

تأثير بعض أجزاء المستخلصات النباتية فى تعديل إرتفاع السكر فى الدم بإستخدام الفئران
المصابة بالسكرى المستحث بالألوكسان
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**Effect of some plant parts extract in modulating the serum
hyperglycemia using alloxan-induced diabetic rat model**

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المستخلص:

توضح الدراسة تأثير استخدام مستخلصات الأجزاء النباتية الثلاثة (المستخلص المائي لثمار البامية، المستخلص المائي للتوت الأبيض، المستخلص المائي لأوراق الكرفس، وخليطهم)، وفحص أثر تلك النواتج على مستوى الجلوكوز في الدم، وذلك عن طريق استخدام فئران مصابة بمرض السكري بعد حقنها بالألوكسان. أظهرت نتائج الدراسة فروق معنوية كبيرة للحيوانات المحقونة بالألوكسان في تركيز الجلوكوز في الدم مقارنة بالمجموعة السالبة (-). أما الفئران التي تغذت على 2% w/w (مستخلص نبات البامية، مستخلص أوراق التوت، مستخلص نبات الكرفس، وخليطهم) قلت نسبة إرتفاع السكر في الدم مقارنة بالمجموعة الموجبة (+)، وسجلت 57.35%، 38.69%، 52.27%، 35.48% على التوالي. كما أن المجموعة التي تغذت على المخلوط سجلت الحد الأقصى لنقص السكر في الدم مقارنة بباقي المجموع التي تغذت على باقى أجزاء النبات المستخلصة بشكل فردي، إلى جانب وجود فروق معنوية كبيرة ($P \leq 0.05$)، وتحسين وظائف الكبد والكلية والدهون بالدم. أظهرت نتائج الدراسة .. أن المستخلصات النباتية وخليطها تستخدم كمضادات أكسدة طبيعية في العديد من التطبيقات الطبية مثل: تحسين مستوى الكلوكرز في الدم ووظائف الكبد والكلية وكذلك الدهون في الدم.

الكلمات المفتاحية: ثمار البامية، ورق التوت ، ورق الكرفس، مرض السكري، وظائف الكبد والكلية، صورة دهون الدم.

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Effect of some plant parts extract in modulating the serum hyperglycemia using alloxan-induced diabetic rat model

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Abstract:

The present study aims to investigate the effect of three plant parts extract [Okra fruits water extract (OFWE), White mulberry leaves water extract (MLWE), Celery leaves water extract (CLWE) and their Mixture in modulating the serum hyperglycemia using alloxan-induced diabetic rat model. The data revealed that treatment of animals with alloxan caused a significant increased ($p \leq 0.05$) in serum glucose concentration by the ratio 136.51% compared to normal animals (negative control group). Supplementation of the rat diets with 2% w/w by OFWE, MLWE, CLWE and their mixture decreased this elevation value compared to normal controls and recorded 57.35, 38.69, 52.27 and 35.48%, respectively. The maximum hypoglycemic yield was recorded for the extracts mixture treatment when compared with the rest selected plant parts extracts individually. Beside the hypoglycemic effect was observed by the selected plant extracts high significant ($p \leq 0.05$) improvements were exhibited for liver and kidney functions as well as serum lipid profile. In conclusion, the data of the present work with that carried out by the others could be represent the mile stone towards the extension of using plant parts extracts such MLWE, CLWE, OFWE and their mixture as natural antioxidants in many different medical applications such improve the serum glucose level, liver and kidney functions as well as blood lipid profile.

Key Words:

Okra fruits, white mulberry leaves, celery leaves, diabetes, kidney and liver functions, serum lipid profile.

Introduction

Diabetes mellitus is widely distributed all over the world including Egypt, and nearly one of each 10 person is diabetic. There is an estimated 143 million people worldwide suffering from diabetes, almost five times more than the estimates ten years ago. This number may probably double by the year 2030 (reviewed in Nagib, 2009). Therefore, the human population worldwide appears to be in the midst of an epidemic of diabetes. Reports from the World Health Organization (WHO) indicate that diabetes mellitus is one of the major killers of our time, with people in Southeast Asia and Western Pacific being most at risk. Diabetes is defined as a state in which homeostasis of carbohydrate and lipid metabolism is improperly regulated by insulin. This results primarily in elevated fasting and postprandial blood glucose levels. If this imbalanced homeostasis does not return to normalcy and continues for a protracted period of time, it leads to hyperglycemia that in due course turns into a syndrome called diabetes mellitus. There are two main categories of this disease. Type 1 (T1DM) diabetes mellitus also called insulin-dependent diabetes mellitus (IDDM) and Type 2 (T2DM), the noninsulin dependent diabetes mellitus (NIDDM). Type 2 diabetes mellitus (T2DM) is one of the world's most common chronic diseases as changing lifestyles lead to reduced physical activity and increased obesity (Wild et al., 2004). Early phenomenon of T2DM is insulin insensitivity, which not only has negative metabolic consequences (Panda and Kar, 2007 and Cunha et al., 2008) but also contributes subsequent pancreas β -cell exhaustion, resulting in the onset of clinical hyperglycemia (Stumvoll et al., 2005). Thus, understanding the regulation of the insulin response and identifying the related mechanisms are important to early treatment and prevention of T2DM. Several hypotheses have been proposed to explain the pathogenesis of T2DM, and during last decades, much attention has been given to the lipid toxicity and low-grade inflammation as major causes of diabetic complications (reviewed in Nagib, 2009).

A number of ways to improve diabetic complications have been proposed, because early treatment and prevention play a pivotal role in reducing the population burden of diabetes. Lifestyle changes such as losing weight, exercising, and watching the diet are often recommended. Benefits of pharmaceutical factors to treat the disease aggressively early have been recommended, but medications may have unwanted side effects. Thus, there has been a growing interest in herbal remedies that can be used but have been difficult to maintain over a long term introduced into the general population with the least side effects and the maximal preventive outcome (Matsui et al., 2006). In this context, many phytochemicals naturally occurring in plant foods would be desirable options. Amongst all of these bioactive compounds flavonoids, phenolic

compounds, organosulfur compounds and anthocyanins are represent the central position. Such compounds has been reported to improve diabetic status by decreasing oxidative stress (Dias et al., 2005 and Coskunet al., 2005) or by reducing the disturbance of hepatic gene expressions (Koboriet al., 2009).

Extensively studied sources of such natural compounds arefruits and vegetables, seeds, cereals, berries, wine, tea, onion bulbs, olive oil and aromatic plants. Attempts are also made to identify and evaluate these bioactive compounds in agricultural by-products, ethnic and traditional products, herbal teas, cold pressed seed oils, exudates resins, hydrolysis products, not evaluate fruits and edible leaves and other raw materials rich in antioxidant phenols that have nutritionalimportance and/or the potential for applications in thepromotion of health and prevention against damages/complecations caused by many diseases including diabetes mellitus.The present study aims to open new avenue for extending the using of three plant parts extract (mulberry leaves, okra fruits and celery leaves) in therapeutic nutrition throught evaluating their effectiveness in modulating hyperglycemia using alloxan-induced diabetic rat model.

Materials and Methods

Materials

Plant parts

Okra fruits, white mulberry leaves and celery leaves were purchased from Port Said local markets, Port Said City, Egypt.

Experimental animals

Normal male albino rats (150-170 g) were obtained from Research Institute of Ophthalmology, Medical Analysis Department, Giza, Egypt.

Chemicals

Alloxan, used for induction of diabetes mellitus among rats, was obtained from Sigma Chemical Co., St. Loues, CA); Casein, as main source of protein from Morgan Co for Chemicals. Cairo, Egypt and Vitamin and salt mixtures, from El-Gomhoriya Company for Chemical, Drugs and Medical Instruments, Cairo, Egypt. All solvents, buffers and specific kits were high analytical grade and purchased from El- Gomhoriya Company for Chemical, Drugs and Medical Instruments, Cairo, Egypt.

Methods

Plant parts extract preparation

Plant parts extracts were prepared according to the methods ofMatazu *et al.*, (2018). Okra fruits, white mulberry leaves and celery leaves were cleaned and cut into pieces, then mashed using a blender (Moulinex Egypt, Al-Araby Co., Egypt) with enough water. The mixture was filtered using a filter paper and the filtrate was concentrated using freeze drier.

Biological experimental

Animals

Animals used in this study, adult male albino rats (130-150 g per each) were obtained from Helwan Station, Ministry of Health and Population, Helwan, Cairo, Egypt.

Basal Diet

The basic diet prepared according to the following formula as mentioned by (AIN, 1993) as follow: protein (10%), corn oil (10%), vitamin mixture (1%), mineral mixture (4%), choline chloride (0.2%), methionine (0.3%), cellulose (5%), and the remained is corn starch (69.5%). The used vitamin mixture component was that recommended by Campbell, (1963) while the salt mixture used was formulated according to Hegsted, (1941).

Induction of diabetes

Diabetes was induced in forty nine normal healthy rats by injection into operationally with freshly prepared alloxan monohydrate in saline at a dose level of 150 mg/ kg body weight (Lazarow and palay, 1954). Immediately after injection animals were received 5% glucose solution over night to overcome drug induced hypoglycemia (Wohaieb & Godin, 1987 and Kakkar et al., 1998). After five days blood glucose was analyzed by a drop of blood was obtained from tail vein and subjected to a strip of haemogluco test. All rats with fasting blood sugar > 126 mg/dl were considered to be diabetics and included in the experiment. Their initial weights were recorded.

Experimental design

All biological experiments performed complied with the rulings of the Institute of Laboratory Animal Resources, Commission on life Sciences, National Research Council (NRC, 1996). Rats (n=42 rats), 130-150g per each, were housed individually in wire cages in a room maintained at 25 ± 2 °C and kept under normal healthy conditions. Concentrations of the tested parts extracts were decided according to many different studies carried out by Elmaadawy, (2016), Hassan, (2014), Salama et al., (2017). All rats were fed on basal diet for one-week before starting the experiment for acclimatization. After one week period, the rats were divided into two main groups, the first group (Group 1, 6 rats) still fed on basal diet and the other main group (36 rats) was injected subcutaneous by alloxan monohydrate to induce diabetic rats then classified into sex sub groups as follow:

- Group (2): Fed on standard diet only as a positive control (rats with diabetes).
- Group (3): Fed on standard diet containing 2% (w/w) of okra fruits water extract (OFWE).

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- Group (4): Fed on standard diet containing 2% (w/w) of mulberry leaves water extract (MLWE).
- Group (5): Fed on standard diet containing 2% (w/w) of Celery leaves water extract (CLWE).
- Group (6): Fed on standard diet containing 2% (w/w) mixture OFWE+ MLWE+ CLWE by equal parts.

Blood sampling

At the end of experiment period, 28 days, blood samples were collected after 12 hours fasting using the abdominal aorta and rats were scarified under ether anesthetized. Blood samples were received into clean dry centrifuge tubes and left to clot at room temperature, then centrifuged for 10 minutes at 3000 rpm to separate the serum according to Drury and Wallington, (1980). Serum was carefully aspirate, transferred into clean covet tubes and stored frozen at -20°C until analysis.

Analytical methods

Liver functions

SGPT/ALTactivities were measured in serum using the modified kinetic method of Tietzet al., (1976) by using kit supplied by Biocon Company. SGOT/AST activities were measured in serum using the modified kinetic method of Tietzet al., (1976) by using kit supplied by BioconCompany. Alkalinephosphatase (ALP)activity was determined using modified kinetic method of Vassaultet al., (1999) by using kit supplied by Elitech Company.

Kidney functions

Serum creatinine concentration was determined using the modified kinetic method of Young et al., (1995) by using kit supplied by BioconCompany. Serum urea concentration was determined by Chaney et al., (1962) by using kit supplied by Biocon Company.

Serum glucose

Enzymatic determination of serum glucose was carried out colorimetrically according to Yound, (1975).

Serum lipids profile

Triglycerides (TG), Total cholesterol (TC) and HDL-Cholesterol were determined in serum using specific kits purchased from El-Nasr Pharmaceutical Chemicals Company, Cairo, Egypt. Low density lipoprotein cholesterol (LDL-c) and very low density lipoprotein cholesterol (VLDL-c) were assayed according to the equations of Fniedewaldet al., (1972) as follow:

$$\text{Very low density lipoprotein (VLDL cholesterol)} = \text{TG}/5$$

$$\text{LDL cholesterol} = \text{Total cholesterol} - \text{HDL cholesterol} - \text{V LDL cholesterol}$$

Statistical Analysis

All measurements were done in triplicate and recorded as mean±SD. Statistical analysis was performed with the Student *t*-test and MINITAB 12 computer program (Minitab Inc., State College, PA).

Results and Discussion

The effect of selected plant parts extracts on serum glucose concentration of obese rats

Data in Table (1) were shown the serum glucose concentration of alloxan-induced diabetic rats consumed the selected plant parts extracts. From such data it could be noticed that treatment of animals with alloxan caused a significant increase ($p \leq 0.05$) in serum glucose concentration by the ratio 136.51% compared to normal animals (negative control group). Supplementation of the rat diets with 2% w/w by OFWE, MLWE, CLWE and their mixture decreased this elevation value compared to normal controls and recorded 57.35, 38.69, 52.27 and 35.48%, respectively. So, the maximum hypoglycemic yield was recorded for the extracts mixture treatment when compared with the rest selected plant parts extracts individually. Such data probably mean that a combination of different selected plant parts extracts may be more efficient for reducing the serum glucose level due to the interactive effects occurred by their different categories of bioactive compounds content. Such behavior was recorded in several previous studies on different plant parts carried out by Sayed Ahmed, (2016), Elmaadawy, (2016) and Elhassaneen et al., (2016-a).

In line with the results of the present study, several studies have been done on the effect of plant parts consumption on diabetic conditions. For example, Matazuet al., (2018) reported the ability of the okra based nutraceutical formulation to decrease glycated hemoglobin (HbA1c) levels in diabetic rats showed its potentials to prevent the diabetic-associated complications. This might be connected with its hypoglycemic effect as well as its antioxidants rich compounds (e.g., carotenoids, riboflavin, ascorbic acid, thiamine and nicotinic acid) identified in Okra fruit (Habtamuet al., 2014).

The antioxidant or free radical scavenging property in plants such as Okra fruit may inhibit oxidative reactions associated with glycation. The observed increase in the level of glycated hemoglobin (HbA1c) in the diabetic untreated group (Table 1) could be due to the persistent hyperglycemia in diabetic condition; because in diabetes, the persistent and excess amount of glucose present in the blood reacts with hemoglobin to form glycated hemoglobin which may also induce the generation of oxygen derived free radicals and other diabetes-associated complications in prolonged diabetic condition (Alyassin et al., 1981). Anthocyanins are the main phenolic compounds in some okra species

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which provide a myriad of health benefits including lower blood glucose level, management or control of postprandial hyperglycemia associated with T2DM and reduce free radicals and thereby improve memory deficits caused by T2DM (Nanda et al., 2013; Esther et al., 2013 and Sepidehet al., 2016).

Table 1. Effect of plant parts extracts on serum glucose concentration (mg/dL) of diabetic rats*

Value	Control (-) Std diet	Control (+) Diabetic	Plant parts extracts (2%, w/w)			
			OFWE	MLWE	CLWE	Mix
Mean	90.53 ^d	214.11 ^a	142.45 ^b	125.56 ^c	137.85 ^b	122.65 ^c
SD	4.21	11.45	7.84	10.56	11.37	6.67
% of Change	0.00	136.51	57.35	38.69	52.27	35.48

* OFWE, Okra fruits water extract; MLWE, White mulberry leaves water extract; CLWE, Celery leaves water extract and Mix, mixture extract of OFWE, MLWE and CLWE by equal parts. Means in the same row with different superscript letters are significantly different at $p \leq 0.05$.

On the other side, mulberry leaves contain N-containing sugars, rutin, quercetin, volatile oil, amino acids, vitamins and microelements, which have so many pharmacological activities such as reducing blood glucose, antihyperlipidemia, hypertensive, bacteriostasis and antivirus (Zou and Chen, 2003). Also, mulberry leaves, a traditional Chinese herb, has been used to treat diabetes mellitus and to alleviate thirst. From mulberry leaf extract, 6 N-containing sugars, such as N-methyl-1-deoxynojirimycin, 2-O- α -D-galactopyranosyl- DNJ, and fagomine, have recently been identified and may have antihyperglycemic effects. Furthermore, Li *et al.*, (2013) recorded that mulberry leaf can be used to treat wasting and thirsting (xiaoke) syndrome, which is now recognized as typical of diabetes.

Regarding celery leaves, Atta and Alkofahi, (1998) reported that celery can lower blood pressure, regulate heart function, as well as the blood glucose level by stimulating the pancreas to insulin secretion, so that it can be used to slow down and treat complications caused by DM. *In vivo* analysis of the effects of quercetin (found in all selected plant parts) on human diabetic lymphocytes showed a significant increase in the protection against DNA damage from hydrogen peroxide at the tissue level. Jung *et al.*, (2011) reported that quercetin might improve glucose response and insulin resistance associated with T2DM by alleviating metabolic dysregulation of free fatty acids, suppressing oxidative stress, up-regulating glucose uptake at peripheral tissues, and/or down-regulating inflammatory gene expression in liver. So, data of the present study with the other concluded that the higher improvement in serum glucose recorded in rats feeding of the selected plant parts mixture could be attributed to the antagonism effects induced by their content of different phytochemical categories

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(phenolics, volatile oils components, quercetin, antioxidant vitamins etc which exhibited different mechanisms of actions.

The effect of the selected plant parts on liver functions enzyme activities of diabetic rats

The effect of selected plant parts extracts on serum liver function enzymes activities (ALT, AST and ALP) in plasma of diabetic rats were shown in Table (2). From such data it could be noticed that alloxan induced a significant increased ($p \leq 0.05$) in ALT (58.99%), AST (43.23%) and ALP (39.35%) compared to normal controls. Consumption of OFWE, MLWE, CLWE and their mixture induced significant improvements on serum liver function enzymes activities through decreasing the ALT, AST and ALP compared to normal controls by the ratio of 23.42, 15.45, 20.36 and 13.90%; 22.26, 16.73, 19.38 and 11.20%; and 18.51, 12.79, 15.26 and 10.93%, respectively. The higher effects in improving of the serum liver functions enzymes activities disorders induced by alloxan in rats were recorded for the Mix followed by MLWE, CLWE and OFWE, respectively. It could be mean that a combination of different selected plant parts extracts may be more efficient for reducing serum level of AST, ALT and ALP the biomarkers of liver functions stress, because the interactive effects occurred by different categories of bioactive compounds of such selected plant parts extracts used.

Table 2. Effect of selected plant parts extracts on liver functions enzyme activities of diabetic rats*

Value	Control (-) Std diet	Control (+) Diabetic	Plant parts extracts (2%, w/w)			
			OFWE	MLWE	CLWE	Mix
Serum alanine aminotransferase (ALT) activity (U/L)						
Mean	36.50 ^c	58.03 ^a	45.05 ^b	42.14 ^b	43.93 ^b	41.57 ^b
SD	2.56	1.98	4.77	1.67	5.11	4.08
% of Change	0.00	58.99	23.42	15.45	20.36	13.90
Serum Aspartate aminotransferase (AST) activity (U/L)						
Mean	53.94 ^d	77.25 ^a	65.94 ^b	62.96 ^b	64.39 ^b	59.97 ^c
SD	3.67	5.11	4.78	4.54	3.84	7.90
% of Change	0.00	43.23	22.26	16.73	19.38	11.20
Serum alkaline phosphatase (ALP, U/L)						
Mean	152.91 ^d	213.08 ^a	181.22 ^b	172.47 ^c	176.25 ^c	169.62 ^c
SD	11.89	14.92	7.88	9.91	10.94	9.81
% of Change	0.00	39.35	18.51	12.79	15.26	10.93

* OFWE, Okra fruits water extract; MLWE, White mulberry leaves water extract; CLWE, Celery leaves water extract and Mix, mixture extract of OFWE, MLWE and CLWE by equal



parts. Means in the same row with different superscript letters are significantly different at $p \leq 0.05$.

In general, aminotransferases are normally intracellular enzymes. Thus, the presence of elevated levels of aminotransferase in the plasma indicates damage to cells rich in these enzymes. For example, physical trauma or a disease process can cause cell lysis, resulting release of intracellular enzymes into the blood. Two amino transferases were found in plasma are of particular diagnostic value AST and ALT. The effect of different plant parts extracts on decreasing the serum liver function enzymes activity have been reported by many studies (Elhassaneen *et al.*, 2013, Elmaadawy, 2016, Sayed Ahmed, 2016 and Aly, *et al.*, 2017). Such effects could be attributed to their high level content of bioactive compounds. Our present data with the others reported that MLWE, CLWE and OFWE are a rich source of different classes of bioactive compounds/ antioxidants rich compounds such flavonols, phenolic acids, anthocyanins, alkaloids, carotenoids and phytosterols (Onyeneho and Hettiarachchy, 1993; Rodriguez *et al.*, 1994; Singh *et al.*, 2002; Beatticet *al.*, 2005; Habtamu *et al.*, 2014 and Elhassaneen *et al.*, 2016). The possible mode of action of liver serum enzymes-lowering activity of the tested plant parts including MLWE, CLWE and OFWE, as individually or mixture could be explained by one or more of the following process. Phenolic compounds including flavonoids found in all of the selected plant parts are known to block the hepatocellular uptake of bile acids. Phenolics pretreatment improved the antioxidant capacity of the liver, diminished the bilirubin concentration and reduced the elevated levels of the following serum enzymes, AST, ALT and ALP, reduce the damage of hepatocytes, and scavengers of reactive oxygen species (ROS) compared with the groups without treatment (Beatticet *al.*, 2005, Sayed Ahmed, 2016). Recently, Matazuet *al.*, (2018) reported that the ability of the okra based nutraceutical formulation to decrease HbA1c levels in diabetic rats showed its potentials to prevent the diabetic-associated complications. This might be connected with its hypoglycemic effect as well as its antioxidants rich compounds (e.g., carotenoids, riboflavin, ascorbic acid, thiamine and nicotinic acid) identified in Okra fruit (Habtamu *et al.*, 2014). The antioxidant or free radical scavenging property in plants such as Okra fruit may inhibit oxidative reactions associated with glycation. Also, a study of Ortaçet *al.*, (2018) have reported that 'Okra have strong antioxidant properties through free radicals scavenging such as superoxide anion, hydroxyl radical and nitric oxide with strong synergic effects'. So, the higher improvement in liver function parameters recorded in rats feeding of the selected plant parts mixture could be attributed to the antagonism effects induced by their content of different phytochemical categories which exhibited different mechanisms of actions.



The effect of selected plant parts extracts on kidney functions of diabetic rats

Data in Table (3) illustrated the kidney functions (urea and creatinine concentrations) in serum of alloxan-induced diabetic rats consumed the selected plant parts extracts. From such data it could be noticed that treatment of animals with alloxan caused a significant increased ($p \leq 0.05$) in serum urea concentration (13.62 and 13.73%) compared to normal control group. From such data it could be noticed that alloxan induced a significant increased ($p \leq 0.05$) in urea (13.62%), and ALP (13.73%) compared to normal controls. Consumption of OFWE, MLWE, CLWE and their mixture induced significant improvements on serum kidney function enzymes activities through decreasing the urea and creatinine compared to normal controls by the ratio of 9.69, 5.85, 7.91 and 5.13%; and 7.84, 5.88, 7.84 and 3.9%, respectively. The higher effects in improving of the serum kidney functions enzymes activities disorders induced by alloxan in rats were recorded for the Mix followed by MLWE, CLWE and OFWE, respectively. It could be mean that a combination of different selected plant parts extracts may be more efficient for reducing serum level of urea and creatinine the biomarkers of kidney functions stress, because the interactive effects occurred by different categories of bioactive compounds of such selected plant parts extracts used.

The effect of selected plant parts extracts on decreasing the serum kidney function parameters have been reported by many studies (Rodriguez *et al.*, 1994; El-Nashar, 2007; Mohamed, 2012; Elhassaneen *et al.*, 2013; Elhassaneen *et al.*, 2016 and Sayed Ahmed, 2016). Such as reviewed in these studies the decreasing in serum uric acid and creatinine as the result of feeding selected plant parts extracts including MLWE, CLWE and OFWE could be attributed to their higher content of phytochemicals such flavonols, phenolic acids, anthocyanins, alkaloids, carotenoids and phytosterols. The possible mode of action of kidney serum parameters-lowering level of the selected plant parts extracts could be explained by one or more of the following process. Polyphenols found in such selected plant parts improved the kidney weight and serum levels of urea nitrogen, creatinine and creatinine clearance as well as increased the activity of superoxide dismutase in the kidney (reviewed in El-Nashar, 2007). While, many authors such Badary *et al.*, (2005) and Mohamed *et al.*, (2005) found that flavanone produced significant protection of renal function by significant reduction in serum urea and creatinine concentrations, decreased polyuria and reduction in body weight loss, marked reduction in urinary fractional sodium excretion as well as protected kidney tissues. Finally, Van Hoorn *et al.*, (2006) noticed that flavonoids lowered plasma creatinine and urea concentration, both indicating a better postoperative kidney functions.

تأثير بعض أجزاء المستخلصات النباتية في تعديل ارتفاع السكر في الدم باستخدام الفئران المصابة بالسكري المستحث بالألوكسان
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Table 3. Effect of plant parts extracts on kidney functions parameters of diabetic rats*

Value	Control (-) Std diet	Control (+) Diabetic	Plant parts extracts (2%, w/w)			
			OFWE	MLWE	CLWE	Mix
Serum urea concentration (mg/dl)						
Mean	51.09 ^c	58.05 ^a	56.04 ^a	54.08 ^a	55.13 ^a	53.71 ^b
SD	2.56	1.98	4.77	1.67	5.11	4.08
% of Change	0.00	13.62	9.69	5.85	7.91	5.13
Serum creatinine concentration (g/dl)						
Mean	0.51 ^{bc}	0.58 ^a	0.55 ^b	0.54 ^b	0.55 ^b	0.53 ^{bc}
SD	3.67	5.11	4.78	4.54	3.84	7.90
% of Change	0.00	13.73	7.84	5.88	7.84	3.92

* OFWE, Okra fruits water extract; MLWE, White mulberry leaves water extract; CLWE, Celery leaves water extract and Mix, mixture extract of OFWE, MLWE and CLWE by equal parts. Means in the same row with different superscript letters are significantly different at $p \leq 0.05$.

The effect of selected plant parts extracts on serum lipid profile of diabetic rats

The effect of selected plant parts extracts consumption on some blood lipid profile parameters in plasma of diabetic rats were shown in Table (4). From such data it could be noticed that alloxan induced a significant increased ($p \leq 0.05$) in triglycerides (TG, 31.12%), total cholesterol (TC, 34.08%), low density lipoprotein (LDL, 100.17%) and very low density lipoprotein (VLDL, 31.12) while significant decreased ($p \leq 0.05$) in high density lipoprotein (HDL, -37.98%) compared to normal controls. Consumption of OFWE, MLWE, CLWE and their mixture (Mix) induced significant improvements on blood lipid profile through decreasing the TG, TC, LDL and VLDL compared to normal controls by the ratio of 23.01, 16.20, 21.41 and 15.58%; 22.39, 17.50, 20.12 and 15.06%; 60.67, 45.44, 53.13 and 36.93%; and 23.01, 16.20, 21.41 and 15.58%, respectively. The opposite direction was observed for the HDL levels. The higher effects in improving of the blood lipid profile disorders induced by DM in rats were recorded for the Mix followed by MLWE, CLWE and OFWE, respectively. Such data are in accordance with that reported by many authors who have been working in different plant parts (Elhassaneen *et al.*, 2016 a-b; Elmaadawy, 2016; Sayed Ahmed, 2016 and Alyet *et al.*, 2017)



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Table 4. Effect of plant parts extracts on serum lipids profile concentration of diabetic rats*

Value	Control (-) Std diet	Control (+) Diabetic	Plant parts extracts (2 %, w/w)			
			OFWE	MLWE	CLWE	Mix
Triglycerides (TG, mg/dL)						
Mean	54.49 ^d	71.45 ^a	67.03 ^b	63.32 ^c	66.16 ^b	62.98 ^c
SD	4.17	7.45	7.08	5.51	4.91	8.45
% of Change	0.00	31.12	23.01	16.20	21.41	15.58
Total cholesterol (TC, mg/dL)						
Mean	105.99 ^d	142.11 ^a	129.72 ^b	124.54 ^b	127.32 ^b	121.95 ^c
SD	10.21	12.09	7.19	6.32	5.03	7.87
% of Change	0.00	34.08	22.39	17.50	20.12	15.06
High density lipoprotein (HDL, mg/dL)						
Mean	45.26 ^a	28.07 ^d	36.25 ^b	39.40 ^b	37.78 ^b	41.12 ^c
SD	4.22	2.98	5.08	3.76	4.18	6.03
% of Change	0.00	-37.98	-19.91	-12.95	-16.53	-9.15
Low density lipoprotein (LDL, mg/dL)						
Mean	49.83 ^c	99.75 ^a	80.06 ^b	72.48 ^c	76.31 ^c	68.23 ^d
SD	5.21	7.02	6.16	8.17	5.89	5.98
% of Change	0.00	100.17	60.67	45.44	53.13	36.93
Very low density lipoprotein (VHDL, mg/dL)						
Mean	10.90 ^b	14.29 ^a	13.41 ^a	12.66 ^a	13.23 ^a	12.60 ^a
SD	2.17	3.41	0.79	3.09	1.91	2.08
% of Change	0.00	31.12	23.01	16.20	21.41	15.58

* OFWE, Okra fruits water extract; MLWE, White mulberry leaves water extract; CLWE, Celery leaves water extract and Mix, mixture extract of OFWE, MLWE and CLWE by equal parts. Means in the same row with different superscript letters are significantly different at $p \leq 0.05$.

Coronary heart disease (CHD) represents one of the most complications induced by DM. It is a major health problem in both industrial and developing countries including Egypt. Many studies have shown that blood elevated concentrations of total or LDL cholesterol in the blood are powerful risk factors for CHD, whereas high concentrations of HDL cholesterol or a low LDL (or total) to HDL (Bedawy, 2008 and Aly, 2017). The composition of the human diet plays an important role in the management of lipid and lipoprotein concentrations in the blood. Reduction in saturated fat and cholesterol intake has traditionally been the first goal of dietary therapy in lowering the risk for cardiovascular disease. In recent years, however, the possible hypocholesterolemic



effects of several dietary components, such as found in our selected plant parts (MLWE, CLWE and OFWE) including, flavonols, phenolic acids, anthocyanins, alkaloids, carotenoids, phytosterols and volatile compounds etc., have attracted much interest. Also, phenolic compounds found in such extracts exerts its beneficial effects on cardiovascular health by antioxidant and anti-inflammatory activities (Kuhlmann et al., 1998). LDL oxidation and endothelial cell damage is believed to be involved in the early development of atherosclerosis. Researchers found that presence of phenolics such quercetin and carotenoids such lycopene significantly reduced LDL oxidation in vitro from various oxidases including 15-lipoxygenase, copper-ion and linoleic acid hydroperoxide (Alaaet al., 2015 and Aly, 2017).

Also, the presence of some macro and micro nutrients as well as other vital antioxidant substances in okra fruit (Habtamuet al., 2014) may work in a way similar to the effect of insulin or enhance insulin sensitivity / secretion of insulin from the beta cells of pancreas. This may leads to increase in uptake of glucose and thereby decrease the rate of lipolysis. Further, the hypolipidemic effect of the formulation may also be associated with the fiber/mucilage content of the formulation which could decrease the absorption of dietary cholesterol from the intestine. It has been reported that okra fruit is rich in pectin in addition to other dietary fiber content (Viuda-Martos et al., 2010). Pectin helps in reducing high blood cholesterol by modifying the synthesis of bile within the intestines. It could also bind with the bile salts and reduces their enterohepatic circulation there by resulting in increased degradation of cholesterol to bile salts (Matzuet al., 2018). This corroborated the findings of Hong et al., (2013) which reported that “the Hypolipidemic Activity of Okra is mediated through inhibition of lipogenesis and upregulation of cholesterol degradation”.

In conclusion, the data of the present work with that carried out by the others could be represent the mile stone towards the extension of using plant parts extracts such MLWE, CLWE and OFWE as natural antioxidants in many different medical applications such improve the serum glucose, liver and kidney functions as well as prevent the lipid oxidation on serum.

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