the control group, rats fed tomato peel, seeds, pulp and whole fruit had significantly increased body weight gain and food efficiency ratio. Compared to the control group, the tomato-fed groups had decreased total cholesterol, triglycerides and low- and very low-density lipoprotein cholesterol and increased high-density lipoprotein cholesterol. A decrease in serum liver enzyme activity and an increase in antioxidant enzymes in the tomato-fed rats were detected. **Conclusion:** Administration of tomato and its components has protective effects against isoproterenol-induced myocardial infarction in rats.

Key words: Tomato, chemical composition, isoproterenol, lipid profile, antioxidant, myocardial infarction, rats

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Data Availability: All relevant data are within the paper and its supporting information files.

INTRODUCTION

Tomato (*Lycopersicon esculentum*) is known as the poor man's orange and is a widely consumed fresh fruit. Tomato fruit is also used to produce stewed fruit, marmalade, syrup and several types of soft drinks. The commercial processing of tomato produces a large amount of waste. The wet tomato pomace constitutes the major part of this waste, which consists of 27% skin, 33% seed and 40% pulp, while the dried pomace contains 56% pulp and skin and 44% seed[1,2]. Tomato fruits are a rich source of dietary fiber and contain many vitamins, including vitamins C, E and A as well as minerals, such as selenium, copper, manganese and zinc, which act as co-factors for antioxidant enzymes. Tomato peel can be used to extract lycopene[3]. Because tomatoes are rich in active components, such as polyphenols and carotenoids as well as several rutins and naringenins, tomatoes can be considered a functional vegetable[4]. Thus, tomatoes promote health by preventing oxidative stress-related diseases, such as cancer, diabetes and coronary heart diseases. Tomato juice and extract reduce plasma levels of low-density lipoprotein cholesterol and blood pressure and might prevent coronary heart disease[5-7].

Myocardial infarction develops as a result of an imbalance between oxygen supply and demand, resulting in ischemic heart disease, causing morbidity and mortality[8]. Subcutaneous injection of isoproterenol (a synthetic β-adrenoceptor agonist) to rats creates irreversible cellular necrosis and infarction characterized by the same symptoms as in myocardial infarction patients[9].

Because of high consumption of tomato and increase tomato waste product(peels and seeds),this study assessed the chemical composition of tomato fruits and the possible ameliorative effects of tomato fruits and their pomace (as peel, pulp and seeds separately) against isoproterenol-induced myocardial infarction in rats.

MATERIALS AND METHODS

Chemicals: All materials used in this experiment were of analytical grade. Kits were purchased from BioMerieux, RCS Lyon, France.

Preparations of tomato, peel, seed and pulp powder: Tomato fruits were purchased from the local market in Riyadh in January, 2017. The skin of the tomatoes with attached flesh pulp was separated from the core of the fruit using a sharp knife and frozen immediately (-18°C). The peel of the tomatoes was then separated from the pulp. The core of the tomato was sieved to obtain seeds. Whole tomato fruit, seeds, peel and pulp were freeze-dried, then crushed to a fine powder and stored at -20°C.

Chemical composition of tomato fruit powder: The moisture, protein, lipid, ash and crude fiber contents of the tomato fruit powder were determined[10]. The carbohydrate content was estimated by the sum of these contents percentage and subtracting from100. Ca, Fe, Zn and K were determined by atomic absorption spectrophotometry (Mod AAnalyst 800, Perkin Elmer, CT, USA) using the corresponding standards. Vitamin C, vitamin A, riboflavin (B2), thiamin (B1), pyridoxine (B6), lycopene and β-carotene content as well as total phenolic content (TPC), were determined as described[11]. Tomato peel, seed, pulp and whole tomato fruit powder were added separately at 10% of a standard diet, with consideration of their nutritional values.

Animals and biological experiment: Forty adult male albino rats (weighing 110-120 g) were provided by the experimental animal center of the Research Center in Prince Sultan Military Medical City, (PSMMC), Riyadh. Food and water were provided *ad libitum*. Ethical guidelines for investigations involving experimental animals were followed throughout the study. This was performed in animal center of the Research Center in Prince Sultan Military Medical City,(PSMMC), Riyadh. The approval Number is: REC AP11/6.

The experiments were carried out with the help of the staff of the Scientific Research Center of the MSD, at their experimental animal facility. Rats were placed in separate cages and housed under suitable airflow with a 12-h light-dark cycle at 22±2°C during the whole period of experimentation. The duration of the biological experiment was 77 days.

Animals received a standard diet according to National Research Council (NRC)[12] and water *ad libitum*. After 2 weeks of acclimatization, blood samples were taken. The rats were injected subcutaneously by isoproterenol (100 mg kg^{-1}) dissolved in normal salinedaily for three consecutive days to induce acute myocardial infarction, which was confirmed by increased lipid parameters and cardiac markers in blood after injection[13]. The rats were then classified into the untreated group (positive control) and four treated groups (tomato peel, tomato seed, tomato pulp and whole tomato fruit). The daily food intake (FI) and weekly body weight were used to calculate the body weight gain (BWG) and food efficiency ratio (FER) of the rats.

Laboratory analyses: After 60 days, rats were sacrificed to obtain blood for plasma lipid profile analysis. Total cholesterol (TC), high-density lipoprotein (HDLc) and triglycerides (TG) were measured using assay kits from Alkan Medical Co., Saudi Arabia. Low- and very low-density lipoprotein cholesterol (LDLc and VLDLc) concentrations and the LDLc/HDLc ratio were calculated. Oxidative stress biomarkers (glutathione peroxidase [GSH-Px], superoxide dismutase [SOD] and malondialdehyde [MDA] as a lipid peroxidation index) were measured using commercially available specific kits(Alkan Medical Co., Saudi Arabia). Serum alanine and aspartate aminotransferase (ALT and AST), alkaline phosphatase (ALP) and lactate dehydrogenase (LDH) activities were also measured. For analyses of cardiac markers, heart tissue was lysed and homogenized with 0.1 M PBS and centrifuged at 12,000 rpm for 10 min at 4°C. Cardiac lactate dehydrogenase (LDH), nitric oxide (NO) and xanthine oxidase (XO) were estimated[14,15].

Statistical analysis: All statistical analyses were performed using SPSS statistical version 16 software package (SPSS® Inc, USA). Mean values were compared between concentration/ animal groups using one-way analysis of variance (ANOVA). The least significant difference test (LSD) was used to calculate the statistical difference between various groups. A value of $p<0.05$ was considered statistically significant.

RESULTS AND DISCUSSION

Proximate composition, vitamin contents and antioxidant contents of tomato fruit: The tomatoes were rich in carbohydrate, protein, fiber and ash but relatively poor in lipid. The moisture content of the tomato. Tomato fruits were rich in total phenolic compounds (TPC), vitamin C and lycopene, respectively and contained considerable amounts of vitamin A, B6 and β-carotene but relatively little vitamin B1 and B2. Tomatoes were rich in calcium and contained variable amounts of potassium, zinc and iron as illustrated in Table 1.

Nutrient analysis of tomatoes are important for evaluating their nutritional significance. The moisture content of food can be used as an indicator of its lifespan. Ash content indicates the amount of inorganic matter and oxides. Fat provides an excellent source of energy, enhances the transport of fat-soluble vitamins, insulates and protects internal tissues and contributes to vital cellular process. Proteins are a class of nitrogenous compounds composed of one or more amino acid chains. Differences between the tomato composition reported here and in other studies might be due to the use of different drying methods, different genotypes, fruit maturities or storage or growing conditions[3,16,17].

Phenolics, lycopene, anthocyanin, ascorbic acid, glycoalkaloids, tomatine and carotenoids are enriched in tomatoes and they have many health benefits[18]. Polyphenols are a major class of secondary metabolites and more than 100 different compounds (e.g., caffeic acid and chlorogenic acid) are present in fresh tomatoes. Numerous polyphenols in tomatoes play important protective roles because of their antioxidant and enzyme-modulatory activities[19-21].

Effect of administration of tomato peel, seeds, pulp or whole tomato fruit on nutritional values of the experimental rat groups: Supplementation with tomato peel, seeds, pulp or whole tomato fruit significantly increased BWG and FER ($p<0.05$), although food intake was not significantly different between the groups (Table 2).

Isoproterenol-induced myocardial infarction is used to study the beneficial effects of drugs on cardiac function. Isoproterenol generates an excess amount of electrons after auto-oxidation, which results in the generation of reactive oxygen species[22]. Tomato and tomato-based products are rich sources of important nutrients and contain several phytochemicals, such as lycopene, carotenoids and polyphenol compounds, which might have beneficial health effects[23]. The lycopene, anthocyanin, ascorbicacid, total phenolics, glycoalkaloids and tomatine as well as the low levels of carotenoids, in tomato and processed tomato also

Table 1: Proximate composition, vitamin and antioxidant contents of tomato fruit

Carbohydrate (g/100 g)	Protein(g/100 g)	Fiber (g/100 g)	Ash (g/100 g)	Lipid (g/100 g)	Moisture (g/100 g)
60.29	12.22	9.25	8.11	3.36	6.77
Vitamin C (mg/100)	Vitamin A (I U^{-1})	Riboflavin (B2) (mg/100)	Thiamin (B1) (mg/100)	Pyridoxine (B6) (mg/100)	β-Carotene (mg/100)
325.77	1149.51	0.617	0.639	7.39	4.99
Lycopene (mg/100)	TPC (mg/100)	Calcium (mg/100)	Zinc (mg/100)	Iron (mg/100)	Potassium (mg/100)
125.11	329.38	18.99	1.80	0.85	2.65

Table 2: Effects of tomato on nutritional values of the experimental rat groups

Parameters	Positive control	Tomato peel	Tomato seed	Tomato pulp	Tomato
BWG (g)	45.77±4.80[b]	60.770±6.22[a]	63.550±7.11[a]	69.750±7.88[a]	71.550±5.44[a]
FI (g/day)	14.35±1.33[ab]	16.350±1.51[a]	16.950±1.41[a]	17.200±1.81[a]	17.510±1.85[a]
FER	0.053±0.001[c]	0.061±0.002[ab]	0.062±0.004[a]	0.067±0.001[a]	0.068±0.003[a]

BWG: Body weight gain, FI: Food intake, FER: Feed efficiency ratio, Mean values in each row having different superscript (a, b, c and d) are significantly different at p<0.05

Table 3: Effects of tomato on serum lipid profile of the experimental rat groups

Parameter	Control positive	Tomato peel	Tomato seed	Tomato pulp	Tomato fruit
TC (mg g^{-1} dL^{-1})	240.11±33.61[a]	140.50±15.21[b]	138.79±14.77[b]	131.16±14.35[bc]	130.77±12.33[bc]
TG (mg g^{-1} dL^{-1})	195.77±20.61[a]	105.11±10.21[b]	99.66±11.03[b]	95.70±10.21[b]	91.66±9.60[b]
HDLc (mg g^{-1} dL^{-1})	29.41±2.66[b]	39.66±4.88[a]	40.11±4.29[a]	41.33±4.67[a]	40.77±4.03[a]
LDLc (mg g^{-1} dL^{-1})	171.55±21.74[a]	79.82±8.89[b]	78.75±8.84[b]	70.69±7.96[bc]	71.74±6.99[bc]
VLDLc (mg g^{-1} dL^{-1})	39.15±2.14[a]	21.02±1.80[b]	19.93±1.43[b]	19.14±1.34[b]	18.26±1.59[bc]
LDLc/HDLc	5.83±0.77[a]	2.01±0.33[b]	1.96±0.20[b]	1.71±0.18[bc]	1.75±0.27[bc]

TC: Total cholesterol, TG: Triglycerides, HDLc: High-density lipoprotein cholesterol, LDLc: Low-density lipoprotein cholesterol, VLDLc: Very low-density lipoprotein cholesterol, Mean values in each row having different superscript (a, b, c and d) are significantly different at p<0.05

Table 4: Effects of tomato on liver enzyme activities of the experimental rat groups

Parameters	Positive control	Tomato peel	Tomato seed	Tomato pulp	Tomato fruit
ALT (μ mL^{-1})	42.17±3.19[a]	30.77±3.66[b]	32.11±3.45[b]	31.59±3.08[b]	31.77±3.07[b]
AST (μ mL^{-1})	85.11±8.13[a]	60.15±6.14[b]	57.33±5.11[b]	55.41±5.61[bc]	54.33±6.11[b]
ALP (μ mL^{-1})	91.55±10.22[a]	63.88±6.71[b]	60.78±6.03[b]	58.74±5.81[bc]	57.11±5.21[bc]
LDH (μ mL^{-1})	250.77±39.66[a]	125.11±11.07[b]	130.11±11.35[b]	110.77±9.22[c]	111.22±8.97[c]

ALT: Serum alanine aminotransferase, AST: Serum aspartate aminotransferase, ALP: Serum alkaline phosphatase, LDH: Serum lactate dehydrogenase, Mean values in each row having different superscript (a, b, c and d) are significantly different at p<0.05

promote health[18]. Lycopene-enriched tomato wine reduces white adipose weight in rats fed a high-fat diet[24].

Effect of administration of tomato peel, seeds, pulp or whole tomato fruit on lipid patterns of experimental rat groups: Compared to the control group, a marked decrease in TC, TG, LDLc, VLDLc and LDLc/HDLc and a marked increase in HDLc in the rat groups fed tomato peel, seeds, pulp or whole tomato fruit were detected. These differences were most evident in the group fed the whole fruit. All blood lipid parameters were similar between the groups (Table 3).

Previous studies have suggested that isoproterenol-induced myocardial infarction is associated with altered lipid metabolism, which is a risk factor for cardiovascular and cerebrovascular disease[25]. Tomatoes can ameliorate various health-related problems, including high plasma triglycerides and very low-density lipoprotein as well as increased lipid metabolism. Tomatoes do this by inducing the expression of genes involved in fatty acid oxidation. Lycopene, which is found in tomatoes, protects LDLc or the phospholipids in LDLc from oxidation and inhibits cholesterogenesis as well as being a powerful antioxidant capable of neutralizing free radicals, especially those derived from oxygen, thereby providing protection against chronic disease, especially coronary heart disease[26-28].Tomato skin and seeds contain high levels of lycopene, essential amino acids, minerals (Fe, Mn, Zn and Cu) and monounsaturated fatty acids, especially oleic acid. Tomato fiber reduces glucose absorption and serum cholesterol, which could be used in the treatment of hypercholesterolemic patients[29]. One study found that tomato consumption at 0.017 kg/day reduced the concentration of plasma lipids in a hyperlipidemic rat group compared to controls[30]. Tomato powder also lowered liver triglycerides and had a preventive effect against serum peroxidation products compared to both control and extracted lycopene treatments[31].

Effect of administration of tomato peel, seeds, pulp or whole tomato fruit on liver function values of experimental rat groups: Administration of tomato peel, seeds, pulp or whole fruit resulted in decreased serum ALT, AST, ALP and LDH (indicators of cardiac tissue damage) compared to the positive control group. There was no difference in these cardiac indicators between the treatment groups (Table 4).

Subcutaneous injection of isoproterenol significantly increased the activities of serum cardiac marker enzymes (creatine kinase, LDH, ALT, AST and ALP) (at p<0.05) and significantly lowered the activities of these enzymes in the heart[32]. The destruction of myocardial cells due to glucose and oxygen deficiency increases cell membrane permeability,

Table 5: Effects of tomato on cardiac function values of the experimental rat groups

Parameters	Positive control	Tomato peel	Tomato seed	Tomato pulp	Tomato fruit
LDH (nmol min^{-1} mg^{-1} protein)	30.77±2.78^{a}	10.14±1.08^{b}	9.55±1.11^{b}	8.99±1.10^{bc}	8.69±1.45^{bc}
NO (nmol min^{-1} mg^{-1} protein)	40.96±4.70^{a}	11.60±1.80^{b}	12.41±2.11^{b}	11.98±1.65^{b}	10.13±1.61^{b}
XO (nmol min^{-1} mg^{-1} protein)	13.77±1.11^{a}	5.66±0.55^{b}	6.08±0.89^{b}	5.11±0.75^{bc}	4.96±0.37^{c}

LDH: Cardiac lactate dehydrogenase, NO: Nitric oxide, XO: Xanthine oxidase, Mean values in each row having different superscript (a, b, c and d) are significantly different at p<0.05

Table 6: Effects of tomato on blood antioxidant levels of the experimental rat groups

Parameters	Positive control	Tomato peel	Tomato seed	Tomato pulp	Tomato fruit
GSH-Px (mmol L^{-1})	3.63±0.23^{b}	6.66±0.76^{a}	5.96±0.33^{a}	6.41±0.45^{a}	7.01±0.65^{a}
SOD (mmol L^{-1})	9.67±1.69^{b}	21.66±2.78^{a}	23.16±2.99^{a}	23.77±2.87^{a}	24.77±2.11^{a}
LPX (mmol L^{-1})	5.76±0.51^{a}	2.41±0.19^{b}	2.51±0.13^{b}	2.67±0.11^{b}	2.11±0.12^{b}

GSH-Px: Glutathione peroxidase, SOD: Superoxide dismutase, MDA: Malondialdehyde, Mean values in each row having different superscript (a, b, c and d) are significantly different at p<0.05

potentially leading to rupture, thereby resulting in the leakage and elevation of AST, ALT and LDH enzymes in the blood[33]. Tomato fruits contain essential nutrients, such as carotene, ascorbic acid and several types of minerals and reconsidered a good dietary source of lycopene and phenolic compounds that have a positive effect on the regulation of some oxidative stress and inflammatory biomarkers[34,35]. Supplementation with 9% dry tomato peel lowers the plasma cholesterol, LDL-C and TG concentrations as well as hepatic enzymes (AST, ALT and ALK), in a dose-dependent manner [36].

Effect of administration of tomato peel, seeds, pulp or whole tomato fruit on cardiac function values of experimental rat groups: Compared to the control group, LDH, NO and XO were markedly decreased in the cardiac tissue of the rats fed tomato peel, seeds, pulp or whole tomato fruit ($p<0.05$) and these were most obvious in the group fed the whole fruit (Table 5).

It has been hypothesized that the skin and seeds of the 3 cultivars of tomato contribute 53% of the total phenolics, 52% of the total flavonoids, 48% of the total lycopene, 43% of the total ascorbic acid and 52% of the total antioxidant activity present in tomatoes[37]. Tomato nutrients and phytochemicals, such as folate and vitamin C as well as various other carotenoids and phytochemicals, such as polyphenols, have antioxidant properties and in combination with lycopene, might contribute more efficiently to the protection against oxidative stress than lycopene alone. The health benefits reported here might be due to the direct use of tomato peel and seeds, which are rich in bioactive compounds, lycopene, fiber and vitamin C[34,38,39].

Effect of the administration of tomato peel, seeds, pulp or whole tomato fruit on antioxidant levels of experimental rat groups: Compared to the control group, the blood of rats fed tomato peel, seeds, pulp or whole fruit had significantly higher GSH-Px and SOD activities ($p<0.05$), while the LPX level was lower($p<0.05$). There was a non-significant difference in GSH-Px, SOD and LPX levels between the treatment groups (Table 6).

The myocardial necrosis observed in the animals receiving isoproterenol can also be attributed to peroxidative damage as isoproterenol generates lipid peroxides. Another group found that supplementation with lyophilized powder of tomato juice reduced plasma MDA in hypercholesterolemic mice[40]. Compared to their pulp and seed fractions, the skin fraction of tomato has significantly higher levels of total phenolics, total flavonoids, lycopene, ascorbic acid and antioxidant activity[37]. Previous studies have shown that increased consumption of polyphenols, lycopene and β-carotene from tomato is associated with a reduced risk of oxidative stress-induced disease. This is because these compounds scavenge free radicals, inhibit cell membrane damage and suppress lipid peroxidation, thus preventing the onset of chronic disease. Supplementation with tomato alters the pro-oxidation and anti-oxidation balance and suppresses oxidative stress by modulating the antioxidant system and cholesterol metabolism[21,41]. In an experimental model of myocardial ischemia-reperfusion injury, lycopene, carotenoids and polyphenols enhanced myocardial glutathione content and GSH-Px activity[20,42]. Future research should investigate the mode of action and the metabolism of tomato constituents to explain how they prophylactic against cardiac infarction.

CONCLUSION

Tomato fruits contain carbohydrate, protein, fiber and ash and they are also rich in lycopene, total phenolic compounds and vitamin C, A and B6, which increase its nutritional value. Tomato fruits and their pomace diminish isoproterenol myocardial infarction in rats by improving lipid marker levels, preventing lipid peroxidation and preserving antioxidant enzymes as well as scavenging free radicals. Thus, whole tomato fruits could be a useful intervention in the management of cardiovascular disease.

SIGNIFICANCE STATEMENT

This study discovered the importance of tomato fruit and pulp and tomato waste products (seed and peel) in nutrition and health because of their gross composition in addition to their contents of some minerals (Ca, Fe, Zn and K), vitamins ©, A, B1, B2 and B6) and antioxidants (β-carotene, lycopene and total phenolic compounds). In addition to their nutritional value, tomato fruit, pulp, seed and peel have ameliorative effect against isoproterenol-induced myocardial infarction in rats by improving liver function and lipid profile. This study will help the researchers to use tomato waste products to lower the incidence of cardiac infarction and arteriosclerosis. Additionally, many researchers could explore the use of tomato in the treatment of myocardial infarction.

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