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Chemical, Technological and Biological Evaluation of Mulberry and Persimmon Leaves

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The present study was conducted to determine the total phenolic content (TPC) and total flavonoid content (TFC) in both irradiated and non-irradiated mulberry and persimmon extracts (water and methanolic extract). Additionally, the oxidative stability of these extracts against sunflower oil (SFO) was determined. The water extract has a higher content of both TPC and TFC. Irradiation exposure increased the antioxidant activity, especially at a dose of 1.5 kGy. Chemical composition of persimmon leaves had a higher fiber content than that of mulberry. Sensory evaluation of blends formula mulberry and persimmon herbal tea achieved the best overall acceptability (8.8) at 3% from each. Administration of 1.2 g/Kg from mulberry, persimmon leaves and their blends represented 72.5%, 71.6% and 73.5% reduction in glucose levels, in rats administrated with water extract, and 73.1%, 68.4% and 71% reduction with rats administrated powder. Thyroid hormones thyroxine (T_4) and triiodothyronine (T_3) showed a significant ($P<0.05$) decrease in diabetic rats treated with mulberry and persimmon compared to diabetic rats. Lipid profile, renal and hepatic enzymes were ameliorated in rats treated with the studied leaves. Mulberry and persimmon leaves possess hypoglycemic activity, beneficial effects on lipid profile, renal and hepatic functions in rats treated with mulberry and persimmon leaves.

Keywords: *Mulberry, Persimmon, Extracts, Antioxidant, Diabetic, Hypoglycemic*

Introduction

Tea "term" is the extract of leaves, leaf nodes and internodes of a plant which is consumed as an extract in hot water rather than being eaten as such. It is also referred to as an aromatic liquid product which has been made by curing the leaves by applying hot water [1]. Mulberry (*Morus alba* L.) leaves are known as folk herbal tea in many countries. Mulberry leaves have a very powerful antioxidant effect that comes from the polyphenolic compounds (like flavonoids, such as quercetin, kaempferol, and morin) contained in the leaves.

Mulberry contains polyphenolics such as rutin, quercetin, 1-deoxynojirimycin (DNJ) and some of its derivatives, which are well known α-glucosidase inhibitors [2, 3]. These are used for medicinal purposes in the treatment of several metabolic diseases including dyslipidemia [4], diabetes [5], fatty liver disease [3], and

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hypertension [6]. The mulberry leaf also enhances antioxidant enzyme activities in diabetic rats [7]. Recently, in many countries, mulberry-leaf tea has gained more popularity as a health beverage and is seeking for industrial manufacture. In the process of tea manufacturing, three main steps are needed namely, blanching, whitening and drying [8, 9].

Among the fruits, persimmon (*Diospyros kaki*) is a popular and widespread fruit that is enriched with many bioactive compounds, including polyphenols, terpenoids, steroids, flavonoids, carotenoids, minerals, and dietary fiber [10, 11, 12]. In fresh persimmon leaves, most of the polyphenols are found to be water soluble. The chief components in persimmon leaf tea are unique proanthocyanidin oligomers and oral administration of this tea along with starch resulted in a dose-dependent decline in the blood glucose level in Wistar rats [13]. Persimmon leaves have been used for tea in Korea and many other countries as green tea and oriental medicine [14], since they were thought to be effective against hypertension [15].

Persimmon is naturally bestowed with bioactive molecules including proanthocyanidins, flavonoids, tannins, phenolic, carotenoids, dietary fiber, and etc. Persimmon leaves and fruit have imperative significance for coronary health because of hypocholesterolemic, anti-atherosclerosis and antioxidant perspectives [16-21].

Applications of leaves and seeds of persimmon in preparing different food and beverage have been tested. [22] prepared persimmon leaf powder supplemented cookies and was found to improve them, without compromising on consumer acceptance. Kim et al. [23] mentioned that persimmon leaves could be used to enhance the preference of green tea as well as to enrich its antioxidant potentials. Persimmon leaf extract showed therapeutic potential to alleviate the severity of radiation-induced liver injury, hyperglycemia, hypoinsulinemia, and dyslipidemia in rats [24]. The intake of persimmon leaf extract would be useful for lowering blood pressure in subjects with high normal blood pressure and stage I hypertension and have no safety concern for long terminal take [25].

The present investigation aims at appraising the chemical, technological and biological profile of mulberry and persimmon leaves powder and their aqueous extract with reference to prospective bioactive components and at exploring their functionality and potential applications in the stability of sunflower oil (SFO) and disease prevention.

Materials and Methods

Materials

Fresh mulberry and persimmon leaves was obtained from the Egyptian garden`s. Cairo and Al-Mansoura, Egypt. Sunflower oil (SFO) (Refined and free from artificial antioxidants), Butylated hydroxyl toluene (BHT) as a synthetic antioxidant (of purity 99.9 %), and 2,2-diphenyl-1-picrylhydrazyl (DPPH) were purchased from Arma for food industry Co., 10th of Ramadan, Naarden International Company and Sigma-Aldrich, Germany respectively. Quercetin, Folin-Ciocalteu reagent, iron (III) chloride and aluminum chloride were purchased from Sigma (St. Louis, MO, USA). All other used chemicals were analytical grade.

All biochemical kites [glucose, triglycerides (TG), total cholesterol (TC), high density lipoprotein (HDL), low density lipoprotein (LDL), very low density lipoprotein (VLDL), serum transaminases (ALT and AST), creatinine and urea] were purchased from Linear Chemicals, S.L.U., Barcelona, Spain and radioimmunoassay (RIA) kits [thiroxine (T_4: Cat. No. MG13081 and triiodothironine (T_3: Cat. No. MG13091] IBL, Hamburg, Germany.

Methods

Preparing of mulberry and persimmon leaves tea

Mulberry and persimmon leaves tea were prepared using the aqueous extract technique [26].

Chemical composition of mulberry and persimmon leaves

Moisture, ash, crude protein and crude fat were determined according to the AOAC official methods of analysis [27]. Carbohydrates were determined by difference. Iron, calcium, potassium, sodium and phosphorus were determined according to the previously reported techniques [28] and [27]. Fiber fractions (cellulose, hemi cellulose and lignin) were determined according to the USA-ARS Agricultural Handbook [29].

Determination of total phenolic (TPC) and total flavonoid content (TFC)

Total phenolic content of the extracts of both irradiated and non-irradiated mulberry and persimmon leaves. was determined using the Folin–Ciocalteu micro-method **[30]**. The total flavonoid content (TFC) of the extracts of both irradiated and non-irradiated mulberry and persimmon leaves. was determined using the aluminum chloride ($AlCl_3$) method according to a reliable approach using quercetin as the standard [31, 32].

Antioxidant Activity

Extraction of antioxidants from mulberry and persimmon leaves

Fresh mulberry and persimmon leaves were cleaned and dried in an oven at 50°C (overnight), ground and passed through 60 mesh. A weighed portion (20 g) was taken for extraction in a conical flask. 100 mL each of methanol and water were added and kept in a mechanical shaker for 2 h. It was filtered with Whatman No. 1 filter paper and the residue was again extracted under the same conditions and the filtrates were combined. The methanolic and water extract was concentrated using a rotary evaporator (Buchilaboritoriums-Technik, Flawil/Schweiz, Switzerland) by evaporating at 40°C and 60°C [26], respectively. The dried sample of each extract was weighed to determine the yield of soluble constituents and stored at 4°C until use.

Free radical scavenging activity (DPPH• test)

The DPPH method of **[33]** was used with some modifications. The stock reagent solution ($1x\ 10^{-3}$mol/ L) was prepared by dissolving 22 mg of DPPH in 50 ml of methanol and stored at –20°C until use. Mulberry and persimmon leaves extract (200 and 400 ppm for each) and synthetic antioxidant Butylated Hydroxy Toluene (BHT) solution (200 ppm) (0.1ml of each) were vortexes for 30 s with 3.9 ml of DPPH• solution and left to react for 30 min, after which the absorbance at 517 nm was recorded. A control with no added extract was also analyzed. The results were expressed as a percentage DPPH• radical scavenging activity of a sample and were calculated according to the following equation:

$$\text{DPPH}\bullet\ \text{radical scavenging activity}\ (\%) = \frac{Abs\ control - Abs\ sample}{Abs\ control}\ x\ 100$$

Where, ***Abs control*****=**the absorbance of DPPH• radical + methanol, ***Abs sample*** **=** theabsorbance of DPPH• radical + samples.

The analyses were done in triplicates and the concentration of extract proportional to a 50% inhibition of DPPH• radical (IC_{50}) was obtained through the analysis of the extract solution concentration versus inhibition percentage graphic. Thus, lower extract concentrations (µg / ml, ppm) mean greater antioxidant capacity.

Irradiation treatment

Fine powder of mulberry and persimmon leaves were gamma irradiated at doses of 1.5, 3, and 4.5 kGy using an experimental ^{60}Co Gamma chamber (dose rate 665.6 Gy/h), Cyclotron Project, Nuclear Research Center, Atomic Energy Authority, Egypt.

Oxidative stability of leaves extracts

The following concentrations were used for the addition of leaves extracts: SFO without antioxidants (control oil), SFO + 200 ppm of BHT, SFO + 200 and 400 ppm non-irradiated (0 kGy) Mulberry, SFO + 200 and 400 ppm irradiated (1.5 kGy) Mulberry, SFO + 200 and 400 ppm irradiated (3 kGy) Mulberry, SFO + 200 and 400 ppm irradiated (4.5 kGy) Mulberry, SFO + 200 and 400 ppm non-irradiated (0 kGy) persimmon, SFO + 200 and 400 ppm irradiated (1.5kGy) persimmon, SFO + 200 and 400 ppm irradiated (3kGy) persimmon and SFO + 200 and 400 ppm irradiated (4.5kGy) persimmon.

Oxidative stability of sunflower oil

The oxidative stability of sunflower oil (free from artificial antioxidants) as affected by the addition of the different studied extractions or BHT was determined using A Metrohm Rancimat model 679 (Herisau, Switzerland) [34]. The antioxidant activity and increasing and/or decreasing activity were calculated as follow:

$$\text{Antioxidant Activity} = \frac{Induction\ period\ of\ sample}{Induction\ period\ of\ control}$$

$$\text{Increasing and/or decresing}\ (\%) = \frac{Induction\ period\ of\ sample - Induction\ period\ of\ contol}{Induction\ period\ of\ control}\ x\ 100$$

Sensory evaluation mulberry leaves and persimmon leaves tea

A panel of 10 judges from the staff of Food Science Department Ain Shams University was asked to evaluate the prepared tea from dried mulberry leaves and persimmon leaves for their color, appearance, clarity, flavor, viscosity and overall acceptability giving numerical scores to each of these attributes from 10, using a report sheet referred to in a previous study [35].

Experimental design for biological evaluations

A total of 90 male albino rats with an average weight of (130:140g) were purchased from the animal lab of the Research Institute of Ophthalmology, Giza, Egypt. All rats were housed in individual cages in standard conditions [36]. The rats were divided into four groups and treated as follows: Group (I): a normal group, Group (II): a normal group treated with 6% mulberry, 6% persimmon and 3% mulberry + 3% persimmon, Group (III): a diabetic group and Group (IV): a diabetic treated with 6% mulberry, 6% persimmon and 3% mulberry + 3% persimmon, five rats for each group. Furthermore, each of groups (II) and (IV) is included two sub-group, one of them treated with standard feed (basal diet) mixed with plant powder and other one treated orally gavaged twice a week with plant aqueous extract besides standard feed. The experimental design was performed in accordance with the guide for the care and use of laboratory animals, as adopted and promulgated by the "Institutional Animal Care Committee".

Induction of diabetes in rats

Groups (III) and (IV) of Diabetes were induced by a single intraperitoneal injection of 45 mg/kg body weight streptozotocin (STZ) dissolved in 0.1 M citrate buffer (pH 4.5). After 7 days of STZ injection, the tail vein blood was collected to determine fasting blood glucose level. Only rats with fasting blood glucose over 250 mg/dl were considered diabetic and included in the experiments. The STZ-treated rats were given 5% glucose water for 24 h following STZ injection, to prevent initial drug induced hypoglycemic mortality. Then, after 72 h STZ injection, blood was drawn from retro-orbital plexus of the surviving rats with heparinized capillaries and the fasting blood glucose levels were estimated according to a previously reported technique [37]. The rats with moderate diabetes having hyperglycemia i.e., with a blood glucose level of more than 250 mg/dl were regarded as experimentally induced-diabetic rats and distributed into groups (III and IV).

Blood sampling

Blood samples were taken at the end of the experiment (49 days) for biochemical analyses [38, 39].

Biochemical analysis

All biochemical analyses were determined, enzymatically colorimetric methods as follow: glucose [37], TG [40, 41], TC [40], HDL [41], ALT and AST [42], urea [43] and creatinine [44], mathematically methods as follow: LDL [45] VLDL [46], and conventional radioimmunoassay (RIA) methods for determining T_3 and T_4

Statistical analyses

All the experiments were carried out in triplicate and the mean and standard error values were calculated for all data. Then, the results were subjected to one-way analysis of variance followed by Duncan's significant differences using SAS program (version 9.1.3) software (Cary, NC). Significant levels were defined as ($P < 0.05$) [47].

Results

Chemical composition of mulberry and persimmon leaves

The chemical composition for the leaves of persimmon and mulberry are illustrated in Table (1). The results showed that the mulberry leaves had higher values of total ash, protein, sodium and potassium contents (11.6%, 23.40%, 412.7 mg/kg and 15360 mg/kg, respectively) as compared to persimmon leaves. On the other hand, the persimmon leaves had a higher content of fat, carbohydrates and iron contents (3.84%, 64.81%, and 374.3 mg/kg, respectively) as compared to mulberry leaves. Persimmon contains high amount of fiber compared to mulberry leaves.

Total phenolic and flavonoid content

Figure (1) shows the total phenolics data for different extracts from mulberry and persimmon leaves extracts. The amount of total phenolics in the extracts of both irradiated and non-irradiated mulberry and persimmon (gallic acid equivalents, GAE) expressed as mg GAE per 100 g dray material, ranged from 698 to 774 in water extract to 463 to 552 in methanol extract and ranged from

488 to 533 in water extract and from 310 to 377 in methanolic extract, respectively. Moreover, the amount of total flavonoid content in persimmon leaves extracts (water and methanolic) both irradiated and non-irradiated, was significantly ($P < 0.05$) lower than that obtained from mulberry leaves extract. Moreover, the total flavonoids of extracts obtained from irradiated and non-irradiated persimmon leaves were significantly ($P < 0.05$) higher in water extract than methanolic extract.

The obtained data indicated that the water extract of TPC and TFC were significantly ($P < 0.05$) higher than methanolic extract.

DPPH radical scavenging activity

Table (2) presented the IC_{50}, which means the concentration of extract proportional to a 50% inhibition of DPPH• radical. Low IC_{50} values indicate high radical scavenging activity. However, water extracts in both mulberry and persimmon leaves either irradiated or non-irradiated, possess to have higher scavenging activity than methanolic extract. In persimmon leaves water extract, the lowest IC_{50} at gamma irradiation dose 1.5 kGy. This means that the highest scavenging activity was at this dose (1.5 kGy) compared to other gamma doses (3 and 4.5 kGy) and non-irradiated mulberry leaves. The same observation was noted in methanolic extract were the best dose was 1.5 kGy. Meanwhile, the highest scavenging activity of mulberry water and methanolic extract was in non-irradiated samples compared to irradiated samples at all doses under investigation.

Oxidation stability of sunflower oil

Data in Table (3) show that the induction period of control sunflower oil (SFO), without artificial antioxidants is 3.06 h while, it was 4.98 h in SFO with BHT at 200 ppm commercial concentration. The data, also, show that the concentration of 200 ppm of both water and methanolic extract did not represented any significant increase in the oxidative stability compared to 200 ppm BHT. However, at a concentration of 400 ppm of extracts, the induction period of all samples either irradiated or non-irradiated have higher induction periods than the oxidative stability compared to concentration 200 ppm of both mulberry and persimmon extracts. The index in all samples increased dramatically at concentration 400 ppm. Furthermore, the irradiation doses 1.5 to 4.5 kGy in mulberry leave extract showed higher induction period, oxidative stability, antioxidant activity and increasing index compared to non-irradiated mulberry leaves.

Table (1): Proximate chemical analysis of persimmon and mulberry leaves

	Persimmon leaves	**Mulberry leaves**
Moisture (%)	8.9	8.9
Ash (%)	8.1	11.6
Fat (%)	3.84	3.03
Protein (%)	14.35	23.40
Carbohydrates* (%)	64.81	53.07
Sodium (mg⁄Kg)	341.1	412.7
Potassium (mg⁄Kg)	13520	15360
Iron (mg⁄Kg)	374.3	192
Calcium (%)	1.0	1.71
Phosphorous (%)	0.13	0.35
Tannins (%)	2.685	1.202
Lignin (%)	7.72	0.74
Cellulose (%)	12.84	12.84
Hemicellulose (%)	19.25	18.99

* Total carbohydrate was calculated by difference

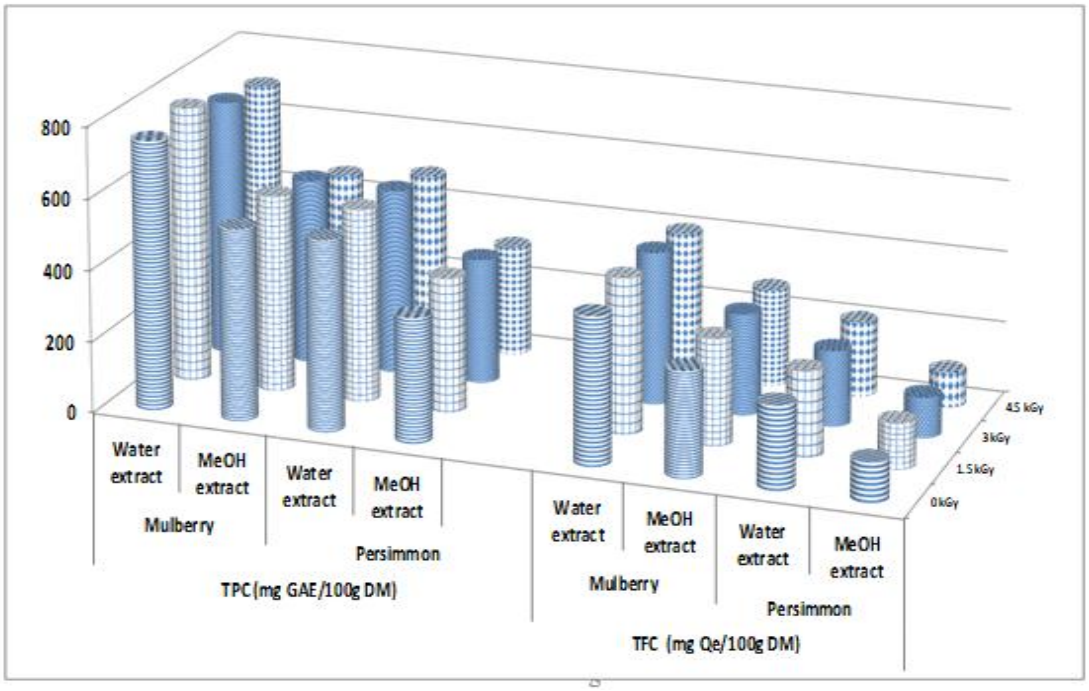

Fig. (1): Total phenolic content TPC and Total flavonoid content of irradiated and non- irradiated mulberry and persimmon leaves extract

Table (2): Radical scavenging activity of mulberry and persimmon extracts

	Irradiation Treatment	Solvent Extraction	DPPH IC_{50} (µg/ml)
persimmon powder	0 kGy	Water	157.97^{d,e}
	1.5 kGy		150.00^{c}
	3 kGy		170.74^{f}
	4.5 kGy		175.06^{f}
	0 kGy	Methanol	182.74^{g}
	1.5 kGy		171.52^{f}
	3 kGy		198.92^{i}
	4.5 kGy		201.75^{i}
Mulberry powder	0 kGy	Water	131.84^{a}
	1.5 kGy		150.33^{c}
	3 kGy		154.58^{c,d}
	4.5 kGy		188.64^{h}
	0 kGy	Methanol	140.50^{h}
	1.5 kGy		150.00^{c}
	3 kGy		161.03^{e}
	4.5 kGy		174.06^{f}

Each value represents the mean, the mean value with different superscript alphabets in the column indicate significant differences ((P<0.05)) using Duncan test

Table (3): Effect of mulberry and persimmon extracts on oxidative stability of sunflower

		Induction Period / h		Antioxidant Activity		Increasing Index %	
SFO* (Control)		**3.06**					
SFO +BHT (200 ppm)		**4.98**					
	γ-irradiation	**200 ppm**	**400 ppm**	**200 ppm**	**400 ppm**	**200 ppm**	**400 ppm**
Mulberry extract	**0.0 kGy+ SFO**	3.08	4.28	1.00	1.40	+ 0.65	+ 39.87
	1.5 kGy+ SFO	3.15	4.35	1.03	1.42	+ 2.94	+ 42.16
	3.0 kGy+ SFO	3.22	4.62	1.05	1.51	+ 5.23	+ 50.98
	4.5 kGy+ SFO	3.27	4.57	1.07	1.49	+ 6.86	+ 49.35
Persimmon extract	**0.0 kGy+ SFO**	3.25	4.51	1.06	1.47	+ 6.21	+ 47.39
	1.5 kGy+ SFO	3.18	4.39	1.04	1.43	+ 3.92	+ 43.46
	3.0 kGy+ SFO	3.25	4.58	1.06	1.50	+ 6.21	+49.67
	4.5 kGy+ SFO	2.97	3.95	0.97	1.29	- 2.94	+ 29.08

***** Sunflower oil

Sensory evaluation of herbal mulberry and persimmon tea leaves

Table (4) shows the effect of different concentrations of persimmon, mulberry and its blends on the color, appearance, clarity, flavor, viscosity and over all acceptability scores of its tea leaves. There was a statistical significance ($P < 0.05$) between the different treatments. Increasing the concentration of persimmon or mulberry tea leaves up to 6% caused an increase in color, appearance, flavor, viscosity, and overall acceptability scores, then decreased at 7%. However, increasing the concentration of persimmon or mulberry tea leaves led to a decrease in Clarity scores. The blends of persimmon and mulberry leaves at ratio (3:3) were the best treatment and improve color, appearance, clarity, flavor, and viscosity (8.4, 8.0, 8.6, 7.6, and 8.6, respectively) and overall acceptability (8.8) of its tea leaves.

Effect of mulberry and persimmon herbal extract on fasting glucose level and thyroid hormones

Table (5) reveals the long-term anti-hyperglycemic effect of mulberry and persimmon. A single intravenous injection of STZ induced an increase of fasting blood glucose levels significantly ($P < 0.05$) to 358.97 mg/dl at the end of the experiment compared to the normal control (84.24 mg/dl) and all other groups. As shown in the normal treated Group (G II), normal 6% mulberry powder as well as normal 6% persimmon powder showed a significant decrease ($P < 0.05$) in blood glucose levels, 80 mg/dl and 86.61 mg/dl, respectively compared to both diabetic control Group (G III) and diabetic treated Group (G IV).

The oral administration from the herbal extract of normal treated Group (G II) 6% mulberry, 6% persimmon and their combination at level 3% represented a significant decrease ($P<0.05$) by 76.92%, 77.84% and 76.53%, respectively in blood glucose level compared to diabetic control.

Group IV, which represents diabetic treated group, clearly showed significant decreases ($P<0.05$) in both herbal powder and herbal extract by 73.24%, 68.42% and 71.06% respectively in herbal powder and 72.51%, 71.65% and 73.50%, respectively in herbal extract, compared to diabetic control. Moreover, normal treated (Group II) represents a significant decrease ($P<0.05$) compared to diabetic treated (Group IV). According to the present data, it could be summarized that Mulberry, Persimmon and their mixture illustrated glucose-lowering effect.

Thyroid hormones thyroxine (T_4) and triiodothyronine (T_3) are tabulated in Table (6). The present data showed that the T_3 and T_4 hormones were significantly decreased ($P<0.05$) in diabetic control (51.56 and 3.08, ng/dl) compared

to normal group (85.86 and 5.63ng/dl). As mentioned before in Table (5), where the serum fasting glucose level was elevated up to 358.97 mg/dl diabetic control. Thus, the higher the level of fasting serum glucose occurs, the lower the thyroid hormones are founded. Moreover, there were no significant differences ($P<0.05$) in T_3 and T_4 hormones within the normal treated group compared to the control group. On the contrary, diabetic treated group represented significant differences in T_3 and T_4 hormones compared to diabetic control except for persimmon leaves, either powder or extract, that showed insignificant differences. Thus, the treatment by the administration of mulberry and the mix of mulberry and persimmon, either powder or extract, proved that these herbal treatments have caused hypoglycemic effect in diabetic rats that led to increase the T_3 and T_4 hormones.

Table (4): Sensory Evaluation of persimmon and mulberry and their blends tea leaves
The mean value with different superscript alphabets in the same row under each plant tea leaves indicate significant differences ($P<0.05$) using Duncan test

	Persimmon (P) tea leaves (6 %)							Mulberry (M) tea leaves (6 %)							Persimmon : Mulberry Blends (3 : 3, %)
	1	2	3	4	5	6	7	1	2	3	4	5	6	7	
Color	5.0^{f}	5.8^{ef}	6.0^{ef}	7.4^{bc}	7.4^{bc}	8.0^{ab}	5.0^{f}	6.4^{de}	6.2^{de}	5.8^{ef}	5.4^{ef}	7.0^{cd}	7.6^{abc}	6.0^{ef}	8.4^{a}
Appearance	5.4^{e}	6.0^{de}	6.2^{cde}	6.4^{cde}	7.2^{abc}	7.6^{ab}	5.6^{e}	7.2^{abc}	6.0^{de}	6.4^{cde}	6.4^{cde}	7.0^{bcd}	8.2^{a}	6.0^{de}	8.0^{ab}
Clarity	8.0^{abc}	7.6^{bcd}	8.0^{abc}	8.0^{abc}	7.2^{cd}	6.0^{f}	5.4^{f}	7.6^{bcd}	8.2^{ab}	7.6^{bcd}	7.0^{fe}	7.2^{cd}	7.2^{cd}	6.2^{ef}	8.6^{a}
Flavor	4.8^{e}	7.2^{abc}	7.2^{abc}	6.8^{abcd}	7.0^{abc}	6.8^{abcd}	7.0^{abc}	5.6^{de}	6.0^{cde}	6.0^{cde}	6.0^{cde}	7.6^{ab}	8.0^{a}	6.6^{bcd}	7.6^{ab}
Viscosity	5.4^{e}	6.2^{e}	5.6^{e}	7.4^{bc}	6.0^{e}	8.0^{abc}	8.2^{ab}	5.4^{e}	6.0^{e}	6.2^{e}	6.4^{de}	7.2^{cd}	8.2^{ab}	7.2^{cd}	8.6^{a}
Overall acceptability	5.0^{f}	6.2^{de}	5.6^{ef}	6.8^{cd}	7.4^{bc}	8.0^{ab}	5.0^{f}	5.2^{f}	5.4^{ef}	5.2^{f}	6.8^{cd}	7.4^{bc}	8.2^{ab}	5.2^{f}	8.8^{a}

Table (5): Effect of mulberry and persimmon leaf administration on fasting blood glucose in chronic diabetic rats

	Glucose (mg/dl)	
	Herbal Powder	**Herbal Extract**
Normal (Group I)	$84.24^{abc} \pm 3.80$	
Normal Treated (Group II)		
Normal (6% Mull.)	$80.00^{a} \pm 3.82$	$82.83^{ab} \pm 4.03$
Normal (6% Pers.)	$86.61^{abcd} \pm 4.30$	$79.54^{a} \pm 3.94$
Normal (3%Mull. + 3%Pers.)	$83.62^{abc} \pm 4.19$	$84.22^{abc} \pm 4.05$
Diabetic (Group III)	$358.97^{g} \pm 4.02$	
Diabetic Treated (Group IV)		
Diabetic (6% Mull.)	$96.41^{cde} \pm 4.08$	$98.66^{de} \pm 4.25$
Diabetic (6% Pers.)	$113.36^{f} \pm 4.91$	$101.74^{ef} \pm 3.60$
Diabetic (3%Mull. + 3%Pers.)	$103.87^{ef} \pm 3.73$	$95.10^{bcde} \pm 3.76$

Each value represents the mean ± Standard Error (S.E.), The mean value with different superscript alphabets indicate significant differences (P<0.05) using Duncan test

Table (6): Effect of mulberry and persimmon leaf administration on thyroid hormones in chronic diabetic rats

Each value represents the mean ± Standard Error (S.E.), The mean value with different superscript alphabets under the same

			Normal treated				Diabetic treated		
		Normal	Normal Mulberry 6%	Normal Persimmon 6%	Normal (Mulberry 3% + Persimmon 3%)	Diabetic	Diabetic Mulberry 6%	Diabetic Persimmon 6%	Diabetic (Mulberry 3% + Persimmon 3%)
Triiodothyronine (T_3) (ng/dl)	powder	$85.86^{g} \pm 1.35$	$89.25^{ef} \pm 1.39$	$93.02^{ef} \pm 2.80$	$92.23^{ef} \pm 2.37$	$51.56^{a} \pm 1.06$	$58.20^{b} \pm 3.99$	$61.76^{bc} \pm 2.44$	$71.28^{d} \pm 2.28$
	extract		$89.37^{ef} \pm 1.40$	$93.94^{f} \pm 2.43$	$96.37^{f} \pm 2.29$		$64.51^{cd} \pm 1.82$	$63.53^{bc} \pm 3.04$	$65.64^{cd} \pm 2.22$
Thyroxine (T_4) (ng/dl)	powder	$5.63^{g} \pm 0.11$	$5.33^{g} \pm 0.15$	$4.95^{f} \pm 0.08$	$4.77^{def} \pm 0.11$	$3.08^{b} \pm 0.06$	$3.71^{c} \pm 0.15$	$3.10^{b} \pm 0.05$	$4.48^{d} \pm 0.11$
	extract		$4.60^{de} \pm 0.15$	$4.83^{ef} \pm 0.05$	$4.87^{ef} \pm 0.04$		$3.68^{c} \pm 0.14$	$3.18^{b} \pm 0.03$	$3.94^{c} \pm 0.11$

measurement indicate significant differences (P<0.05) using Duncan test.

Effect of mulberry and persimmon on plasma lipid profiles

Effects of mulberry and persimmon herbal powder and aqueous extract on plasma lipid profile are tabulated in Table (7), where, triglyceride (TG) and total cholesterol (TC) levels in the diabetic group (G III) were significantly increased(P<0.05) compared to those of the normal control group (G I), the normal treated group (G II) and the diabetic treated group (G IV). High density lipoprotein (HDL) level (56.46 mg/dl) is decreased, but not significantly in diabetic control (G III) compared to all groups in our experimental study. However, very low density lipoprotein (VLDL) did not show any differences in diabetic control compared to all other groups.

Oxidation of low-density lipoprotein (LDL) has been implicated in the development of atherosclerosis and cardiovascular diseases (CVD). Therefore, the normal treated group (G II) and the diabetic treated group (G IV) as well as the normal control group (G I) represented significant decreases(P<0.05) compared to the diabetic control (G III). Furthermore, normal treated 3% mulberry + 3% persimmon in herbal extract (23.93 mg/dl) showed a significant decrease (P<0.05) compared to normal control (34.77 mg/dl) and other sub-treated normal group (6% mulberry and 6% persimmon) in both powder or herbal extract.

Hepatic and renal functions of administration mulberry and persimmon

Table (8) indicated that hepatic and renal functions as results of administration of mulberry and persimmon and their mix in diabetic rats. Both aspartate aminotransferase (AST) and alanine aminotransferase (ALT) showed a significant increase (P<0.05) in control diabetic groups (GIII) compared to all other groups. Meanwhile, there are no significant differences (P<0.05) in-between all other groups (GI, GII and GIV). On the other hand, renal functions showed no significant differences among the normal control, the normal treated and the diabetic treated, expect for diabetic control which showed significantly (P<0.05) increases. The effect on serum urea and creatinine levels is shown in Table (8). Herbal mulberry, persimmon and their mixing, either powder or extract, showed no effect on serum creatinine levels of normal control, normal treated and diabetic treated rats as measured at the end of 7 weeks while, significant differences (P<0.05) were obtained between all groups compared to diabetic control. On the other hand, the elevated plasma urea level of diabetic rats was significantly (P<0.05) countered by herbal administration.

The results of the hematological data (Figure 2) showed that no significant differences appeared in hematology tests (hemoglobin, R.B.Cs., W.B.Cs. and platelets) between the control groups and the groups that had herbal extracts of both mulberry and persimmon.

Discussion

Dietary fiber, known as non-starchy polysaccharides, plays a very important role in stimulating the digestive system and improving its function. Therefore, extracting such rich fiber increases the nutritional importance of the tea produced from persimmon and mulberry leaves, which contain large amount of lignin, tannin, cellulose and hemicellulose [48]. The results showed that the persimmon and mulberry leaves contain a high amount of different nutrient elements.

Phenolic compounds are plant metabolites characterized by the presence of several phenol groups. Some of them are very reactive in neutralizing free radicals by donating a hydrogen atom or an electron, chelating metal ions in aqueous solutions [49].

Table (7): Effect of mulberry and persimmon leaf administration on lipid profile in chronic diabetic rats

			Normal treated (GII)				Diabetic treated (G IV)		
		Normal (G I)	Normal Mulberry 6%	Normal Persimmon 6%	Normal (Mulberry 3% + Persimmon 3%)	Diabetic (G III)	Diabetic Mulberry 6%	Diabetic Persimmon 6%	Diabetic (Mulberry 3% + Persimmon 3%)
TG (mg/dl)	powder	$100.78^{a} \pm 2.86$	$101.89^{a} \pm 3.16$	$102.67^{a} \pm 2.68$	$99.06^{a} \pm 1.83$	$121.47^{b} \pm 3.75$	$102.27^{a} \pm 2.93$	$101.88^{a} \pm 3.07$	$97.33^{a} \pm 3.27$
	extract		$98.92^{a} \pm 2.22$	$102.86^{a} \pm 3.44$	$101.93^{a} \pm 3.78$		$96.39^{a} \pm 3.24$	$95.57^{a} \pm 2.69$	$94.97^{a} \pm 2.91$
TC (mg/dl)	powder	$123.78^{bcdef} \pm 1.19$	$121.02^{abcd} \pm 3.06$	$123.22^{bcde} \pm 2.11$	$118.94^{abc} \pm 2.14$	$151.38^{h} \pm 3.36$	$125.49^{cdef} \pm 0.57$	$131.88^{fg} \pm 1.61$	$114.52^{a} \pm 1.29$
	extract		$134.14^{g} \pm 3.01$	$128.79^{defg} \pm 2.90$	$116.64^{ab} \pm 3.08$		$129.73^{efg} \pm 0.70$	$127.85^{defg} \pm 0.97$	$121.04^{abcd} \pm 0.81$
HDL (mg/dl)	powder	$67.92^{abc} \pm 3.38$	$63.68^{abc} \pm 3.86$	$66.23^{abc} \pm 3.74$	$70.39^{bc} \pm 3.24$	$56.46^{a} \pm 3.24$	$62.64^{abc} \pm 3.88$	$63.80^{abc} \pm 3.77$	$60.83^{ab} \pm 4.00$
	extract		$72.45^{bc} \pm 2.52$	$70.01^{bc} \pm 3.86$	$72.94^{c} \pm 3.85$		$62.44^{abc} \pm 3.24$	$63.64^{abc} \pm 3.31$	$61.73^{abc} \pm 2.75$
LDL (mg/dl)	powder	$34.77^{bc} \pm 1.66$	$36.95^{cd} \pm 1.64$	$36.84^{cd} \pm 1.73$	$28.93^{ab} \pm 1.29$	$70.64^{f} \pm 3.26$	$42.38^{ce} \pm 3.68$	$47.32^{e} \pm 3.25$	$34.48^{bc} \pm 2.00$
	extract		$41.18^{cde} \pm 2.75$	$38.69^{cd} \pm 2.32$	$23.93^{a} \pm 1.20$		$47.28^{e} \pm 2.53$	$44.63^{de} \pm 2.47$	$40.91^{cde} \pm 3.09$
VLDL (mg/dl)	powder	$20.89^{a} \pm 1.08$	$20.51^{a} \pm 0.99$	$20.73^{a} \pm 1.37$	$19.85^{a} \pm 1.40$	$24.26^{a} \pm 1.35$	$20.78^{a} \pm 2.62$	$20.97^{a} \pm 2.96$	$19.46^{a} \pm 1.40$
	extract		$19.77^{a} \pm 1.23$	$20.82^{a} \pm 1.16$	$20.47^{a} \pm 0.87$		$19.68^{a} \pm 1.93$	$19.94^{a} \pm 1.89$	$18.71^{a} \pm 1.67$

Each value represents the mean ± Standard Error (S.E.), The mean value with different superscript alphabets under the same measurement indicate significant differences (P<0.05) using Duncan test

Table (8): Effect of mulberry and persimmon leaf administration on hepatic and renal functions in diabetic rats

			Normal treated (G II)				Diabetic treated (G IV)		
		Normal (G I)	Normal Mulberry 6%	Normal Persimmon 6%	Normal (Mulberry 3% + Persimmon 3%)	Diabetic (G III)	Diabetic Mulberry 6%	Diabetic Persimmon 6%	Diabetic (Mulberry 3% + Persimmon 3%)
AST (U/L)	powder	$42.62^{a} \pm 3.71$	$45.09^{a} \pm 4.03$	$49.96^{a} \pm 4.41$	$45.55^{a} \pm 4.01$	$69.90^{b} \pm 4.46$	$43.58^{a} \pm 3.65$	$45.92^{a} \pm 3.72$	$43.11^{a} \pm 4.32$
	extract		$44.61^{a} \pm 4.00$	$48.83^{a} \pm 4.14$	$48.59^{a} \pm 4.03$		$45.07^{a} \pm 3.86$	$46.50^{a} \pm 3.29$	$46.38^{a} \pm 4.01$
ALT (U/L)	powder	$27.46^{abc} \pm 3.81$	$29.56^{abcd} \pm 4.36$	$27.01^{ab} \pm 3.96$	$25.06^{a} \pm 2.53$	$52.49^{f} \pm 4.21$	$42.59^{ef} \pm 3.71$	$35.98^{abcde} \pm 3.70$	$38.29^{bcde} \pm 3.98$
	extract		$27.41^{abc} \pm 3.49$	$25.08^{a} \pm 4.04$	$27.48^{abc} \pm 2.90$		$40.30^{de} \pm 3.53$	$40.25^{de} \pm 3.72$	$39.44^{cde} \pm 4.07$
Creatinine (mg/dl)	powder	$1.28^{a} \pm 0.14$	$1.27^{a} \pm 0.11$	$1.29^{a} \pm 0.27$	$1.27^{a} \pm 0.23$	$2.95^{b} \pm 0.29$	$1.62^{a} \pm 0.27$	$1.55^{a} \pm 0.16$	$1.44^{a} \pm 0.17$
	extract		$1.27^{a} \pm 0.22$	$1.24^{a} \pm 0.28$	$1.26^{a} \pm 0.14$		$1.77^{a} \pm 0.27$	$1.61^{a} \pm 0.30$	$1.60^{a} \pm 0.23$
Urea (mg/dl)	powder	$30.53^{ab} \pm 0.59$	$31.47^{abcd} \pm 0.82$	$30.55^{ab} \pm 0.88$	$28.52^{a} \pm 0.84$	$35.91^{e} \pm 1.03$	$34.64^{cde} \pm 1.54$	$34.72^{de} \pm 0.54$	$32.77^{bcde} \pm 1.20$
	extract		$31.34^{abcd} \pm 1.04$	$30.98^{abc} \pm 0.87$	$33.53^{bcde} \pm 1.38$		$33.65^{bcde} \pm 1.25$	$33.28^{bcde} \pm 1.44$	$36.36^{e} \pm 1.63$

Each value represents the mean ± Standard Error (S.E.), The mean value with different superscript alphabets under the same measurement indicate significant differences (P<0.05) using Duncan test

Besides, the phenolic compounds possess multiple biological properties such as antitumor, antimutagenic and antibacterial properties, and these activities might be related to their antioxidant activity [50].

Persimmon leaves contain four flavonols [51]. The leaves of persimmon have been reported to contain the following compounds: 40-dihydroxy-a-truxillic acid, tatarine C, myricetin, annulatin, trifolin, astragalin, hyperin, isoquercetin, rutin, quercetin, kampferol, kakispyrone, and kaki saponin [52]. The leaves have been used for tea in Korea, since they were was thought to be effective against hypertension [15]. Persimmon leaves and extracts are being used as a green tea, oriental medicines, deodorants, antiallergic substrates, and cosmetics (especially for dermatitis) as they prevent skin problems and have an antiwrinkle effect [53, 15]. Persimmon leaves have been used as a sushi ingredient [54]. Thus, most of literature reviews stated that persimmon leaves are a good source of antioxidants [55]. Because flavonoids are responsible for antioxidant activity, the high amount of total flavonoids in the extract suggests that the extract possesses an antioxidant activity in vitro [56].

Various solvent extracts from mulberry leaves showed varying degrees of antioxidant activity in different test systems in a dose-dependent manner. The antioxidant activity was correlated with the amount of total phenolics presented in the respective extracts in each assay. Methanol proved to be the most efficient solvent for extraction of antioxidants from mulberry leaves as the related extract contained the highest amount of phenolic compounds and also exhibited the strongest antioxidant capacity in all the assays used [57].

Flavonoids are very important constituents of plants because of the scavenging ability conferred by their hydroxyl groups. Flavonoids are very important constituents of plants because of the scavenging ability conferred by their hydroxyl groups. The flavonoids may contribute directly to anti-oxidative action. It is known that polyphenolic compounds have inhibitory effects on mutagenesis and carcinogenesis in humans when up to 1 g daily is consumed from a diet rich in fruits and vegetables [58]. Flavonoid compounds from plants are known to be good natural antioxidants. However, the activity of synthetic antioxidants was often observed to be higher than that of the natural antioxidants [59]. Flavonoid compounds at certain concentrations markedly slowed down the rate of conjugated diene formation. The interest in phenolics is increasing in the food industry because of their ability to retard oxidative degradation of lipids, thereby improving the quality and nutritional value of foods [60].

The present study revealed that water extract of TFC and TPC are higher than the methanolic extract. These data are in the same trend with Thabti et al. [61] who found that the importance of TPC and TFC were obtained with water extract derived from Morus leaf portions. In addition, Sun et al. [62] found that total flavonoids from persimmon leaves possess a good water-soluble. On the contrary, the present results are different from other authors' who reported that methanol was found to be the most effective solvent in extraction of total phenolics from *Morus indica* leaves compared to acetone and water [57]. Hertog et al. [63] and Yen et al. [64] stated that methanol is a widely used and effective solvent for extraction of antioxidants.

The ability of the total flavonoid persimmon leaves (TFPL) extracts to quench hydroxyl radicals seems to be directly related to the prevention of propagation of lipid peroxidation, because TFPL seems to be a good scavenger of active oxygen species. It will, thus, reduce the rate of the chain reaction [65]. This result may be attributed to the combined effects of reducing power, the donation of hydrogen atoms and the scavenging of active oxygen. Hagerman et al. [66] have also explained that high molecular weight and the proximity of many aromatic rings and hydroxyl groups are more important for the free radical scavenging activity of phenolics than the specific functional groups.

DPPH radical scavenging activity of persimmon leaves are higher than those investigate in recent literature [67] and the Spanish Mediterranean diet [68]. Therefore, they mixed to fully utilize. The consumer in the sensory evaluation, as explained previously accepted the mixing ratio 3: 3. The antioxidant activity of persimmon and mulberry leaves may be due to its content of phenolic acids and flavonoids as indicated by many previous researches, also the results showed that of the superiority of persimmon on mulberry leaves in the value of this activity [69].

The utilization of persimmon, mulberry and its blends leaves, as tea in a ready-to-drink packaging is one of the innovations to get the benefits in

terms of health as well as to fulfill consumers need in practical mode consumption. The results of the panelist's preference test on the taste of the persimmon, mulberry and its blends tea leaves showed that the majority of consumers likes the taste of the tea at 6%. "The color of bright food provides more appeal to consumers". The blends of persimmon and mulberry tealeaves at ratio (3: 3) were the best treatment and improved the sensory parameters. The product mix is everything that can be offered in the market to get customer attention, demand, usage or consumption that can fulfill the customer desire or need. The product mix is also an important factor that influences customer preferences on a certain product. The results showed that the compounds extraction mainly causes decreasing clarity in the prepared tea with increasing the concentration.

In fresh persimmon leaves most of the polyphenols are found to be water soluble. The chief components in persimmon leaf tea are unique proanthocyanidin oligomers and oral administration of this tea along with starch resulted in a dose-dependent decline in the blood glucose level in Wistar rats [13].

The present results showed that long-term daily administration of both powder and aqueous extract of mulberry and persimmon leaves significantly decreased fasting blood glucose levels in STZ-induced diabetic rats. The intraperitoneal injection of STZ at doses of 45 mg/kg into rats damages the pancreas, and insulin levels typically fall to 10–30% of normal levels leading to hyperglycemia [70]. Up to different hypotheses of ability of mulberry induced lowering fasting blood glucose level in diabetic rats, Singab et al. [71] suggested that the lowering blood glucose level is probably due to stimulation of insulin release while, Hansawasdi et al. [72] mentioned that the lowering activity is due to intestinal glucosidase inhibitory activity of the known mulberry-leaf component 1-deoxynojirimycin (DNJ-1) a kind of azasugar, was first isolated from its roots by Yagi et al. [73] in 1976. DNJ is a glucose analogue with a secondary amine group instead of an oxygen atom in the pyranose ring of glucose.DNJ-1potently inhibits α-glucosidase in the small intestine by binding to the active center of α-glucosidase [74].

Furthermore, DNJ-1, a well-known active ingredient in mulberry water extract, affects the final step of carbohydrate digestion in the intestinal lumen and retards the absorption of dietary carbohydrates to suppress postprandial hyperglycemia [75, 76]. So, several studies proved that mulberry administration were effective in controlling systematic blood glucose in addition postprandial glucose levels [77, 78]. Another postulated explanation illustrated by Kim et al. [79] is in spite the DNJ-1 content in mulberry leaves water extract might inhibit sucrase activity in the high sucrose diet, the inhibitory activity could be slight due to low absorption of DNJ-1.

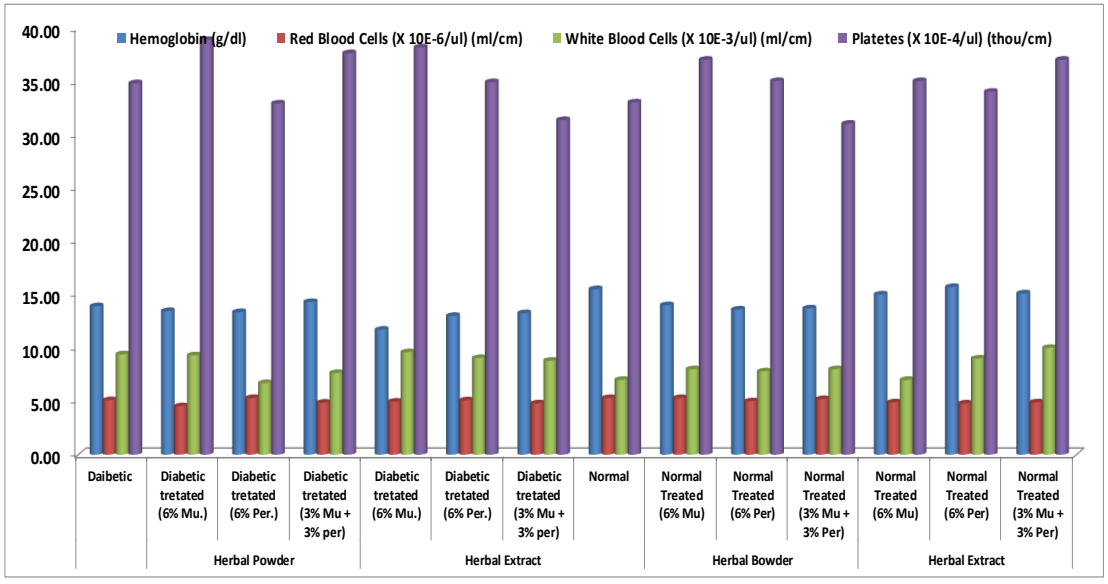

Fig. (2): Complete blood count (CBC) of the administration of either, mulberry, persimmon and their mix leaves, powder or extract

A pervious study showed that mulberry leave ethanolic extract contains several important polyphenolic compounds including DNJ-1 and resveratrol [14]. Moreover, [80] mentioned that resveratrol improved insulin resistance by promoting Heme Oxygenase-1 (HO^{-1}) protein through mediating Nuclear factor erythroid 2-related factor 2 (NrF2) level in HepG2 cell.

On the other hand, owing to rich phytochemicals of persimmon leaves, it could contribute as traditional treatment of hypertension in patients with type 2 diabetes mellitus as well as prevention and cure to diabetes mellitus [15, 19, 81]. Type 2 diabetes mellitus is a heterogeneous metabolic disorder characterized by the impaired insulin secretion from the pancreatic beta cells and the insulin resistance in the peripheral tissues such as liver, adipose tissue, and skeletal muscle [82]. The present data are in agreement with Lee et al.[83] who postulated that persimmon leaves affect the insulin-stimulated muscular glucose transport therefore, it could be used as insulin sensitizers for the treatment of diabetes. However, the inhibition of pancreas alpha-amylase [84, 19] and α-glucosidase [85] could be one of major mechanisms responsible for the antidiabetic role of persimmon. So, the antidiabetic effects are dependent on degree of polymerization of bioactive components of persimmon. Therefore, inhibition of α-glucosidase and/or α-amylase by persimmon leaves extract may prolong overall digestion time, causing a delay in glucose absorption, consequently reducing the rapid increase of postprandial blood glucose.

The hypoglycemic effect of both mulberry and persimmon leaves tea, are in agreement with Andallu et al.[86] andNaowaboot et al. [87] who found that mulberry extract has an anti-hyperglycemia effect while, Lee et al.[83] found that persimmon ethanolic extract has been used as insulin-sensitizers for the treatment of diabetes.

Similarly, Matsuno et al.[88] observed that kaki-tannin found in persimmon fruit flesh and leaves was soluble in artificial stomach liquid and reduced blood alcohol (40%) and acetaldehyde contents (30%). Dietary intake of persimmon tannin was found to prevent hypercholesterolemia in some animal models and humans [89].

In conclusion, the present study revealed that the mixing of 3% mulberry and 3% persimmon leaves in the diabetic rata diet could be control the blood glucose levels according to, - stimulation of insulin release - inhibition of intestinal α-glucosidase - inhibition of pancreas alpha-amylase - inhibition of small intestinal sucrase enzyme - improved insulin resistance by resveratrol.

Thyroid gland plays a central role in the regulation of metabolism. So, abnormal thyroid function can have a major impact on the control of diabetes. Besides, untreated thyroid disorder can increase the risk of certain diabetic complications and can aggravate many diabetes symptoms. The effect of the thyroid hormones(T3 and T4) on metabolism and the major organ systems of the human body appears in stimulating the enzymes concerned with glucose oxidation and enhancing the rate of uptake of glucose, affecting synthesis, mobilization and degradation of lipids, and lowering blood cholesterol [90]. Thyroid hormones act directly in the insulin secretion. In the hypothyroidism condition there is an increase of insulin secretion stimulated by glucose in the β cells, and the opposite occurs in the hyperthyroidism condition, reducing the secretion of insulin stimulated by glucose [91, 92].

Comte et al. [93] reported that the reduction of gluconeogenesis caused hypothyroidism. Thus the mode of action, as herbal powder and extracts reduced higher levels of thyroid hormones in diabetic rats, this is due to the reduction of gluconeogenesis (metabolic pathway that results in the generation of glucose from non-carbohydrate carbon substrates such as lactate, glycerol, and glucogenic amino acids) which led to a reduction in thyroid hormones leading to hypothyroidism (but not *vice versa*) Therefore, it could be concluded that the increase in glucose level led to a reduction in thyroid hormones. More important, hypothyroidism is accompanied by a variety of abnormalities in blood lipid levels. This includes increased total cholesterol and LDL (low-density lipoprotein or "bad") cholesterol levels, and increased triglyceride levels. The abnormal lipid pattern typical of Type 2 diabetes (low HDL, or "good" cholesterol, high triglycerides, and a high proportion of small, dense LDL particles) is usually worsened by hypothyroidism. These changes further raise the already high risk of cardiovascular diseases such as heart disease and stroke among people with diabetes.

Another explanation of the reduction of the thyroid hormones (T_3 and T_4), is the possibilities include caffeic acid phenyl ester induced modulation in

deiodination system, which affects deiodinase activity through its antioxidant properties [94, 95].
In rats, administration of both mulberry and persimmon either individually or in mixing Table (7), no significant differences were seen in serum triglycerides (TG) levels in all groups both normal control, normal treated and diabetic treated compared to diabetic control. In addition, a very low density lipoprotein (VLDL), small and very small LDL fractions, are called "very bad cholesterol" because they are often oxidized and frequently induce adverse effects, including atherosclerosis. The current results are in the same trend with Tsuduki et al. [96] who found that administration of mulberry leaf extract rich in DNJ was strongly attenuated lipid accumulation through β-oxidation.
Furthermore, findings of the present investigation suggest that total cholesterol (TC) showed significant differences as results of improving plasma lipoprotein profile and decrease very bad cholesterol [97].
Persimmon leaf powder improved plasma lipid levels profile partly via increased fecal lipids excretion [81]. These beneficial effects may be due to the properties of its phenolic compounds and high fiber content [98, 99]. Liu et al. [100] suggested that improved lipid profile by lowering of total and LDL cholesterol and triglyceride is might be due to increased expression of cholesterol 7 alpha-hydroxylase (CYP7A1) gene's expression. CYP7A1 regulates bile acid synthesis thus holds imperative role in balancing cholesterol homeostasis. In pervious statistically analysis studies, flavonoids have been reported to have acute and chronic effects on lipid metabolism [101, 102].
Although the activities of aspartate and alanine amino transaminase (AST and ALT) in the serum have been found to be a useful indicator of liver damage in the diagnosis and study of acute hepatic disease, these enzymes are located not only in the liver, but also in the extra-hepatic tissues [103]. In the current study, activities of serum AST and ALT which are known be marker enzymes for liver damage were markedly elevated in hyperglycemic animals compared to normal rats. Administration of mulberry and persimmon extract remarkably prevented hyperlipidemic elevation of serum AST and ALT.

Conclusion

The obtained data can support the use of mulberry and persimmon water extract decoctions by the elderly as natural anti-diabetics, anti-hypertensives, anti inflammatories, and vermifuges. Moreover, these extracts might be potential natural sources for the development of antioxidant function in dietary food. These results encourage a further study of the possibility of improving the extraction of natural antioxidants using water and avoiding organic solvents.

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