Effect of Some Plant leaves extract on diabetic rats

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Abstract:

Searching for effective, low cost and less side effect containing herbal hypoglycemic agents is important therefore, the present study was performed to evaluate the effect of olive leaves and stevia leaves of alcoholic extracts on diabetic rats. A total of thirty six male healthy rats, weighing (201±1.5g) were classified in to 2 main groups of extraction of olive leaves and stevia leaves each group was classified into 2 subgroup (levels of each type of extract at 0.2 and 0.5 %); in addition to the control negative (-ve) and the control positive (+ve) groups. The rats were divided into six groups: Group (1), the control negative (-ve) was fed on the basal diet. Group (2), the control positive (+ve) (diabetic rats) was fed on the basal diet. Groups (3 and 4) are diabetic rats fed on the basal diet containing olive leaves extract at 0.2 and 0.5 % respectively. Groups (5 and 6) are diabetic rats groups fed on the basal diet containing stevia leaves extract at 0.2 and 0.5 % respectively.

At the end of the experimental period (6 weeks), rats were sacrificed and blood samples were collected to obtain serum. The results indicated that, STZ treated rats showed significant increase in glucose levels compared to normal rats. Supplementation with different levels of olive leaves and stevia leaves in the diet caused significant decrease (P<0.05) in the concentration of glucose level compared to the positive control one. It was also observed that the concentration of serum lipid profile, liver functions and kidney functions were significantly improved for all tested groups, compared to the positive control group. In conclusions, diet supplemented olive leaves and stevia leaves caused an improvement of the biochemical results from diabetes, therefore olive leaves and stevia leaves could be used as a suitable supplementation therapy for diabetic patients.

Introduction;

Diabetes mellitus (DM) is one of the world's fastest growing chronic diseases. As the prevalence of diabetes continues to rise, it will eventually reach a global rise by 2025 **(Khavandi, *et al*., 2013)**. According to the International Diabetes Foundation (IDF), there are 415 million people with diabetes in the world. By 2040, the number of diabetes will increase to 642 million worldwide. The greatest increase in the incidence and prevalence of diabetes is in the African population, which is attributed to the dietary habits associated with urbanization and westernization **(Mennen, et al., 2001)**. Diabetes increases the risk of developing heart diseases **(Danesh et al., 2007)**.

Most of the oral drugs are costly and have a lot of side-effects. Moreover, several medicinal plants, used to control diabetes along with life style management, have been investigated for their beneficial effect in different types of diabetes and are being more desired, owing to lesser side-effects and low cost. In addition, during the past few years, many phytoconstituents responsible for antidiabetic effects have been isolated from hypoglycaemic plants. There are about 200 pure compounds from plant sources reported to show blood glucose lowering activity. The compounds may be flavonoids, alkaloids, carbohydrates, glycosides, steroids, peptides and amino acids, phenolics and glycopeptides **(Lo and Wasser, 2011)**. Consumers across the world are becoming more interested in foods with health promoting features as they gain more awareness of the links between food and health. Over the last decades, consumer demands for functional foods as an opportunity to improve food product quality has increased enormously. The main characterization of functional food is fortification with dietary fibre, micronutrients, antioxidants, vitamins or minerals that contributes health benefit effects in certain disorders. One of the promising functional constituents that could be used for developing a functional food is inulin. It has a great potential to be considered as a low glycaemic index (GI) ingredient that could provide a number of health benefits such as managing increased risk of chronic diseases (Diabetes Mellitus,

cardiovascular diseases, obesity, stroke and cancer), improving digestive health prevents constipation, reducing cholesterol and lipids and enhancing mineral absorption from colon with its prebiotic role prevents osteoporosis (**Barclay et al., 2008).**

The olive tree is mentioned in Quran and sunnah as a blessed tree, and it is recommended to eat its fruit and use its oil, Many herbal medicines have been recommended for the treatment of diabetes (**Chanwitheesuk et al., 2005**). Hypoglycemic effects have been reported for some plants that contain terpenoids, iridoid glycosides, flavonoids, and other phenolic compounds (**Li et al., 2004**). In addition, a number of secondary metabolites like flavonoids, phenolic acids, phenylpropanoids, and terpenoids have shown significant antioxidant properties (**Rahimi et al., 2005; Harput et al., 2006 and Topcu et al., 2007**). In fact, Olive tree leaves can be regarded as a particularly rich source of polyphenolic compounds, as their polyphenolic contents may reach up to 40 g per kg of dry tissue.

A great number of medicinal plants have been used in the treatment of diabetes in different part of the world. Evaluation of the antidiabetic potentials of these plants becomes necessary to provide scientific proof and justify their uses in ethnomedicine. Stevia rebaudiana belongs to the Aster family which is indigenous to the northern region of South America. It grows in many parts of Brazil, Paraguay, central America, Thiland and Chine (**Kolb et al., 2001**).

Aim of the Study:

The present study was performed carry out to study the hypoglycemic agent of some leaves plant effect of olive leaves and stevia leaves extracts on diabetic rats and searching for effective, low cost and less side effect.

Materials and Methods:

This study and all stages of experiment and analysis were conducted at Graduate labs, Nutrition and Food Science Department, Faculty of Home Economics, Helwan University. It was also be hiring some specialized laboratories to conduct some determinations and examinations.

Materials:

Chemicals: Streptozotocin was obtained from Sigma Company. Kits for biochemical analysis were purchased from Gama Trade Company for Pharmaceutical and chemicals, Dokki, Egypt. Casein, vitamins, minerals, cellulose and choline were obtained from El-Gomhoria Company, Cairo, Egypt.

Animals: Forty eight Male Sprague-Dawley rats weighing (201±1.5g) were purchased from Farm of experimental animals in Helwan, Egypt.

Preparation of the basal diet:

The basal was prepared of protein 14 % (casein ≥85%), corn oil 4%, vitamin mixture 1%, salt mixture 3.5%, cellulose 5%, sucrose 1% and reminder was corn starch as mentioned (**Reeves et al., 1993**).

Preparation of extraction of olive leaves and stevia leaves:

A mixture of ethanol and water (20 ml, 70:30 (v/v)) were added to the olive leaves and stevia leaves and flaxseed powdered (1 g). The mixture was lifted to stand for at least one week at room temperature in the dark. Subsequently, the solution was filtered using a 0.45 μm filter paper. The extract was dried at 45 °C in rotary evaporator to produce a semisolid mass and stored in airtight containers in refrigerator below 10°C (**Ben Salah et al., 2012**).

Experimental animal design:

Injection with Streptozotocin: Streptozotocin (STZ) was dissolved in a citrate buffer (pH 4.4) with a concentration of 15 mg/ml. All animals were fasted overnight and were injected intraperitoneally (IP) with a low dose STZ (60 mg/kg b.w.) for induction of diabetes, after 4 days, blood samples were obtained from medial canthus of eyes of each rat to estimate glucose levels. Serum glucose was 100.34±1.22 and 300.01±2.15 mg/dl in healthy and injected rats respectively. Three days later, the level of the blood glucose was assessed and the level ≥250 mg/dl was considered as diabetic (**Ghauri et al .,2020).**

A total of thirty six male healthy rats, weighing (201±1.5g) were classified in to 2 main groups of extraction of olive leaves and stevia leaves each group was classified into 2 subgroup (Levels of each type of extract at 0.2 and 0.5 %); in addition to the control negative (-ve) and the control positive (+ve) groups. The rats were divided into six groups: **Group (1):** The control (-ve) was fed on the basal diet. **Group (2):** The

control (+ve) (diabetic rats) was fed on the basal diet. **Groups (3 and 4):** Diabetic rats groups were fed on the basal diet containing olive leaves extract at the level of 0.2 and 0.5 % respectively. **Groups (5 and 6):** Diabetic rats groups were fed on the basal diet containing stevia leaves extract at the level of 0.2 and 0.5 % respectively.

Blood sampling: At the end of experiment (6 weeks) rats were starved for 12 hr., then sacrificed under ether anesthesia. Blood samples were collected from the aortic vein into clean dry centrifuge tubes and stored at room temperature for 15 minutes, put into a refrigerator for 2 hour, then centrifuged for 15 minutes at 3000 rpm to separate serum. Serum was carefully aspirated and transferred into dry clean Wasser –man tubes by using a Pasteur pipette and kept frozen at (-20c) until analysis.

Biological Evaluation: Biological evaluations were carried out by determination of feed intake (FI) which was recorded every day throughout the experimental period. Body weight gain% (BWG) and feed efficiency ratio (FER) were determined according to **Chapman *et al.*, 1959**, using the following equations:

$$\textbf{BWG\%} = \frac{intial\ body\ weight - final\ body\ weight}{initial\ body\ weight} \times 100$$

$$\textbf{FER} = \text{Weight gain (g) / Feed intake (g)}$$

Biochemical analysis: For each group analyses included the following: Serum total cholesterol (TC) were determined according to **Allen (1974)**.Triglycerides (TG) was done according to **Fassati and Prencipe (1982).**High density lipoprotein–cholesterol (HDL-c) was determined according to **Lopez (1977)**, whereas low density lipoprotein–cholesterol (LDL-c) and very low density lipoprotein were determined according to **Friedewable et al.,(1972)**.

LDL-c = TC - (HDL-c + VLDL-c)

Determination of aspartate aminotransferase (AST) and alanine aminotransferase (ALT) were determined according to **Reitman and Frankel, (1957).** Serum alkaline phosphates (ALP) was carried out according to **Belfield and Goldberg (1971).**Urea was determined according to **Pattn and Crouch (1977),** the determination of Creatinine was according to **Henry (1974)**, whereas glucose was determined according to **Trinder (1959).**

Statistical analysis: The results were expressed as mean ± standard error (SE). The statistical analysis was carried out by using SPSS, PC statistical software (Verion 18.0 SPSS Inc., Chieago, USA) using the Dunk 'test multiple range post-hoc test. All differences were considered significant if P-values were (P< 0.05) **(SPSS, 1999)**.
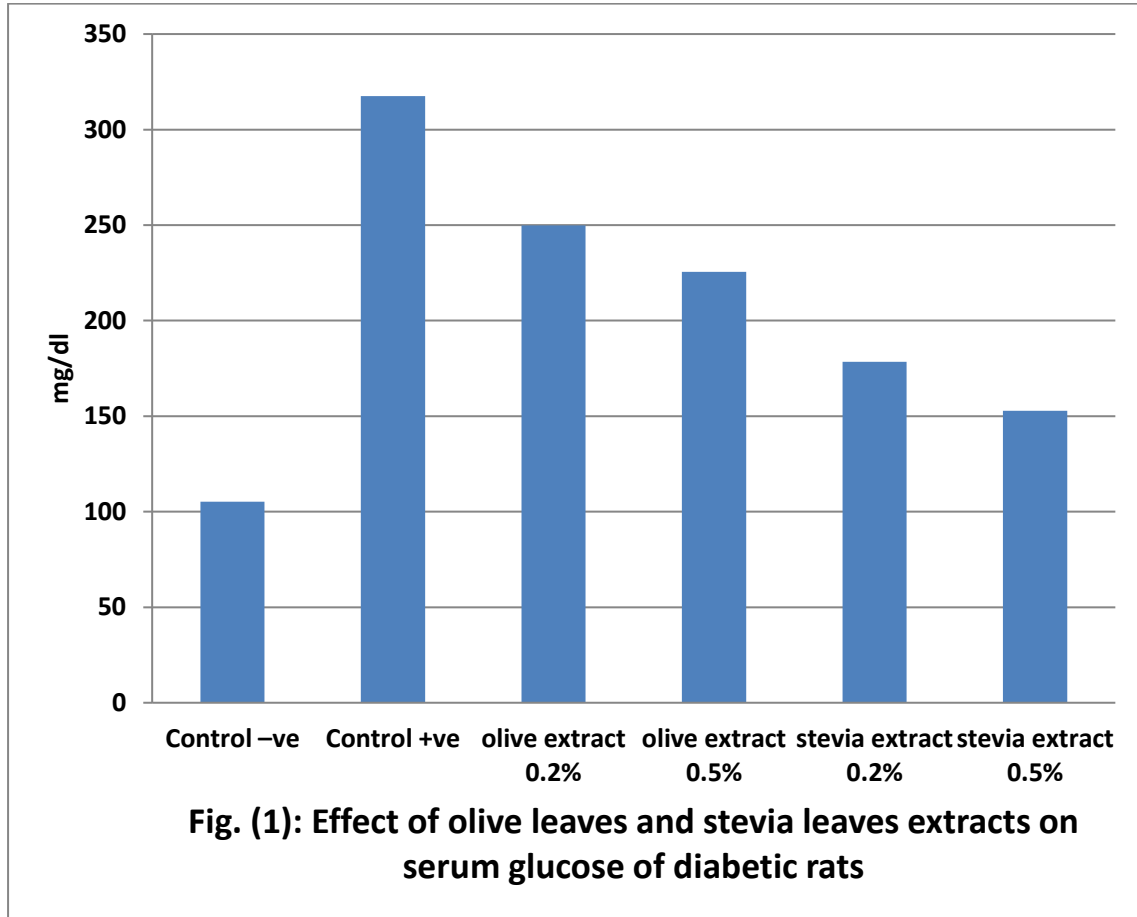
Results:

Rats injected with STZ had significant (P≤0.05) higher glucose level compared to the control negative group Table (1). Feeding diabetic rats on diet supplemented with stevia leaves and olive leaves extract at the level of 0.2 and 0.5% caused a significant decrease (P<0.05) in the elevated serum glucose level, compared to the control positive group. It was clear that, there were significant differences (P<0.05) in glucose level among the treated groups with different two levels of stevia leaves and olive leaves extract. While no significant difference in glucose level among the treated groups with extract of olive at the level of 0.5% was detected. The percent of glucose reduction as a result of supplementation with stevia leaves and olive leaves extracts are (43.77%, 51.88, 21.33%, 28.97%) respectively, as compared to the value of glucose level in the positive control group. Supplementation with extract of stevia caused the highest reduction in glucose level.

Table (1) Effect of stevia leaves and olive leaves extracts on serum glucose of diabetic rats

Parameters / Groups	Glucose (mg/dl)	% of glucose reduction
Control –ve	105.25±5.12 [g]	-
Control +ve	317.50±3.30 [a]	-
Stevia extract 0.2 %	178.50±1.93 [e]	43.77
Stevia extract 0.5%	152.75±4.23 [f]	51.88
Olive extract 0.2%	249.75±3.54 [b]	21.33
Olive extract 0.5%	225.50±3.42 [c]	28.97

Data are expressed as **mean ± SE.**

Means with different superscript letters in the column are significantly differences at **(P ≤ 0.05).**

Fig. (1): Effect of olive leaves and stevia leaves extracts on serum glucose of diabetic rats

The results in Table (2) revealed the effect of stevia leaves and olive leaves extract at the level of 0.2 and 0.5% on liver function of diabetic rats. The activities of serum ALT and AST significantly increased (P<0.05) in the diabetic group, compared with the corresponding value of normal control group .

Supplementation with stevia leaves and olive leaves extract at the level of 0.2 and 0.5% significantly decreased (P<0.05) the elevated levels of both serum ALT and AST compared to the negative control group. It was clear that, no significant difference in AST and ALT levels among the treated groups with different two levels of stevia extract. But extract of olive at the level of 0.5% were significantly different (P<0.05) among the treated groups. Supplementation with extract of olive at the level of 0.5% caused the highest reduction in liver function.

Table (2): Effect of olive leaves and stevia leaves extracts on liver functions of diabetic rats

Parameters / Groups	AST (µ/L)	ALT (µ/L)
Control –ve	83.00±2.88 [d]	40.20±2.16 [d]
Control +ve	119.60±2.58 [a]	99.67±0.95 [a]
Stevia extract 0.2 %	104.57±4.33 [bc]	74.25±2.80 [b]
Stevia extract 0.5%	103.37±1.74 [bc]	72.35±2.83 [b]
Olive extract 0.2%	99.42±4.46 [c]	69.07±3.36 [b]
Olive extract 0.5%	87.80±3.20 [d]	59.00±3.53 [c]

Data are expressed as **mean ± SE.**

Means with different superscript letters in the column are significantly differences at **(P ≤ 0.05).**

Fig. (2): Effect of olive leaves and stevia leaves extracts on serum AST of diabetic rats
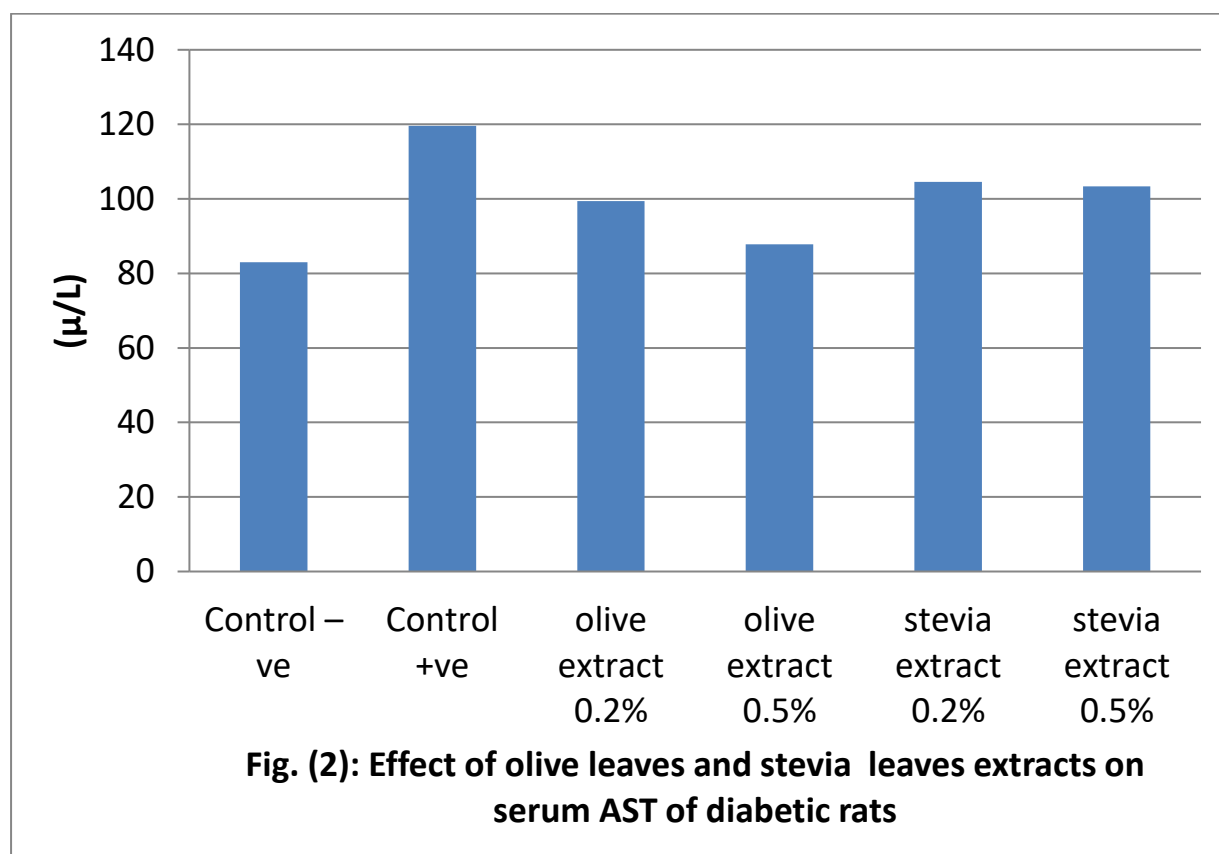
Fig. (3): Effect of olive leaves and stevia leaves extracts on serum ALT of diabetic rats
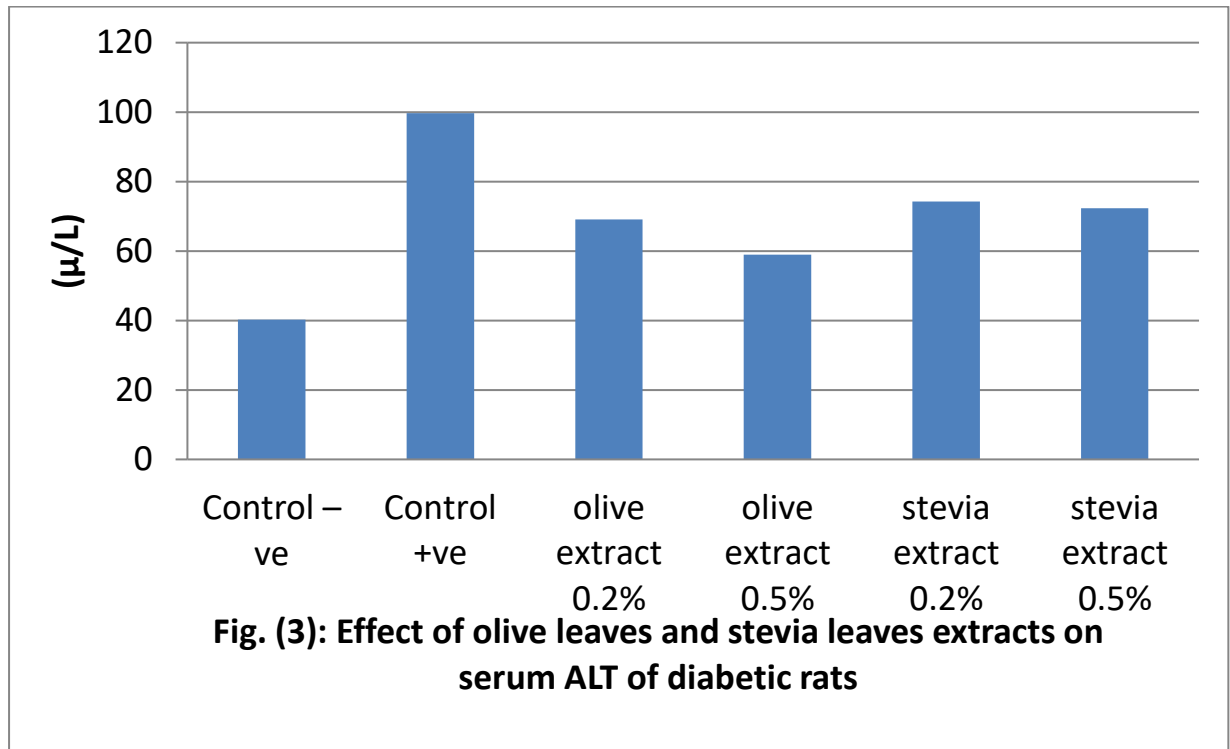
Table (3) illustrates the effects of stevia leaves and olive leaves extract at the level of 0.2 and 0.5% in serum kidney functions on diabetic rats. Injection with STZ significantly increase ($P<0.05$) the level of creatinine, urea and uric acid, compared to the control normal group (control –ve). Feeding diabetic rats on diet supplemented with stevia leaves and olive leaves extract at the tested level caused a significant decrease ($P<0.05$) in the mean values of creatinine, urea and uric acid as compared to the positive control group. There were no significant differences in serum creatinine, urea and uric acid between the treated groups.
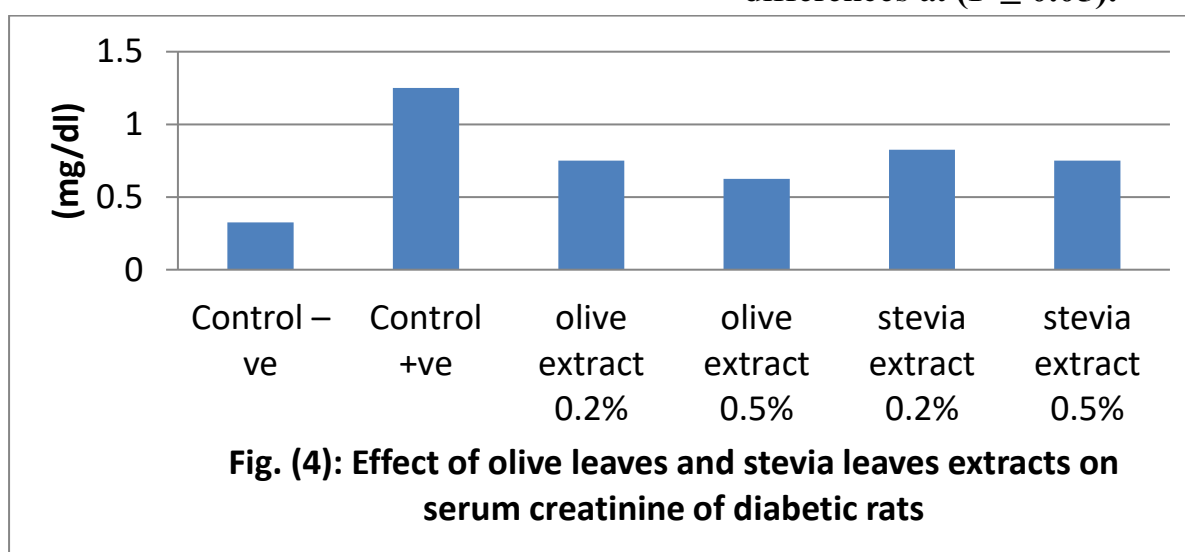
Table (3): Effect of olive leaves and stevia leaves extracts on kidney functions of diabetic rats
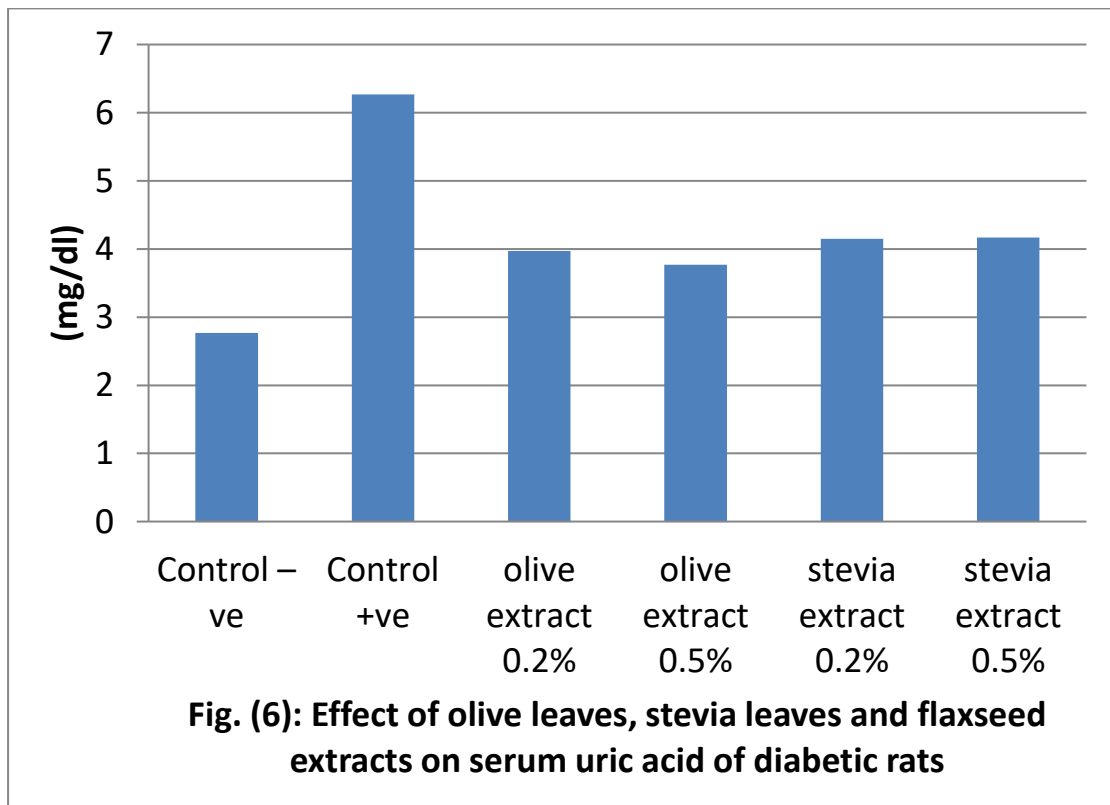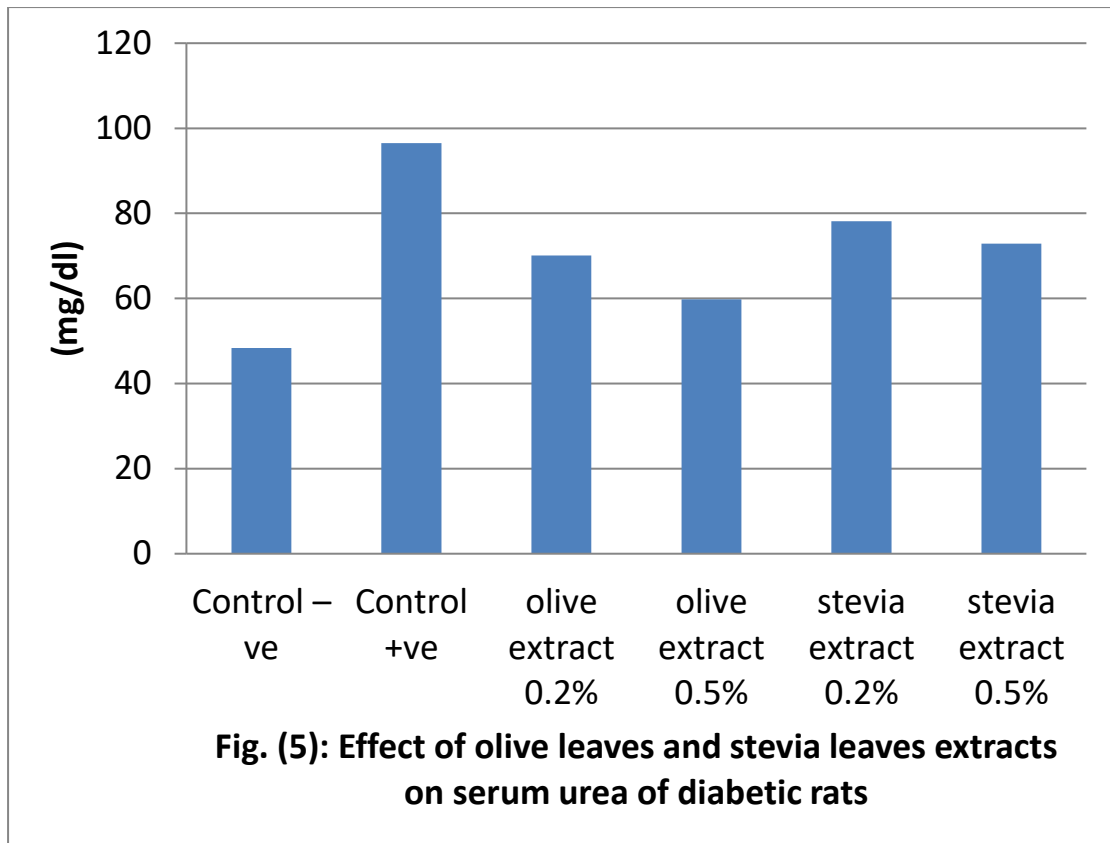
Parameters / Groups	Creatinine	Urea	Uric acid mg/dl
Control –ve	0.325±0.08 c	48.35±1.55 d	2.77±0.13 c

Control +ve	1.25±0.15 [a]	96.50±3.01 [a]	6.27±0.34 a
Stevia extract 0.2 %	0.825±0.08 [b]	78.12±2.13 [b]	4.15±0.40 b
Stevia extract 0.5%	0.750±0.06 [b]	72.85±4.50 [b]	4.17±0.41 b
Olive extract 0.2%	0.750±0.06 [b]	70.12±4.00 [bc]	3.97±0.16 b
Olive extract 0.5%	0.625±0.07 [b]	59.77±2.39 [c]	3.77±0.14 b

Data are expressed as **mean ± SE.**

Means with different superscript letters in the column are significantly differences at **(P ≤ 0.05).**

Fig. (4): Effect of olive leaves and stevia leaves extracts on serum creatinine of diabetic rats

Fig. (5): Effect of olive leaves and stevia leaves extracts on serum urea of diabetic rats

Fig. (6): Effect of olive leaves, stevia leaves and flaxseed extracts on serum uric acid of diabetic rats

Results illustrated in Table (4) shows the effect of stevia leaves and olive leaves extract on lipids profile of diabetic rats. STZ injection to rats caused a significant increase (P<0.05) in serum lipid profile, however, serum HDL-C was significantly lowered, compared to the healthy rats. Diet supplemented with stevia leaves and olive leaves extract at the level of 0.2 and 0.5% significantly decrease (P<0.05) the mean value of serum TC, TG, VLDL-C and LDL-C, however, serum HDL-C level was increased significantly (P<0.05), compared to the positive control group.

It was clear that, no significant difference in TC, TG and VLDL levels but there were significant differences (P<0.05) in HDL and LDL levels among the treated groups with different two levels of stevia extract. Moreover, no significant difference in lipid profile among the treated groups with different two levels of olive extract. Also, no significant difference in TG and VLDL levels but there were significant differences (P<0.05) in TC, HDL and LDL levels among the treated groups with different two levels of flaxseed extract. There were no significant differences in serum TC between different two levels of stevia leaves and olive leaves extract. It was obvious that, the treatments with flaxseed extract at the level of 0.5% gave the highest beneficial effect in improving lipid profile in diabetic rats.
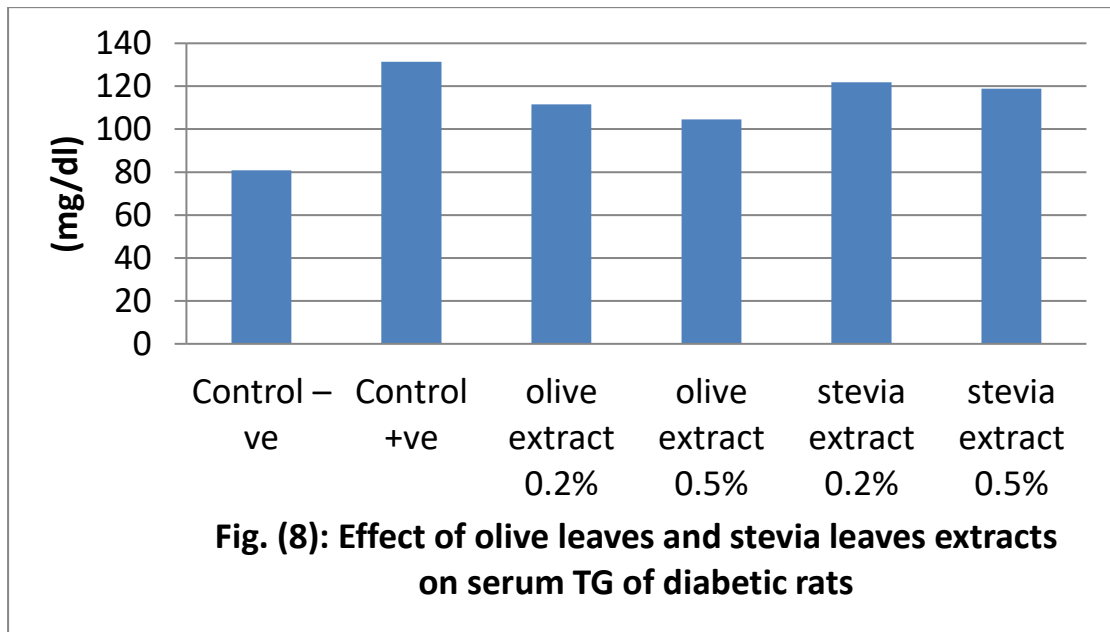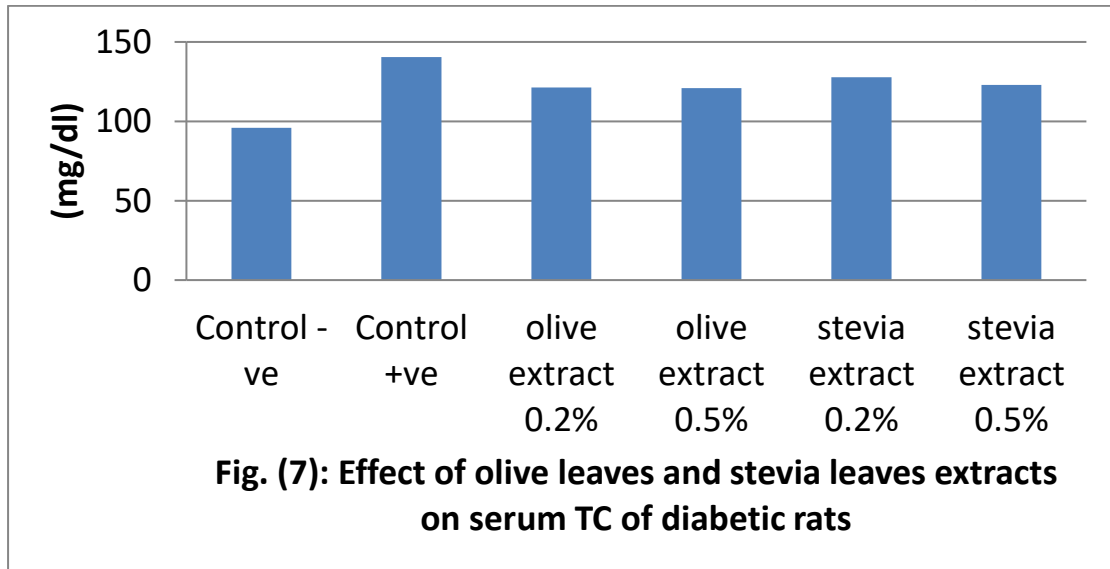
Table (4): Effect of stevia leaves and olive leaves extracts on lipid profile of diabetic rats

Parameters / Groups	TC	TG	HDL-C	VLDL-C	LDL-C
	(mg/dl)				
Control –ve	95.97±3.56 e	80.87±4.95 f	59.25±2.39 a	16.17±0.99 f	20.55±2.61 e
Control +ve	140.47±2.57 a	131.35±1.78 a	25.75±1.10 d	26.27±0.35 a	88.45±3.81 a
Stevia extract 0.2 %	127.80±1.87 b	121.82±2.76 b	34.75±1.70 c	24.36±0.55 b	68.68±11.88 b
Stevia extract 0.5%	122.92±3.19 bc	118.82±1.35 bc	45.25±1.25 b	23.76±0.27 bc	53.91±2.23 c

Olive extract 0.2%	121.35±1.42 bc	111.50±2.87 cd	47.92±2.71 b	22.30±0.57 cd	51.12±3.28 c
Olive extract 0.5%	120.90±1.82 bc	104.50±2.25 de	48.75±1.75 b	20.90±0.45 de	51.25±1.20 c

Data are expressed as **mean ± SE.**

Means with different superscript letters in the column are significantly differences at **(P ≤ 0.05)**

Fig. (7): Effect of olive leaves and stevia leaves extracts on serum TC of diabetic rats

Fig. (8): Effect of olive leaves and stevia leaves extracts on serum TG of diabetic rats

Fig. (9): Effect of olive leaves and stevia leaves extracts on serum HDL-C of diabetic rats

Fig. (10): Effect of olive leaves and stevia leaves extracts on serum VLDL-C of diabetic rats

Fig. (11): Effect of olive leaves and stevia leaves extracts on serum LDL-C of diabetic rats
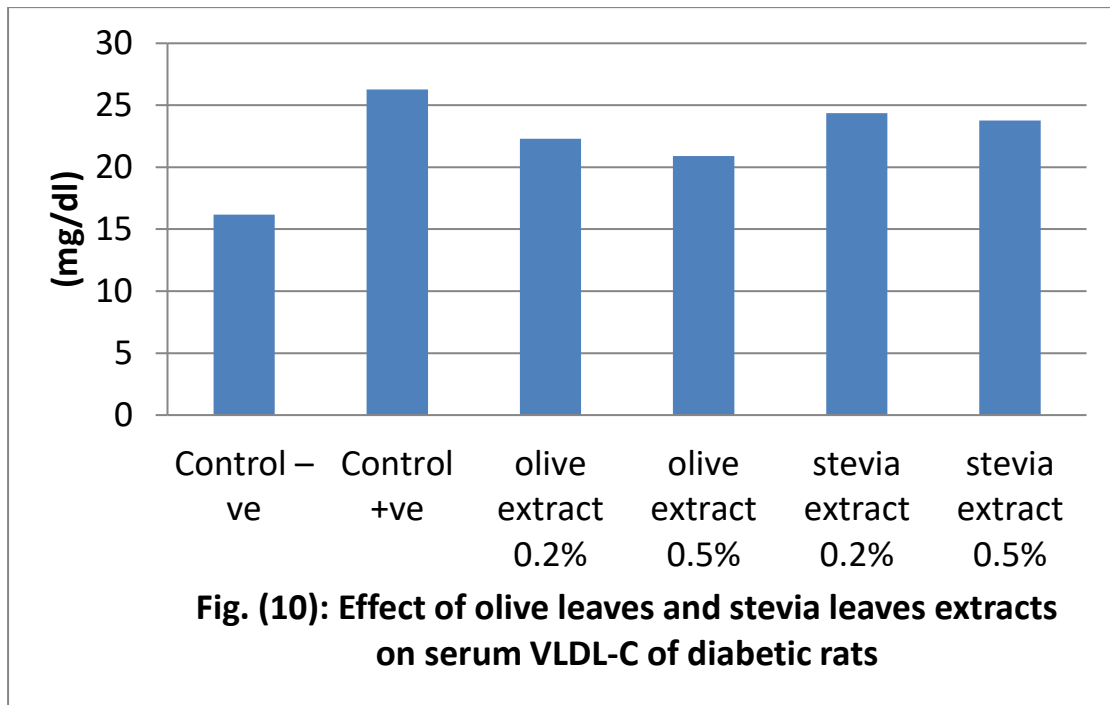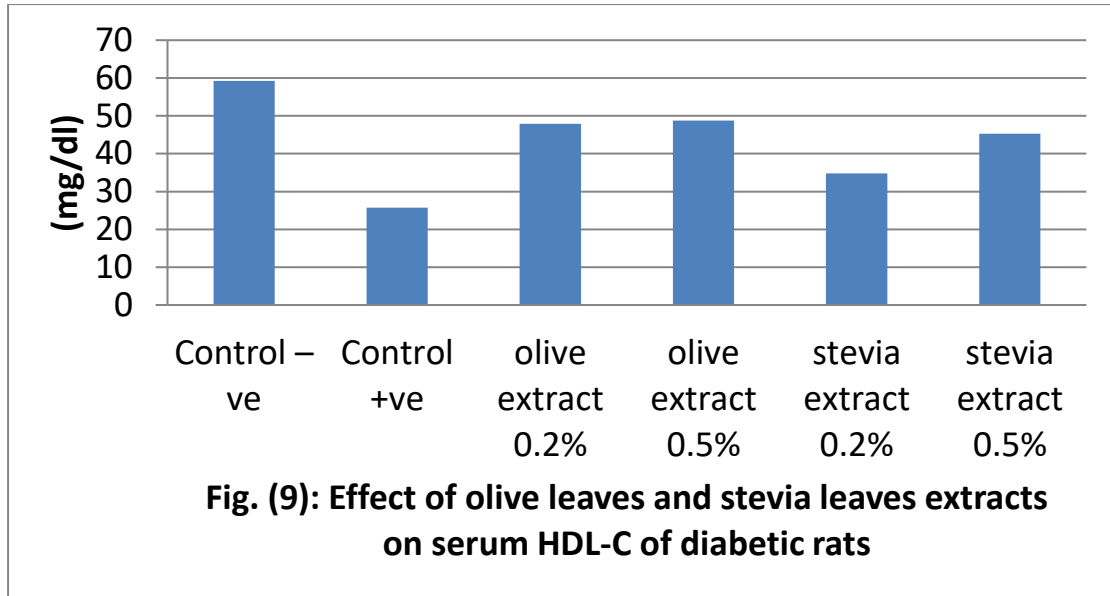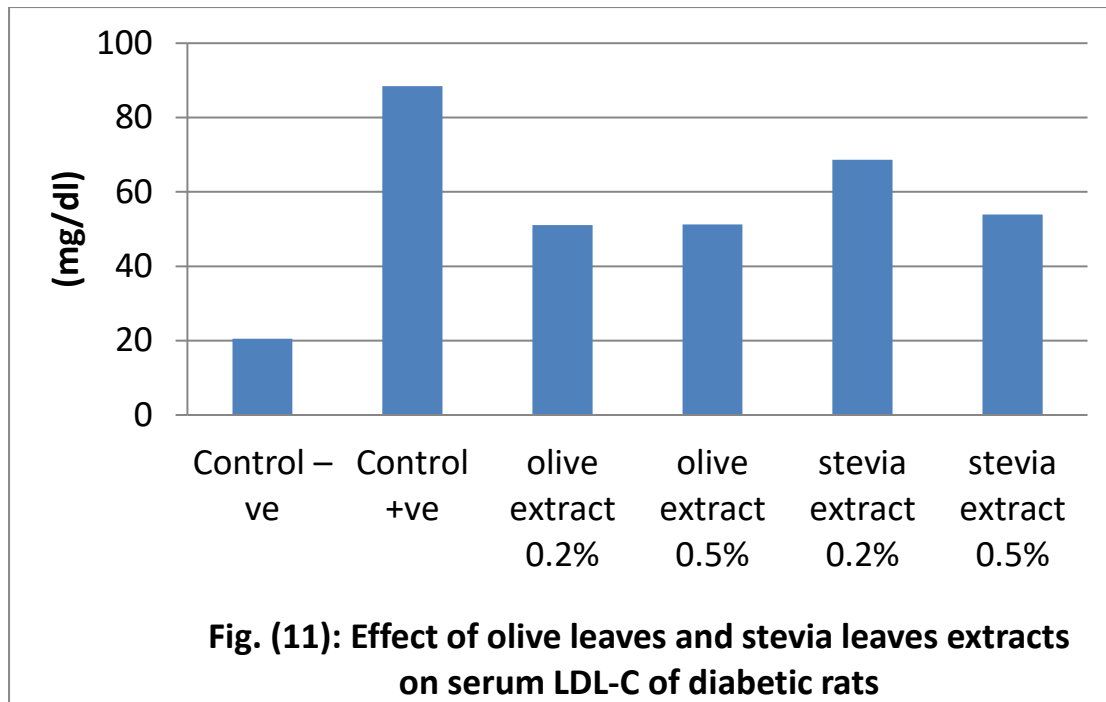
Regarding to changes in body weight status, Table (5) illustrated the changes of body weight, feed intake and FER in the diabetic rats fed on diet supplemented with of stevia leaves and olive leaves extracts. The initial body weight of rats was (201.50±1.85 g), there were no significant differences in IBW among all groups. Diabetic rats had significant decrease (P<0.05) in the FBW compared to the negative control group. It was observed that STZ induced diabetic in rats caused significant decrease (P<0.05) in FBW compared to the healthy rats .

The supplementation with stevia leaves and olive leaves extracts significantly (P<0.05) increased the lowered FBW compared to the positive control group. There were significant differences (P<0.05) in FBW among the treated groups . There were significant differences (P<0.05) in FBW among the treated groups with different two levels of Stevia extract, while no significant change in FBW among the treated groups with different two levels of olive leaves extract.

Stevia extract at the level of 0.5% caused the highest increase in FBW compared to other treatments. In regarding to BWG% and FER, diabetic rats had significantly (P<0.05) lowered BWG% and FER but a significant increase in FI compared to the negative control group. There were no significant differences in BWG% and FER between the groups fed on (0.2 and 0.5%) of olive leaves extract, while the supplementation with St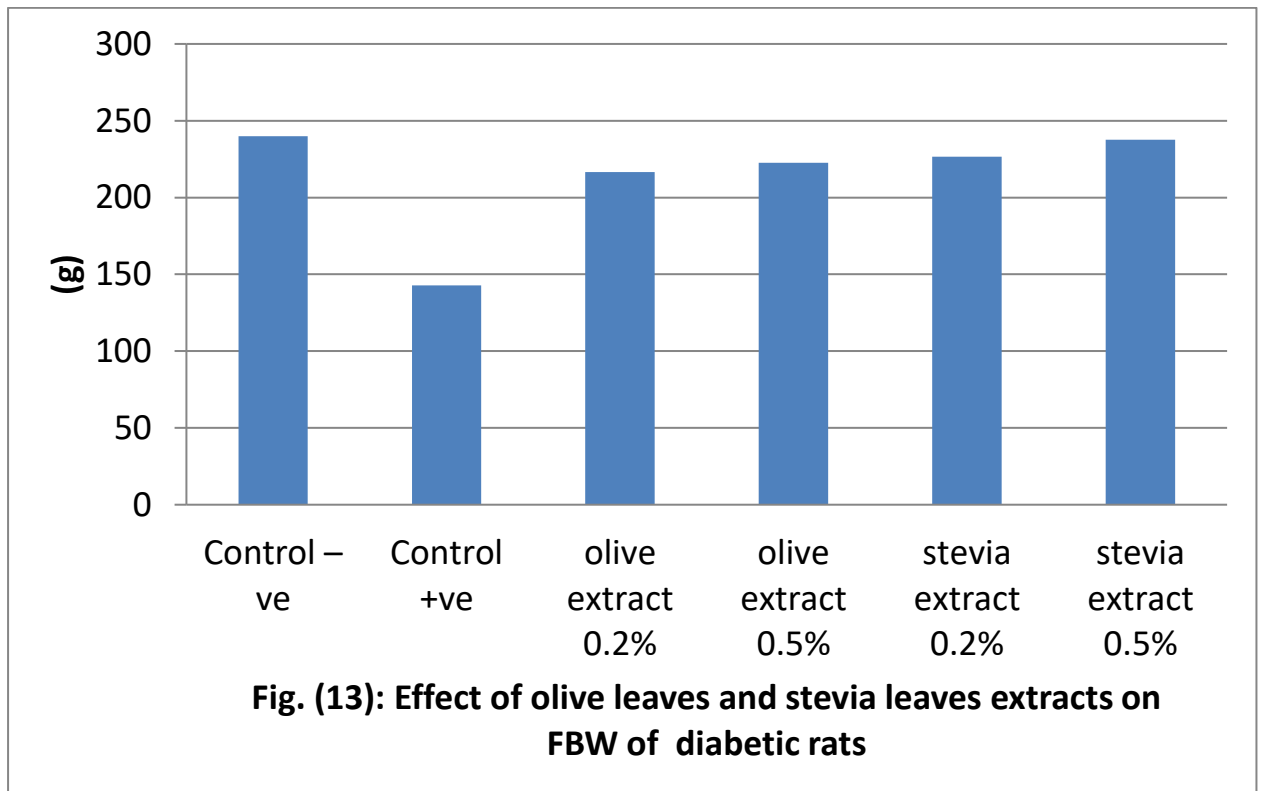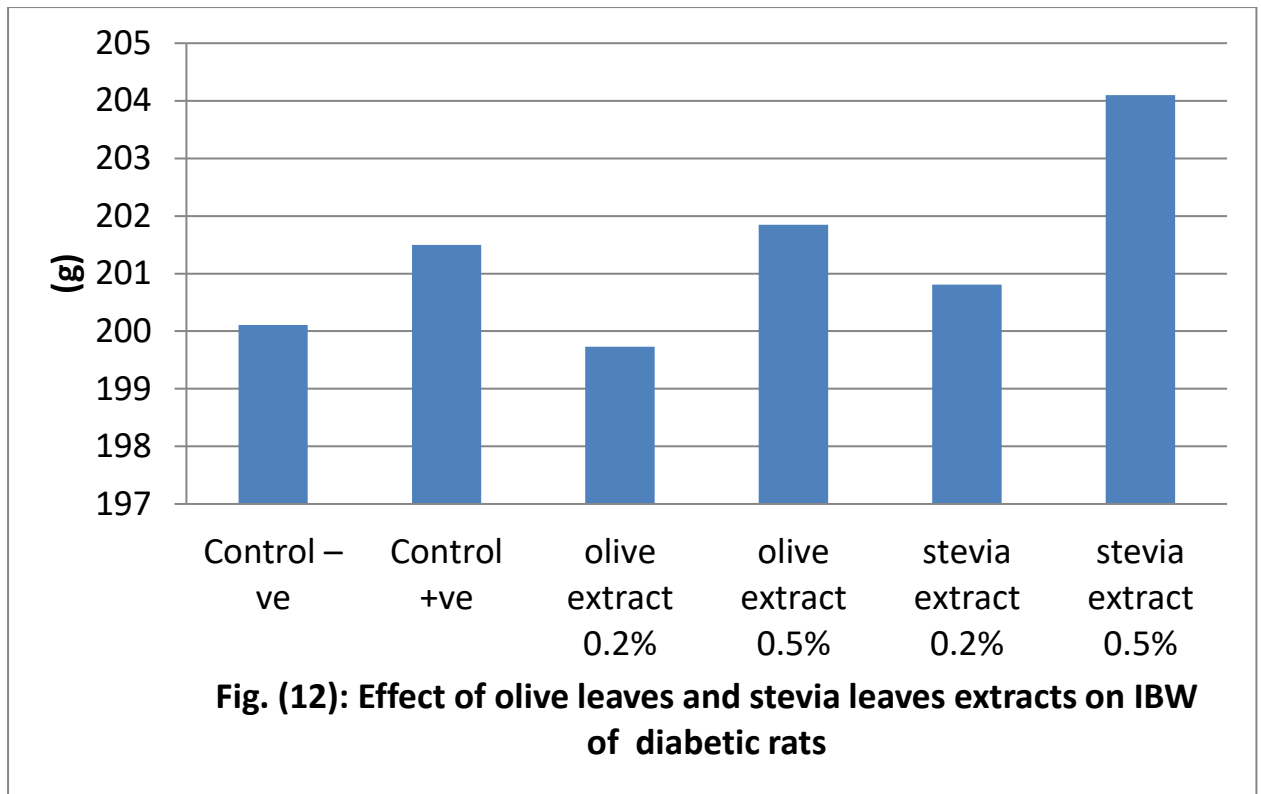evia extract showed significant differences (P<0.05) in BWG%. However, the supplementation with the tested materials caused a significant increase (P<0.05) in BWG% and FER compared to the positive control group, while no significant change in FER among the treated groups with different two levels of stevia extract. Stevia extract at the level of 0.5% caused the highest increase in BWG% and FER compared to other treatments.
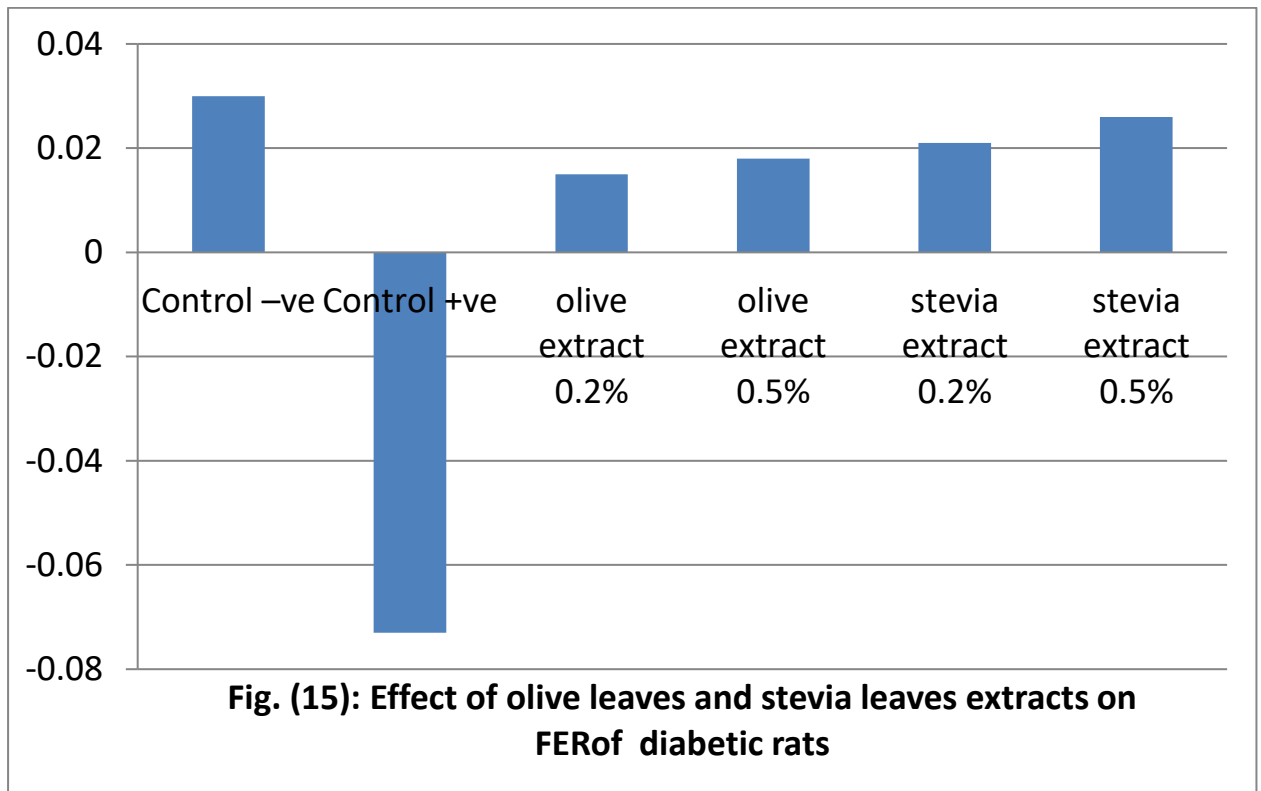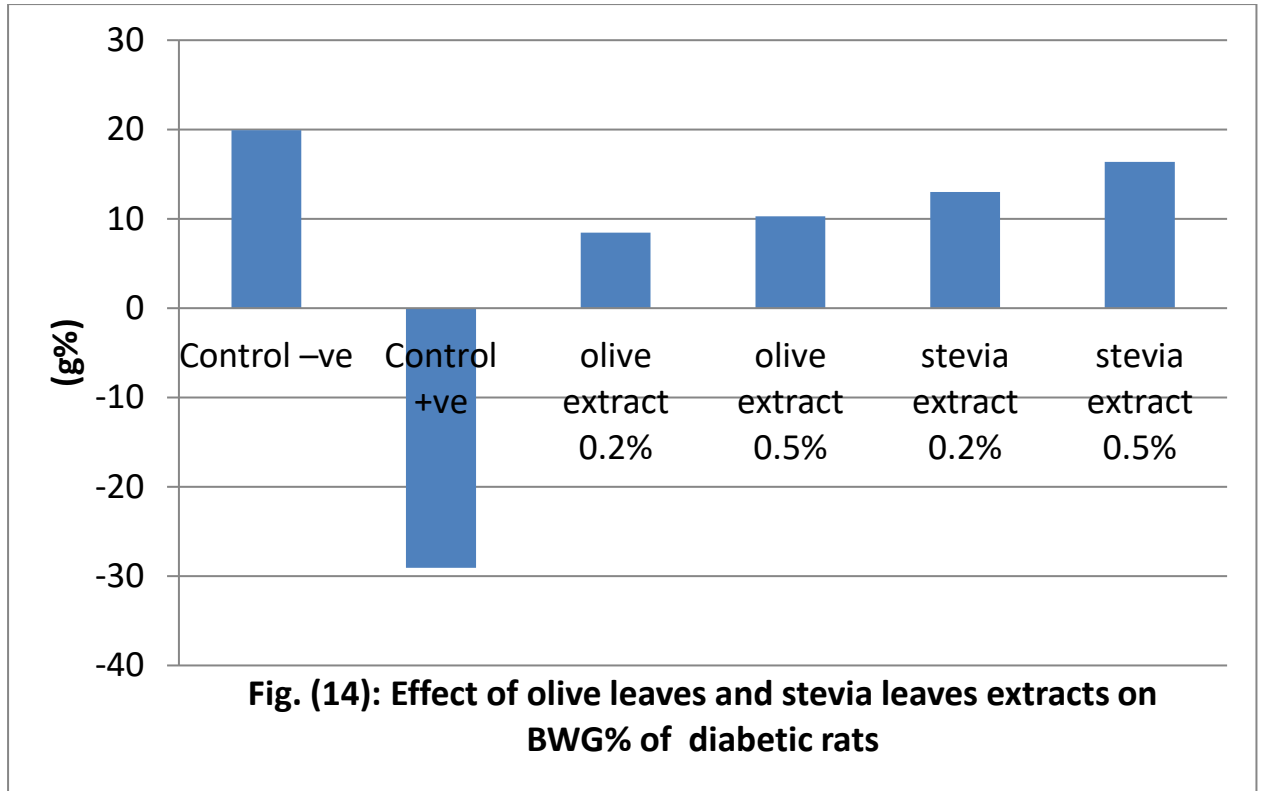
Table (5) Effect of stevia leaves and olive leaves extracts on FI, BWG and FER of diabetic rats

Parameters / Groups	IBW (g)	FBW (g)	BWG%	FI (g/d/rat)	FER
Control –ve	200.11±1.91 a	239.86±2.42 a	19.93±1.60 a	22.00	0.030±0.02 a
Control +ve	201.50±1.85 a	142.80±3.00 e	- 29.06±1.77 f	13.30	- 0.073±0.04 e
Stevia extract 0.2 %	200.81±3.50 a	226.67±2.41 b	12.99±1.10 c	20.00	0.021±0.01 bc
Stevia extract 0.5%	204.10±1.81 a	237.53±1.99 a	16.39±0.48 b	21.00	0.026±0.007 ab
Olive extract 0.2%	199.73±2.21 a	216.60±1.86 cd	8.47±0.67 de	18.40	0.015±0.01 cd
Olive extract 0.5%	201.85±1.78 a	222.61±1.51 bc	10.30±0.41 cd	19.00	0.018±0.006 cd

Data are expressed as **mean ± SE.**

Means with different superscript letters in the column are significantly differences at **(P ≤ 0.05)**

Fig. (12): Effect of olive leaves and stevia leaves extracts on IBW of diabetic rats

Fig. (13): Effect of olive leaves and stevia leaves extracts on FBW of diabetic rats

Fig. (14): Effect of olive leaves and stevia leaves extracts on BWG% of diabetic rats

Fig. (15): Effect of olive leaves and stevia leaves extracts on FERof diabetic rats

Discussion:

DM is a chronic condition that grows the most, especially in developing countries. The disease is highlighted for the severity of its complications (**Whiting et al., 2011**). Controlling the blood glucose

level is vital for protecting complications and improving the diabetics' health (**Ceriello, 2005**). The available hypoglycemic drugs have numerous limitations, therefore herbal medicine can help to minimize diabetic complications.

In the present study feeding diabetic rats on diet supplemented with olive, stevia leaves and flaxseed extracts caused a significant decrease (P<0.05) in the elevated serum glucose level, compared to the control positive group. These results are in agreement with a study carried out by **Azzawie and Alhamdani, (2006)** who found that ethanol extract of olive leaf decreased blood glucose with diabetic rabbits. In the study by **poudyal et al., (2010)** showed that treatment with OLE lowered blood glucose levels and improved glucose tolerance in OLE rats compared with control group. Another study examined the effect of 500 mg olive leaf extract on both diabetic patients and streptozotocin-induced diabetic rats for 1 week , the results indicated a significant decreased in blood glucose (**Wainstein et al., 2012**).

The anti-hyperglycemic effect of S. rebaudiana was investigated in both rats and humans by (**Jeppesen et al., 2003 and Thomas, 2010**). **Ahmad and Ahmad, (2018)** showed that stevia extract decrease blood glucose level in treated diabetic rats, compared with the diabetic and non-diabetic control rats after 8 weeks. The aqueous extract of stevia has anti-diabetic effects in albino rats, and therefore could be promising nutraceutical therapy for the management of diabetes and its associated complications.

Jemai et al., (2009) reported that 8 and 16 mg/kg doses of olive leaf extract decreased serum glucose level. Olive leaf extract was able to cure glucose metabolism in liver and kidneys of rats by minimizing oxidative stress in rats (**Salah et al., 2013**). **Abunab et al., (2017)** found that olive leaf extract decreased blood glucose level in diabetic rats. Similarly, **Ajwad et al., (2020)** showed that the diabetic rats treated with olive extract showed reduction in fasting blood glucose by enhanced insulin sensitivity, improved some antioxidative parameters. These results imply that olive leaf extract may have a potential effect in the treatment of Type 2 diabetes and prevention of its complications (**Acar-Tek and Ağagündüz 2020**). **Khattab, et al (2020)** showed that olive leave extract

may exert a protective role against STZ induced diabetic nephropathy via an antioxidant mechanism.

Regarding to liver functions, **Al-Sahib and Alsaadi, (2020)** showed that 4% and 8% olive leaves improved ALT and AST enzymes activities compared to (diabetic) positive control group. The decrease in the liver enzymes may be due to the presence of some active constituent like flavonoids and terpenoids in the OL which have hepatoprotective effect against hepatotoxins **(Miles et al., 2005). Fki et al., (2020)** suggest that the oleuropein- and hydroxytyrosol-rich olive leaf extracts possessed hypolipidemic and hepatoprotective effects against the HFD-induced metabolic disorders. These results are in the same line with the obtained results.

Shivanna et al., (2013) showed a reduction of blood glucose, ALT and AST in the stevia whole leaves powder. **Assaei et al., (2016)** suggested that supplementation with an aquatic extract of stevia (400 mg/kg) for the period of 28 days significantly reduced triglycerides, ALT, AST levels, Creatinine, Urea and Uric acid compared with diabetic rats (p<0.05). So stevia acts exerts beneficial anti-hyperglycemic effects through stevia's antioxidant properties.

Hyperproteinemia and hyperalbuminemia associated with dysfunctions of liver and kidney, and the increased rate of body water loss **(Kalaiselvi et al., 2015)**.These observations are generally in agreement with other investigations on STZ and alloxan induce relative influences **(Abdel-Kader et al., 2019 and Al-Attar and Alsalmi, 2019)**.

Laaboudi et al., (2016) suggested that olive tree extract consumption can improve lipid profile, and reduce glycemia. It was found that olive oil improve lipid profiles and blood glucose in type-2 diabetic patients through the effect of monounsaturated fatty acids (MUFA), the minor components of olive oil which prevents central fat redistribution and the postprandial decrease in peripheral adiponectin gene expression and insulin resistance induced by a carbohydrate-rich diet in insulin-resistant subjects **(Al Jamal and Ibrahim, 2011)**. Diabetes is associated with fundamental changes in serum lipids profile **(Ani and Aginam, 2018)**, that is mainly attributable to increased TC and TG levels and impaired lipoprotein profile **(Ormazabal et al., 2018)**.

Long-term oral consumption of olive leaves by streptozocin-induced diabetic rats has been hypoglycemic effect, decreases serum

triglyceride, total cholesterol and LDL cholesterol and increases HDL level **(Basuny and Mohammed, 2020)**.

Al-Attar and Alsalmi, (2019) noticed the extract of olive leaves (200 and 400 mg/kg body weight) was investigated for antidiabetic activity on STZ diabetic rats. Significant declines of body weight gain in STZ-diabetic rats were noted after eight weeks. Similar observations were noted in many experimental diabetes researches **(Zhang et al., 2016 and Abdel-Kader et al., 2019)**. Also, **Jung et al., (2019)** suggest that OLE is useful for preventing or treating obesity in which the administration of the oleuropein- and hydroxytyrosol-rich olive leaf extracts identically reduced the body weight, the weight gain, and the epididymal fat accumulation.

Ahmad and Ahmad, (2018) showed that stevia aqueous extract (200, 300, 400 and 500 ppm/kg b.w) for 8 weeks improved weight control in diabetic rats by decreasing the feed intake and body weight gain.

Regimen diet containing supplemented bakery with flaxseed or flaxseed oil for 12 weeks decrease BMI, blood glucose, lipid profile in type 2 diabetics **(Tharwat et al., 2017)**. **Soltanian and Janghorbani, (2018)** suggested that flaxseed cookies (10 g of flaxseed pre-mixed in cookies twice per day) used as a snack may be a useful tool for decreasing, weight, glycemic and lipid levels.

Conclusion: Olive leaves and stevia leaves have long been utilized for their various beneficial effects in traditional medicine. There are still a long way ahead of these plants and their compounds to find their place among drugs actively used in modern medicine to alleviate blood glucose, their remarkable health-benefitting effects should not be overlooked, which are very much worthy of further investments and investigations.

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المستخلص

تأثير المستخلص لبعض أوراق النباتات علي الفئران المصابة بالسكر

من المهم البحث عن نباتات فعالة ومنخفضة التكلفة واقل في إحداث آثار جانبية في تقليل سكر الدم ، لذلك أجريت الدراسة الحالية لتقييم تأثير المستخلصات الكحولية لأوراق الزيتون وأوراق الإستيفيا على الفئران المصابة بمرض السكري. تم تقسيم ستة و ثلاثون من ذكور الفئران السليمة البالغة ، وزنها (201 ± 1.5 جم) إلى 3 مجموعات رئيسية من (أوراق الزيتون و الاستيفيا وبذور الكتان) تم تقسيم كل مجموعة إلى مجموعتين فرعيتين (0.2%، 0.5% لكل مستخلص) ؛ بالإضافة إلى مجموعة الضابطة السالبة والمجموعة الضابطة الموجبة . قسمت الفئران إلى ستة مجموعات: المجموعة (1) المجموعة الضابطة السالبة تم تغذيتها على النظام الغذائي الأساسي. المجموعة (2) المجموعة الضابطة الموجبة (الفئران المصابة بمرض السكري) تم تغذيتها على النظام الغذائي الأساسي. المجموعتان (3 ، 4) عبارة عن فئران مصابة بداء السكري تتغذى على النظام الغذائي الأساسي الذي يحتوي على مستخلص أوراق الزيتون بنسبة 0.2 و 0.5% على التوالي. المجموعتان (5 ، 6) عبارة عن فئران مصابة بداء السكري تتغذى على النظام الغذائي الأساسي الذي يحتوي على مستخلص أوراق الاستيفيا بنسبة 0.2 و 0.5% على التوالي. في نهاية فترة التجربة (6 أسابيع) تم ذبح الفئران وتم جمع عينات الدم للحصول على سيرم الدم.

أشارت النتائج إلى أن الفئران المعالجة بمادة STZ أظهرت زيادة معنوية في مستويات الجلوكوز مقارنة بالفئران السليمة. التدعيم بمستويات مختلفة من أوراق الزيتون وأوراق الإستيفيا أدي الي انخفاض معنوي ($P < 0.05$) في تركيز الجلوكوز مقارنة بالمجموعة الضابطة الموجبة. كما لوحظ أن تركيز الدهون في الدم ووظائف الكبد ووظائف الكلى قد تحسنت بشكل ملحوظ لجميع المجموعات المختبرة، مقارنة بالمجموعة الضابطة الموجبة. الخلاصة: التدعيم باوراق الزيتون وأوراق الاستيفيا أدي الي تحسين النتائج البيوكيميائية لمرض السكري ، لذلك يمكن استخدام أوراق الزيتون وأوراق الاستيفيا كعلاج مكمل مناسب لمرضى السكري.