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Anti- diabetic and Antioxidant Effects of Grapefruit, Mango and Strawberry Juice in Streptozotocin – Induced Diabetic Rats

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Authors' contributions

This work was carried out in collaboration between all authors. All authors equally designed the study, performed the statistical analysis, wrote the protocol, wrote the first draft of the manuscript, managed the analyses of the study and managed the literature searches. All authors read and approved the final manuscript.

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Original Research Article

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ABSTRACT

Aim: The aim of the present study is to evaluate the phytochemical screening of mango, grapefruit and strawberry juice using HPLC and to investigate the anti- diabetic and antioxidant effects of grapefruit, mango and strawberry juice in streptozotocin – induced diabetic rats

Methodology: Mango, grapefruit and strawberry juice were orally administered at a dose of 1ml/100g body weight/day to streptozotocin - induced diabetic rats for four weeks. Blood samples were collected for analysis of Serum triglycerides (TAG), glucose, Insulin, total lipid (TL), total cholesterol (TC), low-density lipoprotein (LDL) and high-density lipoprotein (HDL) in diabetic rats

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compared with control negative rats and diabetic rats fed on different fruit juice.
Results: The results showed that mango has the highest levels of protein, crude fiber, ash content and total carbohydrates (0.82, 0.72, 0.51 and 9.61 g/100g fresh weight) followed by strawberry (0.50, 0.35, 0.27 and 8.95 g/100g fresh weight) and grapefruit was 0.40, 0.25, 0.19 and 8.76 g/100g fresh weight, respectively. There was no significant difference the pH at 20 ºC, titratable acidity (TA) g/L, total soluble solids (TSS °Brix), Vit. C. mg/100g and density g/cm (at 20ºC) between different fruit juices. Results also revealed that all fruit juices had rich content of the polyphenols and the results also illustrated that the mango, grapefruit, and strawberry juice oral adminstration decreased serum triglycerides (TAG), serum glucose, serum insulin, total lipid (TL), total cholesterol (TC), low-density lipoprotein (LDL) and MDA in diabetic rats. On the other hand, oral administration of fruit juices significantly increased serum HDL- cholesterol and modified oxidative stress.
Conclusion: From the obvious results, we can conclude that the grapefruit, mango, and strawberry juice have a strong antioxidant and hypolipidemic effects which might be attributed to their high polyphenols and flavonoid content.

Keywords: Mango; grapefruit and strawberry juice; phenolic acids and flavonoids compounds.

1. INTRODUCTION

The popularity of citrus fruit juice is certainly due to its pleasant and refreshing flavor plus consumers know that they get the nutritional benefits from Vitamin C, folic acid, flavonoids and dietary fiber, but the quick changes and degradation of the chemical and physical characteristics of the juice which is reflected in the taste, flavor, and appearance need to be treated carefully with different technological processes [1].

Consuming citrus fruit e.g. grapefruit and grapefruit juice can help boost the absorption of non-heme iron. This means that if you drink a glass of grapefruit juice before eating a meal rich in iron, for example, a spinach salad the body absorbs two or four times as such iron [2].

One-half of a piece of grapefruit has more dietary fiber than many other popular fruits including, bananas, apples, and strawberries. It has been demonstrated that, low-fat diets high in fruits and vegetables has many health benefits, especially in the reduction of cardiovascular disease risk and cancer [2]. One grapefruit can provide more than 188 mg potassium which meets the daily requirement and also provides the necessary daily requirement for Vitamin C, which is important to support a healthy immune system. The high level of pectin and fiber found in citrus fruits like grapefruit may help to maintain healthy cholesterol and glucose levels [2].

Mango (*Mangifera indica* L.) from *Anacardiaceae* family is one of the most widely eaten tropical fruit because of its unique taste, attractive color and flavor, affordability and nutritional qualities. It is a rich source of vitamins, organic acids, carbohydrates, amino acids, phenolic acids (e.g., gallic acid, caffeic acid, and tannic acid) and certain volatile compounds [3,4]. Many of the pharmacological properties attributed to mango might be due to the presence of phenolic acids. These phenolic compounds possess potent antioxidant activity that plays an important role in human nutrition as preventative agents against several diseases caused by oxidative stress, protecting the body tissues against oxidative stress with their antioxidant, antimutagen, anti-inflammatory, and anti-carcinogenic properties [5,6]. Apart from the fruit, mango flesh also has been reported to have antilithiatic and free radical scavenging properties, which reduce lipid peroxidation and enhance antioxidant enzymes (superoxide dismutase and catalase) against isoproterenol [7].

Strawberries (*Fragaria x ananassa* Duch.) have unique, highly desirable taste and flavor. Among the most important factors that can affect the taste quality of a product, ripeness, maturity, cultivar, irrigation, and fertilization [8,9].

Strawberries is a good source of ascorbic acid (vitamin C) which is a very important nutrient, being essential, e.g. for the synthesis of collagen. Ascorbic acid is also a natural antioxidant used in foodstuff formulations in order to prevent browning, discoloring and to enhance shelf life [10].

The aim of the present study is to evaluate the phytochemical screening of mango, grapefruit and strawberry juice using HPLC and to investigate the anti- diabetic and antioxidant effects of grapefruit, mango and strawberry juice in streptozotocin – induced diabetic rats.

2. MATERIALS AND METHODS

2.1 Materials

Grapefruit (*Fragaria x ananassa* Duch.), mango (*Mangifera indica* L.) and strawberry (*Fragaria x ananassa* Duch.) fruits were purchased from Giza-Egypt.

Authentic samples of phenolic acids and flavonoids compounds were purchased from Sigma Co. (St. Louis, MO, USA). All other solvents and chemicals were of analytical grade.

2.2 Preparation of Raw Material Juice

Fresh mango, grapefruit and strawberry cultivars were washed, manually peeled and seed removed. The pulp of mango, grapefruit, and strawberry was sliced using a stainless steel knife.

Fruit juices were prepared using a robot type fruit squeezer. Grapefruit, mango, and strawberry were prepared as clear juice. Fruit juice was filtered and stored in labeled plastic containers at -4℃ for analysis.

2.3 Physicochemical Properties of Fruits Juice

Protein content, ash, crude fiber, lipids content and total carbohydrates were determined in mango, grapefruit and strawberry juice according to [11].

Total soluble solids (TSS) expressed as ^{o}Brix, were measured with an Abbe refractometer (A. Kruss, Germany) calibrated against sucrose. Titratable acidity (TA), total sugar and density g/cm (at 20ºC) were measured according to [11]. pH was measured with a pH meter (Mettler-toledo, Switzerland). Ascorbic acid (AA) was determined using dinitrophenylhydrazine method of [12].

2.4 Identification of Phenolic Acids Compounds Using HPLC

Phenolic compounds were determined by HPLC according to the method of [13] as follow: 5 g of different samples (mango, grapefruit and strawberry fruits) were mixed with ethanol and centrifuged at 10000 rpm for 10 min and the supernatant was filtered through a 0.2 µm Millipore membrane filter then 1-3 ml was collected in a vial for injection into HPLC Agilent (series 1200) equipped with auto-sampling injector, solvent degasser, ultraviolet (UV) detector set at 280 nm and quaternary HP pump (series 1100). The column temperature was maintained at 350C. Gradient separation was carried out with ethanol and acetonitrile as a mobile phase at a flow rate of 1 ml/min. phenolic acid standard from sigma Co was dissolved in a mobile phase and injected into HPLC. Retention time and peak area were used to calculate the phenolic compounds concentration by the data analysis of HEWLLET Packard software. Standard compounds were prepared as stock solutions at 2 mg mL−1 in 80% ethanol. The stock solutions were stored in darkness at 18 ^{o}C and remained stable for at least 3 months. All samples were analyzed in duplicate unless otherwise stated, and concentrations of individual phenolic acids were expressed in mg/100 of dry matter.

2.5 Identification of Flavonoids Compounds Using HPLC

Flavonoid compounds were determined by HPLC according to the method of [14] as follows: 5 g of different samples (mango, grapefruit and strawberry fruits) were mixed with ethanol and centrifuged at 10000 rpm for 10 min and the supernatant was filtered through a 0.2 µm Millipore membrane filter then 1 - 3 ml was collected in a vial for injection into HPLC Hewllet Packared (series 1050) equipped with auto-sampling injector, solvent degasser, ultraviolet (UV) detector set at 330 nm and quarter HP pump (series 1050). The column temperature was maintained at 350C. Gradient separation was carried out with ethanol and acetonitrile as a mobile phase at a flow rate of 1 ml/min. Flavonoids acid standard from sigma Co. were dissolved in a mobile phase and injected into HPLC. Retention time and peak area were used to the calculation of phenolic compounds concentration by the data analysis of HEWLLT Packared software.

2.6 Biological Experiment Protocol

Male adult rats (40 rats) 150-160g were purchased from National Organization for Drug and Control Research, Giza, Egypt. Animals were housed in individual cages with screen bottoms and fed on a basal diet for eight days. The basal diet consisted of corn starch 70%, casein 10% corn oil 10%, salt mixture 4%, vitamin mixture 1% and cellulose 5% according to [11].

After feeding on a basal diet for eight days, rats were divided into two groups. The first group (8 rats) was fed on the basal diet for another four weeks (30 days) and considered as negative control. The second main group (32 rats) fasted overnight and injected with streptozotocin (50 mg/kg b. w.) dissolved in 0.1M citric acid buffer and adjusted to pH 4.5) into the leg muscle (5mg /100g body weight) to induce diabetic rats according to [15]. After 48 hr. of injection the second main group was divided into four subgroups (8 rats for each). The first one (group 2) (8 rats) was continued to be fed on basal diet and considered as positive control. From the third to fifth groups (8 rats each) were fed on basal diet and the animals were treated by oral gavage with 1 mL of different fruit juice as follow group 3 (mango), group 4 (strawberry) and group 5 (grapefruit) per 100 body weight for 4weeks. The chosen juice dose corresponds to approximately 500-600 mL of juice consumed daily by an average-weight adult individual. Each rat was weighed every two days and the food consumption was calculated.

At the end of experimental period (four weeks), the blood samples were withdrawn from the orbital plexus and centrifuged at 3000 rpm to obtain the sera. After that, the sera were kept on a deep-freeze at -20°C until their analyses.

The organs as liver, heart, kidney and lung were weighted at the end of experimental.

The serum parameters were analyzed spectrophotometrically by using double beam UV-Visible spectrophotometer. Serum glucose was measured following the colorimetric method using the assay kit [16], Serum insulin levels were determined by ultra sensitive rat insulin kit, using double antibody enzyme-linked immunosorbent assay (ELISA) [17], total lipids [18], Serum total cholesterol (TC) and triacylglycerols (TAG) were measured according to the colorimetric methods and using the assay kits according to [19] and [20], respectively. Also, high-density lipoprotein cholesterol (HDL-C) measurement in serum followed the instructions of the assay kit according to [21]. Serum low-density lipoprotein cholesterol (LDL-C) and very-low-density lipoprotein cholesterol (VLDL-C) were calculated by the following equations:

LDL-C (mg/dl) = TC – (VLDL-C + HDL-C)

VLDL-C (mg/dl) = TAG concentration/5 [22]

2.7 Induction of Diabetes Mellitus

Diabetes was induced by administering 50 mg/kg of Streptozotocin in cold citrate buffer, pH 4.5, intraperitoneally to overnight fasted male rats. Hyperglycemia was confirmed after 72 hrs by the elevated blood glucose and the behavioral changes (excess thirst and frequent urination). The rats with blood glucose level more than 240 mg/dL were glucose >200 mg were considered to be diabetic and included for the study [15].

2.8 Statistical Analysis

The data obtained in the present study was analyzed by ANOVA. The results were analyzed with the aid of the software SAS System for Windows [23].

3. RESULTS AND DISCUSSION

3.1 The Physicochemical Screening of Grapefruit, Mango, and Strawberry Fruit Juice

Chemical composition and physical properties of grapefruit, mango, and strawberry juice were determined and the results are recorded in Tables 1 and 2. The results from Table 1 showed that mango has the highest levels of protein, crude fiber, ash content and total carbohydrates (0.82, 0.72, 0.51 and 9.61 g/100g fresh weight) followed by strawberry (0.50, 0.35, 0.27 and 8.95 g/100g fresh weight) and also, grapefruit was 0.40, 0.25, 0.19 and 8.76 g/100g fresh weight, respectively. Moreover, the strawberry was higher in fat (0.25 g/100 g fresh weight) compared with mango and grapefruit were 0.24 and 0.20 g/100g fresh weight, respectively. The percent of total sugar in grapefruit and mango were 9.90 and 8.13% respectively and the strawberry was the lowest (5.08%).

Mango is an important fruit, a good source of nutrients, particularly vitamin A and C and dietary fiber [24,25]. The importance of optimal intakes of essential mineral elements to maintain peak health is widely recognized. According to [26]**,** mango plays an important role in balancing the diet of a human being by providing 64-86 calories of energy.

Grapefruit (Citrus paradisi) has been used as a folk medicine in many countries as anti-fungal, anti-inflammatory, antimicrobial, antioxidant, antiviral, astringent and preservative. It has also been used for cancer prevention, cellular regeneration lowering cholesterol, diabetics, cleansing, detoxification, heart health maintenance, arthritis and weight loss [27]. Great interest has developed in strawberries because of their extremely high content of vitamin C, which makes them an important source of this vitamin for human nutrition.Together with vitamin C, folate plays a crucial role in emphasizing the micronutrient content of the strawberry when considering that, among fruits, it is one of the richest natural sources of this essential micronutrient; its content is considered in the range of 20 to 25 mg/100 g fresh weight (FW) [28].

Table 2 showed the physical properties of grapefruit, mango and strawberry juice and it could be noticed that, there was no signioficant difference in the pH at 20ºC, titratable acidity (TA) g/l, total soluble solids (TSS ^{o}Brix), Vit. C. mg/100g and density g/cm (at 20ºC) between all fruits juice.

The pH in the fruit pulp plays an important role in flavor promotion as well as a preservation factor [29].

Strawberry flavor is conditioned in part by the balance between sugars and acids expressed in ripe fruits, and the organic acids are the second contributors (after sugars) to the soluble solids of strawberries. Besides their importance in flavor, acids are important in processing because they affect the gelling properties of pectin. Citric acid contributes 92% and malic acid 9% of acidity [30]. Strawberries are considered to be a good source of vitamin C, having an average Ascorbic Acid (AA) content from 50 to 60 mg/100 g [30].

3.2 Identification of Phenolic Acids in the Grapefruit, Mango, and Strawberry Juice Using HPLC

Distribution of the polyphenolic and related compounds in the grapefruit, mango and strawberry juice are shown in Table 3. The results illustrated that grapefruit juice has higher levels of the phenolic acid salicylic (1.658 mg/100g). However mango juice has the highest levels of syringe, pyrogllol and benzoic acids (2.307, 1.226 and 1.600 mg/100g, respectively). Moreover, Ssyrinigc, salycilic and ferulic acids were detected in higher concentration in strawberry juice (1.631, 1.591 and 2.193 mg/100g, respectively).

The phenolic acids play an important role in combating oxidative stress in the human body by maintaining a balance between oxidants and antioxidants [31]. The average percentage contributions to totally free and bound phenolic acid concentrations varied with components and cultivars. Syringic acid represented the most abundant class of free phenolic acids, contributing from 29.8% to 36.8% of the total concentrations among cultivars; whereas ferulic represented the most abundant class of the total bound phenolic acid, contributing from 46.0% to 55.8% of the concentrations among cultivars. Therefore, the free phenolic extracts of the grain were mostly contributed by syringic rather than ferulic, whereas ferulic acid primarily existed in the bound form [32]. Moreover, the bound form contributed 95.8% of the grain ferulic acid concentration determined, similar to the previous results [33]. Ferulic acid was, as expected, the dominant component in the bound fraction, consistent with previous reports by [34]. The second most abundant phenolic acids in whole grain were caffeine and p- coumaric, largely in agreement with [35].

Table 1. Chemical compositions of grapefruit, mango and strawberry juice, g /100g fresh weight (Mean±S.D)

Chemical analysis	Grapefruit	Mango	Strawberry
Moisture (g/100g fresh weight)	90.2±0.23	89.9±0.21	98.68 ± 0.17
Protein (g/100g fresh weight)	0.40±0.011	0.82±0.014	0.50 ± 0.02
Fat (g/100g fresh weight)	0.20 ±0.012	0.24±0.014	0.25 ± 0.02
Crude fiber (g/100g fresh weight)	0.25±0.011	0.72±0.015	0.35 ± 0.02
Ash (g/100g fresh weight)	0.19±0.014	0.51±0.007	0.27 ± 0.01
Total carbohydrates (g/100 g fresh weight)	8.76±0.16	9.61±0.26	8.95 ± 0.13
Total sugar %	9.90±0.13	8.13±0.21	5.08 ± 0.39

Table 2. The values of the determined physical properties of fresh weight (Mean±S.D)

Physical properties	Grapefruit	Mango	Strawberry
pH (at 20ºC)	3.61±0.07	3.81±0.087	3.73 ± 0.01
Titratable acidity (TA) g/l	0.92±0.04	0.69±0.032	0.86 ± 0.10
TSS (ºBrix)	12.10±0.19	15.60±0.40	10.50 ± 0.50
Vit. C. mg/100g	35.8±0.25	36.4±0.27	50.2±0.29
Density g/cm (at 20ºC)	1.047±0.009	1.056±0.008	1.096±0.003

Table 3. Identification of phenolic acids in the grapefruit, mango and strawberry juice using HPLC (mg/100 g)

Phenolic compounds	Grapefruit	Mango	Strawberry
Syringic acid	0.760	2.307	0.723
Gallic acid	0.124	0.100	0.100
Protocatechuic acid	0.338	0.256	0.241
4- Amino-benzoic acid	0.012	--	0.007
Chlorogenic acid	0.121	0.200	0.124
4-Hydroxybenzoic acid	0.145	0.350	0.100
Caffeic acid	--	0.085	0.052
Vanillic acid	0.023	0.050	0.039
Caffeine	0.361	0.271	0.118
Ferulic acid	--	0.788	2.193
Benzoic acid	0.107	1.600	--
Salicylic acid	1.658	--	1.591
Ellagic acid	0.443	0.467	0.334
Cinnamic Acid	0.102	0.527	0.237
Rosmarinic	0.040	0.201	0.155

Citrus products consumption has been recognized as an important factor in reducing the risk of several chronic diseases such as cancer [36,37], osteoporosis [38] and cerebrocardio-vascular diseases [39,40]. Grapefruit juices and jams are highly appreciated due to their specific taste, flavor and nutritional value.

The presence of bioactive compounds such as flavonoids and ellagic acid derivatives makes the consumption of strawberry suitable for potential health benefits. Dietary intake of flavonoids has been associated with lower risk of heart disease as well as cancer, probably related to the antioxidative activity of these compounds. Recent studies illustrated that, the compounds in strawberries have potential power in reducing the risk of cardiovascular diseases by inhibition of LDL cholesterol oxidation, promotion of plaque stability, improved vascular endothelial function, and decreased tendency for thrombosis, modulation of the inflammatory process, blocking initiation of carcinogenesis, suppressing progression and proliferation of tumors [41], inhibition of proliferation of human liver cancer cells [42], inhibition of esophageal cancer [43], anticarcinogenic activities to breast and cervical cancer cells [44] and inhibition of growth and stimulation of apoptosis of human cancer cells [45]. Moreover, the extracts from strawberry showed antithrombotic effect [46] and inhibition of Helicobacter pylori with enhanced susceptibility to clarithromycin [47].

3.3 Identification of Flavonoids Compounds in the Grapefruit, Mango and Strawberry Juice Using HPLC

The results of isolation and identification of flavonoids compounds in the grapefruit, mango and strawberry juice are shown in Table (4). Contents of the flavonoids compounds are expressed as mg of compounds per 100g of the dry weight. From the results of the present study, it could be observed that the grapefruit juice is a good source of hesperidin compound (1.419 mg/100g) and mango juice containe 2.835 mg/100g from luteolin compound. Moreover, the compounds contained in strawberry juice and all flavonoids compounds in the grapefruit, mango and strawberry juice were less than 1 mg/100g.

The concentration of flavonoids in plant extracts depends on the polarity of solvents used in the extract preparation [48].

Although some investigators have suggested that flavonoid glucosides may utilize the sodium-dependent glucose transporter for uptake by the gut, it has been shown that the h-glycosides genistin and daidzin, and by implication other flavonoid glucosides, are hydrolyzed in the gut wall by lactose phlorizin hydrolase, an enzyme in the apical membrane of the villi of the small intestine [49] and by intestinal microflora that convert them into aglycone forms [50]. The flavonoid algycones that are produced by hydrolysis are then absorbed into the intestinal cells by passive mechanisms. This is followed by a conjugation step in the intestinal cell with glucuronic acid by the phase II enzyme UDP-glucuronosyl transferase. Those aglycones that escape this initial metabolism pass into the circulation and are converted to glucuronidated, methylated, and sulfated phase II metabolites by enzymes in the liver and other organs [51].

The flavonoid phase II metabolites are taken up from the blood by the liver and are excreted in bile, thus transporting them back into the intestines. Intestinal hglucuronidases and sulfatases then release the aglucones these can be reabsorbed or enter the bacterial rich large bowel for further metabolism [52]. Flavonoids are converted to several other phenolic acids. Some of these metabolites have shown higher anti-oxidative and estrogenic activities (measured in vitro) than their parent compounds, for instance, equal compared with daidzein [53].

3.4 Effect of Mango, Strawberry and Grapefruit Juice on Body Weight Gain, Food Intake and Feed Efficiency Ratio in Diabetic Rats

The results from Table 5 indicated that the negative control group had the highest final body weight 169.28 g and feed efficiency ratio (0.97%) at the end experimental period (four weeks). While the positive control group had a significant decrease in final body weight 140.40 g and feed efficiency ratio was decreased -1.10%. Meanwhile, there was no significant difference in final body weight and feed efficiency ratio in rat groups orally administered with mango, strawberry and grapefruit juice at 1 ml/day for four weeks.

Table 4. Identification of flavonoids compounds in the grapefruit, mango and strawberry juice using HPLC (mg/100 g)

Flavonoid compounds	Grapefruit	Mango	Strawberry
Luteolin	0.765	2.835	0.938
Rutin	0.495	0.534	0.770
Hesperidin	1.419	0.100	0.389
Quercitrin	0.050	0.128	0.454
Quercetin	0.096	0.200	0.137
Hispertin	0.221	0.428	0.670
Kaempferol	0.058	0.2122	0.085
Apigenin	0.044	0.042	0.028
7-Hydroxyflavone	0.010	0.007	0.037

Table 5. Effect of mango, strawberry and grapefruit juice on initial body weight, final body weight, food intake and feed efficiency ratio in diabetic rats (Mean ±SE)

Groups	Initial body weight (g)	Food intake (g/day)	Final body weight(g)	Total food intake(g)	Feed efficiency ratio
Group 1 Negative control	155.64± 0.037^{a}	15.96±0.10^{a}	169.28±1.05^{a}	446.88± 3.56^{a}	0.97±0.014^{a}
Group 2 Diabetic control	153.20±.042^{c}	9.54±0.06^{c}	140.40±1.24^{c}	267.12±.4.21^{c}	-1.10±0.011^{c}
Group 3 (Mango juice)	157.92± .039^{b}	14.85±0.09^{b}	163.84±1.08^{b}	415.80± 3.91^{b}	0.96±0.012^{b}
Group 4 (Strawberry juice)	159.56± 0.082^{b}	14.89±0.075^{b}	165.12±1.35^{b}	416.92± 4.25^{b}	0.97±0.013^{b}
Group 5 (Grapefruit juice)	158.24± 0.075^{b}	14.79± 0.07^{b}	163.48±1.71^{b}	414.12± 5.24^{b}	0.97±0.012^{b}

Values are expressed as means ± SE. Means with similar superscript (a, b c, d) letters in columns indicate the non-significant difference (P< 0.05)

3.5 Effect of Mango, Strawberry and Grapefruit Juice on the Relative Weight of Organs in Diabetic Rats

Data presented in Table 6 showed that, there was no significant difference in relative weight of organs between different treatment groups.

3.6 Effect of Mango, Strawberry and Grapefruit Juice on Triglycerides (Tag), Serum Glucose and Insulin in Diabetic Rats

Table 7 showed the effect of mango, strawberry and grapefruit juice at a dose of 1 ml taken orally every day for four weeks on triglycerides (TAG), serum glucose and serum insulin in diabetic rats. The results illustrated that the triglycerides (TAG), serum glucose and serum insulin in control negative were 96.42 and 93.50 mg/dl and 15.80 U/ml respectively. Whereas, in the diabetic rats there was a significant increase in these parameters they were 201.04 and 241.80 mg/dl and 8.01 µU/ml respectively. On the other hand, the diabetic rats treated orally with 1ml/day of mango, strawberry and grapefruit juice, there was a significant improvement (decrease) in different parameters as compared to the diabetic control positive group. But there were no significant differences between these three treatment groups (mango, strawberry and grapefruit juice). From the results, it could be noticed that, dietary supplementation with grapefruit, mango and strawberry juice, a rich source of bioactive compounds, especially the polyphenols, have been associated with protective effects especially lowering serum glucose and triglycerides.

Streptozotocin administration causes a reduction in the number of β-cells and induces hyperglycemia [54]. The different juice were observed to decrease serum glucose level and increase serum insulin concentration in treated rats. The possible mechanism of the hypoglycemic action of different juice may be through potentiating the plasma insulin effect by increasing either pancreatic secretion of insulin from regenerated β-cells or its discharge from bound insulin. In this context, other plants have also been observed previously to have hypoglycemic effects [55]. Moreover, streptozotocin-induced diabetes is due to the excess production of reactive oxygen species (ROS) leading to cytotoxicity in β-cells, thus decreasing the synthesis and release of insulin [56] and also affecting the pancreas [57]. Increased levels of the pancreatic thiobarbituric acid reactive substances (TBARS) could be due to the increase in free radicals and decrease in nonenzymatic antioxidants [58].

3.7 Effect of Mango, Strawberry and Grapefruit Juice on Lipid Parameters in Diabetic Rats

Total lipids (TL), total cholesterol (TC), low-density lipoprotein (LDL) and high-density lipoprotein (HDL) were determined in diabetic rats fed on basal diet and mango, strawberry and grapefruit juice at 1 ml/ day for four weeks and the results are reported in Table (8). From the results, it could be noticed that the group 1 as a negative control was the lowest in TC, LDL, and TL (98.14 and 24.11 mg/dl and 0.65 g/dl respectively) when compared to the positive control diabetic group. On the other hand, TC, TAG, LDL were significantly decreased in

Table 6. Effect of mango, strawberry and grapefruit juice on relative weight of organs in diabetic rats (Mean ±SE)

Groups	Liver (g)	Heart (g)	Kidney (g)	Lung (g)
Group 1 Negative control	3.56 ±1.60[a]	0.65 ±0.01[a]	1.32 ± 0.36[a]	1.13 ±0.15[a]
Group 2 Diabetic control	4.01 ±1.14[a]	0.48 ±0.16[a]	1.01 ± 0.26[a]	1.19 ±0.66[a]
Group 3 (Mango juice)	3.86 ±0.51[a]	0.44 ±0.12[a]	1.02 ± 0.22[a]	1.04 ±0.12[a]
Group 4 (Strawberry juice)	3.57 ±0.14[a]	0.47 ±0.05[a]	1.21 ± 0.34[a]	1.10 ±0.14[a]
Group 5 (Grapefruit juice)	3.62±0.005[a]	0.45±0.003[a]	1.15±0.005[a]	1.08 ±0.14[a]

Values are expressed as means ± SE. Means with similar superscript (a, b c, d) letters in columns indicate non-significant difference (P< 0.05)

Table 7. Effect of mango, strawberry and grapefruit juice on triglycerides (TAG), serum glucose and insulin in diabetic rats (Mean ±SE)

Groups	TAG (mg/dl)	Serum glucose (mg/dl)	Serum insulin (μU/ml)
Group 1 Negative control	96.42± 2.04[a]	93.5± 1.4[a]	15.80± 0.17[a]
Group 2 Diabetic control	201.04±3.99[c]	241.80± 2.9[c]	8.01± 0.19[c]
Group 3 (Mango juice)	105.7± 2.33[b]	132.3± 1.99[b]	12.18± 0.15[b]
Group 4 (Strawberry juice)	103.97± 1.22[b]	136.9± 2.10[b]	12.02± 0.12[b]
Group 5 (Grapefruit juice)	103.45± 2.81[b]	137.28± 1.40[b]	11.96± 0.12[b]

Values are expressed as means ± SE. Means with similar superscript (a, b c, d) letters in columns indicate non-significant difference (P< 0.05)

Table 8. Effect of mango, strawberry and grapefruit juice on lipid parameters in diabetic rats (Mean ±SE)

Groups	Total cholesterol (TC) (mg/dl)	LDL-C (mg/dl)	HDL-C (mg/dl)	Total Lipid (TL) g/dl
Group 1 Negative control	98.14± 2.44[a]	24.11 ± 0.96[a]	50.74± 1.44[a]	0.65 ±0.03[a]
Group 2 Diabetic control	185.9± 2.64[c]	116.64± 2.28[c]	43.08± 2.49[c]	1.42 ±0.17[c]
Group 3 (Mango juice)	108.54± 2.99[b]	52.41± 2.61[b]	48.99± 2.05[b]	0.78±0.13[b]
Group 4 (Strawberry juice)	106.19± 249[b]	50.49± 2.34[b]	46.9± 2.44[b]	0.73 ± 0.06[b]
Group 5 (Grapefruit juice)	107.50± 3.02[b]	54.05± 2.04[b]	47.76± 1.87[b]	0.77±0.12[b]

Values are expressed as means ± SE. Means with similar superscript (a, b c, d) letters in columns indicate non-significant difference (P< 0.05)

Table 9. Comparative effect of mango, strawberry and grapefruit juice on serum MDA and GSH in Streptozotocin- induced diabetic rats (Mean ±SE)

Parameters / Groups	Serum MDA (nmol\L)	Blood GSH(mg/dl)
Group 1 Negative control	1.67±0.03	12.76±0.25
Group 2 Diabetic control	3.67±0.04	6.98 ±0.16
Group 3 (Mango juice)	2.42±0.04 [a]	7.74 ± .11
Group 4 (Strawberry juice)	2.41±0.08 [a]	9.3 ± 0.09[a]
Group 5 (Grapefruit juice)	2.59±0.03	9.4 ± 0.083[a]

Values are expressed as means ± standard Error. Means with similar superscript (a, b c, d) letters in columns indicate non-significant difference (P< 0.05)

groups treated with mango, strawberry and grapefruit juice at 1 ml/day for four weeks as compared to the positive diabetic control group which was the highest in all parameter TC, LDL and TL. These results are similar to several studies which demonstrated that, the uniquely high levels of polyphenols in grapefruit, mango, and strawberry juice, may play an important role in contributing to the health benefit such as lowering total cholesterol level, diabetes and reducing the risk of cardiovascular diseases [59].

On the other hand serum HDL- cholesterol was significantly increased by supplementation of mango, strawberry and grapefruit juice at 1 ml/ day as compared to positive control diabetic rats.

The results of the current study are in harmony with the previous finding which demonstrated that treatment with aqueous extract of *Mangifera indica* leaves showed a significant decrease in elevated total cholesterol (TC), triglyceride (TG), low-density lipoprotein (LDL-C) and very low-density lipoprotein (VLDL), with a significant increase in high-density lipoprotein (HDL-C) [60]. Moreover, [61] found that Single oral administration of a dose of 250 mg/ kg body weight produces a potent and strong hypoglycemic effect in Type-2 diabetes on rats. A similar result was found by [62]. A significant decrease in mean concentration of plasma glucose two weeks after administration of high (1 g/kg/d) dose of the powdered part, aqueous extract and alcoholic extract of leaves of *Mangifera indica* were found [63].

There was a significant increase in MDA in diabetic rats as compared to normal control however blood GSH was significantly decreased in diabetic rats. Different juice treatment leads to a significant improvement in oxidative status where MDA significantly reduced and Blood GSH was significantly increased in groups treated with mango, strawberry and grapefruit juice which may be attributed to their high antioxidant content.

4. CONCLUSION

From the results of the present study, it may be concluded that mango has the highest levels of protein, crude fiber, ash content and total carbohydrates followed by strawberry and then by grapefruit. The identification of phenolic acids and flavonoids compound in mango, grapefruit, and strawberry juice reported that all juice had high levels of polyphenols and flavonoids.

Also, we can conclude that the different fruit juices (grapefruit, mango, and strawberry) at a dose of 1mL /100g body weight for 4 weeks play an important role in controlling blood glucose level of streptozotocin - induced diabetic rats. In addition, different fruit juices lead to a significant improvement in lipid profile and antioxidant status. Also, we can conclude that grapefruit, mango, and strawberry juice showing strong anti-diabetic and antioxidant activities which might be attributed to their high polyphenols and flavonoid content which may be promising alternative therapy for treatment of diabetes and related lipid and vascular abnormalities.

ETHICAL APPROVAL

All authors hereby declare that "Principles of laboratory animal care" (NIH publication No. 85-23, revised 1985) were followed, as well as specific national laws where applicable. All experiments have been examined and approved by the appropriate ethics committee.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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