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Influence of functional and biological properties of Damsissa (*Ambrosia martima*) on rats suffering from Diabetic

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ABSTRACT

The present research was conducted to study the influence of functional and biological properties of *Damsissa* leaves powder (*DLP*) under various concentrations (5%; 10% & 15%) to give more protection against diabetic disease. Thirty five adult male albino rats were used in this experiment. These rats were fed on the basal diet for two weeks for adaptation prior to commencement of the experiment before then divided into five groups (7 rats of each). The first group was fed on basal diet as a (negative control group). The second group (positive control group) was injected with Alloxan to induce hyperglycemia and fed on basal diet. Groups (3; 4 & 5) were fed as the second group + 5%; 10% & 15% (*DLP*). At the end of the experimental period (60 days) rats were fasted over night and sacrificed; blood samples were collected from the aorta to determine glucose, insulin, HbA1c, total cholesterol and other lipids, also for liver and kidney functions. Besides, nutritional parameters were recorded on body weight gain; feed intake and feed efficiency ratio. Liver and pancreas removed surgically for histopathological observation. From the obtained results we concluded that group of rats injected with Alloxan were considered as a major risk factor for hyperglycemia disease. Our results could be summarized that diet fortified at 10% and 15% (*DLP*) can reduced the adverse effect of hyperglycemia; reduced blood cholesterol and other lipids as well as reducing hazards on liver and kidney function compared with positive control group.

Keywords: Diabetes, Albino rats, Damsissa powder, Lipid profile, Liver & Kidney functions, Histopathology.

Introduction

Diabetes mellitus (DM) is one of the common and widely distributed metabolic diseases all over the world. Globally, the prevalence of diabetes was estimated and the latest statistical data of the *International Diabetes Federation (IDF)* showed that at least 382 million people worldwide had diabetes in 2013. Compared with 371 million cases in 2012, the increasing rate reached 8.4 percent, and by 2025, the organization predicts that there will be 592 million cases. Moreover, *IDF* showed that there are 5.1 million deaths caused by this disease per year, or one death every 6 seconds. The expense for the treatment of diabetes is high according to Xing *et al.* (2015).

The experts agreed that in both type 1 and type 2 diabetes, various genetic and environmental factors can result in the progressive loss of β-cell mass and/or function that manifests clinically as hyperglycemia. Once hyperglycemia occurs, patients with all forms of diabetes are at risk for developing the same complications, although rates of progression may differ revealed by American Diabetes Association, (2018). Moreover, Punthakee *et al.* (2018) they confirmed that the (*DM*) is a heterogeneous metabolic disorder characterized by the presence of hyperglycemia due to impairment of insulin secretion, defective insulin action or both. The chronic hyperglycemia of diabetes is associated with relatively specific long term micro vascular complications affecting the eyes, kidneys and nerves, as well as an increased risk for cardiovascular disease; the diagnostic criteria for diabetes are based on thresholds of glycemia that are associated with micro vascular disease, especially retinopathy.

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A wide variety of medicinal plants are used in the treatment of diabetes. One of these plants is the *Ambrosia maritima, L*. is known locally as (*Damsissa*) family composite (*Asteraceae*), widely grown in Egypt, south Sinia and Alwady Algaded showed by Abdelgaleil (2010) and Helal *et al.* (2015).

There is an increasing demand for healthy food products, natural and high quality, among Egyptian consumers. Therefore, one recent trend is to enrich the components in food products to overcome health problems and many of them are known to be effective against diabetes (Halaby *et al.,* 2014 and Baynest, *2015)*. In view of the increasing interest in the use of medicinal plants as a functional foods and natural antioxidant. The present study was planned to evaluate the antioxidant effect of *Damsissa* leaves powder against biochemical changes induced by alloxan-induced diabetic rats.

Materials and Methods

Materials:

Egyptian cultivar of *Damsissa* (*Ambrosia maritima* L.) was obtained from Horticultural Research Institute, Agricultural Research Center. Giza, Egypt. Casein, cellulose, vitamins and minerals ingredients were obtained from El-Gomhorya Pharmaceutical Company Cairo, Egypt. Corn oil and starch were purchased from the local market. Thirty five adult male albino rats (*Sprague Dawley*) weighting an average (150 – 180 g) were obtained from Animal House Colony of Vacsera Helwan, Egypt. Kits used to determine serum cholesterol, triglycerides, LDL-C, uric acid, urea nitrogen, creatinine, and transaminases supplied by Alkan Company.

Methods:

Chemical constituents of Damsissa leave powder:

Moisture, protein, ash, crude fiber, fat and tannins content were determined according to the method outlined in A.O.A.C. (2007). Total carbohydrates were determined by difference as mentioned by Abd El-Latif (1990). Total Phenol compounds were determination by HPLC according to the method of Journal Sci. & Food Agric. (1999). Flavonoid compounds were determined by HPLC according to the method described by Journal of Agric. Food Chem. (2000). Determination of antioxidant activity and total carotenoids were determined according to the methods described by Politeo *et al.,* (2006) and Horwitz and Latimer (2007).

Diet composition:

The basal diet was prepared according to Reeves *et al.* (1993). The vitamin and mineral mixture was prepared according to Hegested *et al.* (1941).

Experimental design:

Rats were adapted for two weeks prior to commencement of the experiment. Water was introduced ad-libitum. Rats were divided into five groups and fed on diets for sixty days as follows: The first group (-ve) was fed on basal diet. The second group (+ve) was injected with alloxan to induce hyperglycemia and fed on basal diet. The other groups (3; 4 & 5) after being injected with alloxan were received basal diets fortified with *DLP* at 5%; 10% & 15%. After 60 days the quantities of diet, which were consumed and / or wasted, were recorded every day. In addition, rat's weight was recorded weekly, to determine Body Weight Gain %, Feed Intake and Feed Efficiency Ratio according to Chapman *et al.* (1959).

Blood Sampling:

At the end of the experiment period the rats were fasted over night before sacrificing. Blood

samples were collected from the aorta. They were centrifuged for 15 minutes at 3000 rpm to separate the serum. The serum was carefully separated into dry clean Wassermann tubes by using a Pasteur pipette and kept frozen till analysis at -20°C.

Biochemical analysis of serum:

Serum samples were used for the determination of Glucose (Trinder, 1959), insulin (Burgi *et al.,* 1988), HbA1c Sudhakar and Pattabiraman (1981), triglycerides (Fassati and Prencipe 1982), total cholesterol *(*Allain *et al.,* 1974), HDL-C *(*Lopes *et al.,* 1977), LDL-C and VLDL-C were calculated by using the method of Friedewald *et al.* (1972). Aspartate aminotransferase (AST) and alanine aminotransferase (ALT) were measured according to the method described by Burtis *et al.,* (1999). Uric acid, urea nitrogen and creatinine were determined according to the methods described by Fassati *et al. (1980),* Patton and Crouch (1977) and Bartels *et al.* (1972).

Histopathological examination:

Tissues from liver and pancreas of the sacrificed rats were examined at the Histology laboratory, Faculty of Veterinary Medicine, Cairo University as described by Drury and Walligton, 1980).

Statistical analysis:

Results were expressed as mean ± SD. Data were statistically analyzed for variance using one-way analysis of variance "ANOVA" according to Armitage and Berry, (1987). Computer software system SPSS (version 20) was used for these calculations.

Results and Discussion

Chemical constituents of raw materials:

Damsissa leaves powder *(DLP)* was investigated on dry weight basis. The following parameters in Tables (1) were pointed out for moisture, carbohydrate, protein, oil, ash and crude fibers, the ratios were 5.70, 56.2, 33.2, 4.9, 4.9 and 16.4 (g/100g DW) respectively. The present results are in agreement with those Julie *et al.* (2001) and El-Kamali and El-Amir (2010), they published that both *Damsissa* powder and ethanol extract contained moisture, carbohydrates, flavonoids, tannins, triterpens and alkaloids, volatile oil, and 20% total ash (2.5% oil sulfated ash and 10% insoluble ash**).**

Table 1: Chemical constituents of Damsissa leave powder (g / 100g dry weight basis)

Component (%)	Damsissa leave powder
Moisture	5.70
Carbohydrate	56.2
Protein	33.2
Oil	4.9
Ash	4.9
Crude fibers	16.4

The following parameters for *DLP* were determined for the content of flavonoid compounds. Results in Table (2) indicated that Hisperidin and Hespirtin were the abundant flavonoid compounds in *Damsissa* leaves which were at concentration of 449.97; 126.13 (mg/100g), while, Naringin; Acacetin; Apig.6- glucose 8-rhamnose; Apignin; Luteo 6-arbinose 8-glucose; Kaemp.3,(2-p-comaroyl) glucose; Luteo.7- glucose and Rutin were the moderate abundant flavonoid compounds in *Damsissa* leaves (33.92; 32.37; 30.51; 28.54; 27.43; 22.92; 17.76 & 11.76 mg/100g), respectively. Also, the lowest abundant were Rhamnetin; Quercetrin-3-o- glucoside; Apig.7- glucose; Apig.7-o-neohespiroside; Luteo.6- glucose 8-arbinose; Kampferol and Rosmarinic at concentration of 2.79; 2.56; 2.38; 2.20; 1.66; 0.87 & 0.48 mg/100g respectively. The results reported previously by Abdelgaleil (2010) and Saxena *et al.* (2013) that the flavonoids appear to have played a major role in successful medical treatments of ancient times, and their use has persisted up to now. Confirmed by Helal *et al.* (2015) that the phytochemical screening of *Ambrosia maritima* revealed that, the presence of alkaloids, flavonoids, saponins and terpenes.

Table 2: Types and concentrations of flavonoids compounds of Damsissa leave powder

Types of Flavonoids	*Test Methods By HPLC analysis	Test results of Flavonoids (mg/100g)
Luteo .6-arbinose 8-glucose	Journal of Agric. Food Chem.(2000) 48,5834-5841	27.43
Luteo.6- glucose 8-arbinose		1.66
Apig.6-rhamnose 8-glucose		5.90
Naringin		33.92
Luteo.7- glucose		17.76
Apig.6- glucose 8-rhamnose		30.51
Hespridin		449.97
Rutin		11.76
Quercetrin-3-o- glucoside		2.56
Rosmarinic		0.48
Apig.7-o- neohespiroside		2.20
Apig.7- glucose		2.38
Kaemp.3,7dirhamoside		7.62
Quercetrin		7.63
Quercetin		11.34
Kaemp.3,(2-p-comaroyl) glucose		22.92
Naringenin		5.12
Hespirtin		126.13
Kampferol		0.87
Rhamnetin		2.79
Apigenin		28.54
Acacetin		32.37

Biological evaluation:

The mean values of rats body weight gain% (BWG); their feed intake (FI) (g/ day for each rat)) and feed efficiency ratio (FER) were summarized in Table (3). Data presented could be observed that there was a significant increases in BWG; FI and FER for healthy control group (negative) (+10.51±1.02; 798.48±26.51 & 0.013±0.00) as compared to the control positive group (hyperglycemia) (-46.65±8.43; 567.42±18.57 & -0.082±0.02), respectively. Hyperglycemia groups fed on the diet containing *DLP* showed improving in body weight and feed intake compared to the positive control group, it seems that *DLP* at 5%; 10% and 15% exert a protective effect against overweight. These results are in harmony, with those obtained by Ahmed and Khater (2001) and Mohamed and Saber (2011) indicated that flavonoids in *Ambrosia maritime* acts as an antioxidant agent against the biochemical alterations induced by alloxan effect via inhibiting the liver damage, improving the liver function and reduction in body weight loss.

Table 3: Effect of feeding on Damsissa dried at different levels on body weight gain, feed intake and feed efficiency ratio

	Groups		(BWG %)	(FI/g/day)	(FER)
1	**Negative Control**		+10.51 ±1.02	798.48 ±26.51	0.013 ±0.00
2	**Positive Control**		-46.65 ±8.43	567.42 ±18.57	-0.082 ±0.02
3	**Dry**	**5 %**	-10.18 ±0.92	651.00 ±23.20	-0.016 ±0.00
4		**10 %**	-18.00 ±1.10	627.06 ±20.19	-0.029 ±0.01
5		**15 %**	-18.00 ±2.15	596.40 ±18.51	-0.030 ±0.00

Biochemical analysis of serum:

Data presented in Tables (4 & 5) illustrated that the initial serum glucose and HbA1c levels showed significant decrease (P<0.05) in the control negative group (healthy rats), with increased in insulin secretion as compared to other groups. While, the serum glucose and HbA1c levels were increased as expected in alloxan injected rats (positive group) to reach 369.50±19.16 mg/dl and 20.00±3.11%, compared with negative group 119.00±5.29 mg/dl and 16.00±2.52% since alloxan causes a massive reduction in insulin 9.25±4.43 U/ml, release by the destruction of the β-cells of the islets of Langerhans and inducing hyperglycemia, as reported by Prabu and Natarajan (2013) and Halaby *et al.* (2014), showed that HbA1c concentration is proportionately increased in diabetic patients with ambient hyperglycemic and reflects the extent as well as management of diabetic condition.

Table 4: Glucose in diabetic rats fed on Damsissa leaves powder

	Groups		Glucose (mg/dl)						
			Zero Time	After 2 Weeks	Decrease %	After 4 Weeks	Decrease %	After 6 Weeks	Decrease %
1	Negative Control		119.00^{g} ±5.29	116.50^{g} ±5.20	-2.10	115.25^{g} ±4.03	-3.15	114.00^{g} ±4.32	-4.20
2	Positive Control		369.50^{a} ±19.16	349.25^{b} ±14.86	-5.48	329.25^{b} ±11.81	-9.67	306.50^{bc} ±10.28	-15.91
3	Dry	5 %	356.50^{a} ±15.35	326.75^{b} ±13.72	-8.35	265.00^{d} ±10.61	-21.25	214.75^{e} ±9.60	-36.18
4		10 %	370.25^{a} ±16.40	331.25^{b} ±12.07	-10.53	262.25^{d} ±8.06	-31.03	180.00^{e} ±7.30	-52.66
5		15 %	378.75^{a} ±15.88	322.00^{b} ±13.49	-14.98	230.25^{de} ±9.14	-39.21	149.75^{f} ±8.54	-60.46

Table 5: Insulin and HbA1c in diabetic rats fed on Damsissa dried leaves after six weeks

	Groups		HbA1c %	Insulin µ/ml
1	Negative Control		16.00^{c} ±2.52	16.36^{bc} ±3.90
2	Positive Control		20.00^{a} ±3.11	9.25^{a} ±4.43
3	Dry	5 %	18.40^{b} ±4.95	15.00^{b} ±3.39
4		10 %	16.30^{bc} ±2.19	15.90^{b} ±3.92
5		15 %	15.77^{c} ±3.02	20.55^{d} ±5.03

Feeding diabetic groups on diet contained *DLP* at 5%; 10% & 15% after 2; 4 and 6 weeks resulted in a significant reduction in the blood glucose levels. (P<0.01) reached 214.75±9.60; 180.00±7.30 & 149.75±8.54 mg/dl, at ratios decrease (-36.18%; -52.66% & -60.46%) respectively, compared to the positive control group. At the same time, ratios of HbA1c decreased to 18.40±4.95%; 16.30±2.19% and 15.77±3.02%, respectively, compared to the positive control group (20.00±3.11%). Data was observed that rats fed on 15% dry *Damsissa* were the best results in HbA1c than other

groups compared with negative control group. It's clear from our results that the treatment with *DLP* may increase the activity of the enzyme glucose 6-phosphate dehydrogenase, via increased secretion of insulin, which increases the influxes of glucose into pentose mono-phosphate shunt in an attempt to reduce high blood glucose levels reported by Akbari *et al.* (2012); Hossain, (2013) and Nandhagopal *et al.* (2013).

Moreover, the increase in insulin reached to highly levels (15.00±3.39%; 15.90±3.92% & 20.55±5.03%) after feeding on diet fortified with 5%; 10% & 15% *DLP,* it's observed that the reversed correlations between serum glucose concentration and insulin secretion level. It is well documented that adherence to a healthy diet can improve glycemic control, which may reduce glycosylated hemoglobin (HbA1c) levels confirmed by Prabu and Natarajan (2013). In this respect, Singh *et al.* (2012) noted that the lifestyle factors, genetics and dietary composition are mainly responsible for type 2 diabetes mellitus. Beneficial effects of *Damsissa* dried leaves including antioxidant property (containing flavonoids and tannins), effect on lowering blood sugar in diabetic patients and effects on Glycemic Index, related to containing dietary fibers have a better effect on blood sugar than those lacking such components confirmed by Khorasgani *et al.* (2013) and Helal *et al.* (2015).

Effect of fortification diet with different levels of *DLP* at 5%; 10% & 15% on lipid profile presented in Tables (6 & 7). It could be noticed that the positive control group fed on basal diet has shown a significant increase in the mean values of TC, TG, TL, LDL-C and VLDL-C (72.00±4.83; 87.50±5.51; 157.75±6.02; 25.15±7.75 & 17.35±0.66 mg/dl) compared with the control negative group "healthy" fed on the same basal diet (63.25±5.06; 78.75±1.71; 142.00±5.35; 12.50±5.85 & 15.75±0.34 mg/dl) respectively, these findings are in agreement with Mishra *et al.* (2010). Data also, indicated that no significant variance with TC between positive control (72.00±4.83) and group fed on 5% *DLP* (71.00±3.74). While, diabetic rats which were treated with the diet fortified on 10%; 15% *DLP* were observed reduction in TC (67.50±7.59 and 64.50±3.42 mg/dl) compared with positive control.

Table 6: Effect of diet with DLP on serum cholesterol, triglycerides and total lipids of diabetic rats.

	Parameters / Groups		Cholesterol (mg/dl)	Triglyceride (mg/dl)	Total Lipids (mg/dl)
1	**Negative Control**		63.25^{b} ±5.06	78.75^{b} ±1.71	142.00^{c} ±5.35
2	**Positive Control**		72.00^{a} ±4.83	87.50^{a} ±5.51	157.75^{a} ±6.02
3	**Dry**	**5 %**	71.00^{a} ±3.74	85.00^{a} ±15.00^{a}	157.00^{a} ±3.74
4		**10 %**	67.50^{b} ±7.59	82.75^{ab} ±15.25^{ab}	150.25^{ab} ±9.22
5		**15 %**	64.50^{b} ±3.42	80.50^{b} ±14.00^{c}	145.00^{c} ±8.98

Table 7: Effect of diet with DLP on High-density lipoprotein cholesterol (HDL-C), low and very low density lipoprotein cholesterol (LDL-C & VLDL-C) in diabetic rats

	Parameters / Groups		HDL-C (mg/dl)	LDL-C (mg/dl)	VLDL-C (mg/dl)
1	**Negative Control**		35.00^{b} ±1.83	12.50^{d} ±5.85	15.75^{b} ±0.34
2	**Positive Control**		28.50^{a} ±5.45	25.15^{a} ±7.75	17.35^{a} ±0.66
3	**Dry**	**5 %**	31.25^{ab} ±1.71	23.75^{a} ±7.01	17.00^{a} ±1.45
4		**10 %**	32.75^{ab} ±3.30	18.20^{b} ±4.98	16.55^{a} ±1.50
5		**15 %**	34.00^{b} ±2.94	14.40^{c} ±3.56	16.10^{ab} ±1.23

The reduction of lipid profile associated with an increase of HDL-C in diabetic rats. This might be due to decrease of cholesterol absorption and biosynthesis and increase of fecal bile acid and cholesterol excretion. In the same view, Data in Table (6) showed that decrease significant serum triglyceride in rats group fed on diet containing 10% or 15% dried *Damsissa* (82.75±15.25 and 80.50±14.00 mg/dl), respectively, compared to positive control (87.50±5.51 mg/dl). Moreover, data reflected to the decrement in total serum lipids in rats group fed on 10% and 15% *DLP* were significant (150.25±9.22 and 145.00±8.98 mg/dl) compared to rats fed on positive control group (157.75±6.02 mg/dl). These results were concluded that dried *Damsissa* had a hypolipidaemic effect; the previous studies Gupta *et al.* (2013) proved that the clinical efficacy of *Damsissa* extracts leaves in reducing chronic hypertension by relaxing arteries and help prevent the buildup of calcium on artery walls.

Our results indicated that serum LDL content in rats fed on 10% and 15% dried *Damsissa* (18.20±4.98 and 14.40±3.56 mg/dl) gradually decrease significant compared to rats fed on positive control formula (25.15±7.75 mg/dl). In contrast serum level HDL in rats fed on 10% or 15% dried *Damsissa* were increase significant (32.75±3.30 & 34.00±2.94 mg/dl), respectively, compared to rats fed on positive control group (28.50±5.45 mg/dl) but no significant variance compared to negative control (35.00±1.83 mg/dl). In fact, the best results for all treated groups was noticed in group fed on basal diet fortified with 10% or 15% *DLP* compared with the control positive group. On the other hand serum VLDL.C were significant decrease in rats fed on 15% only (16.10±1.23 mg/dl), compared to rats in positive control (17.35±0.66 mg/dl). While, no significant variance between rats group fed on 5% and 10% *DLP* (17.00±1.45 and 16.55±1.50 mg/dl) respectively, compared to rats in positive control.

There are few studies assessing the effects of *Damsissa* in diabetes, which may be part of vegetarian diet. According to previous studies Hossain (2013) and Prabu and Natarajan (2013) they published that diabetes is a key factor in the predictive equations for cardiovascular disease. In combination, these plant food components may have a very significant impact on blood lipids and cardiovascular disease, which appeared to be complications of diabetes; Type II diabetes patients in combination with hypercholesterolemia, increased fecal cholesterol accompanied with or without bile acid excretion by interfering intestinal micelle formation was proposed to be the mechanisms responsible for the hypocholesterolemic properties. Confirmed by Abdalla and Selem (2014) revealed that *Ambrosin* and damsin considered as the most active ingredients in *Damsisa* plants; moreover, flavonoids in *Damsisa* suppress the glucose level, reduce plasma cholesterol and triglycerides significantly and increase hepatic glucokinase activity probably by enhancing the insulin release from pancreatic islets.

The effect of *DLP* used in fortified diet at (5%; 10% & 15%) on kidney functions of diabetic rats is presented in Table (8). Diabetes is among the leading causes of kidney failure. Ten to twenty percent of people with diabetes die of kidney failure Singh *et al.* (2012). It could be observed that the control positive group has shown a significant increase ($p< 0.05$) in serum uric acid, creatinine, urea nitrogen and blood urea nitrogen, compared with those of the control negative group (3.80±1.82; 0.70±0.02; 80.50±7.68 & 38.50±3.26 *vs.* 1.50±0.04; 0.50±0.04; 43.00±3.85 & 20.02±1.60 mg/dl) respectively, that confirmed previously by Shebl *et al.* (2013) who declared that the chronic elevation of plasma glucose causes many of the major complications of diabetes including nephropathy, retinopathy, neuropathy, macro- and micro vascular damages. Conclusively, Uric acid in rats fed on dried *Damsissa* was gradually significant decrease.

Results indicated that, the treated groups fed on fortified diet with *DLP* at different levels induced significant decrease ($p<0.05$) in the studied parameters, as compared to the positive control group. Also, no significant variance in serum creatinin between rats fed diet containing 10% and 15% *Damsissa* dried for creatinin (0.55±0.09 and 52±0.09 mg/dl) compared to normal rats fed on negative control (0.50±0.04 mg/dl). Nowadays, *Damsissa* used in some renal tea due to it is proved effect in renal colic and expel renal stones published by Mohamed and Saber (2011).

Results in Table (8) noticed that the rats group fed on diet containing different dried *Damsissa* indicated that gradually decrease significant in serum urea compared to positive control. At the same time, rats fed in diet containing 15% dry *Damsissa* was highest decrease significant in BUN (23.36±1.86 mg/dl) level compared to positive control (38.50±3.26 mg/dl).

Table 8: Kidney function in diabetic rats fed on Damsissa dried leaves.

	Groups		Uric Acid (mg/dl)	Creatinin (mg/dl)	UREA (mg/dl)	Blood urea nitrogen (B.U.N) (mg/dl)
1	**Negative Control**		1.50^{e} ±0.40	0.50^{d} ±0.04	43.00^{e} ±3.85	20.02^{d} ±1.60
2	**Positive Control**		3.80^{a} ±1.82	0.70^{a} ±0.02	80.50^{a} ±7.68	38.50^{a} ±3.26
3	**Dry**	**5 %**	2.75^{b} ±0.26	0.64^{ab} ±0.12	71.67^{b} ±5.53	33.30^{b} ±1.68
4		**10 %**	2.47^{c} ±0.40	0.55^{c} ±0.09	68.00^{bc} ±3.94	31.78^{b} ±1.60
5		**15 %**	2.05^{cd} ±0.31	0.52^{c} ±0.09	50.00^{e} ±3.61	23.36^{cd} ±1.86

The effects of *DLP* at different ratios on liver function of diabetic rats are presented in Table (9), which indicated that the feeding diabetic rats on basal diet resulted in significant increase in serum Aspartate Amine Transferase (AST) and Alanine Amine Transferase (ALT), as compared to healthy rats fed on basal diet (73.67±8.94 & 26.50±3.54 *vs.* 29.33±9.18 & 11.00±2.61 IU/L), respectively. Moreover, the mean values ± SD of serum AST & ALT for the positive control groups of diabetic rats showed significant increase ($p<0.05$), compared with other groups fed on different levels of *DLP* at 5%; 10% & 15%. Generally, the best results of liver function recorded for the group fed on dried *Damsissa* because these groups showed non-significant changes in AST & ALT enzymes activity, compared to those of control negative groups. These results of the present study agree with Reda (2006) revealed that, serum AST and ALT levels increased in diabetic rats, compared with negative control rats. Also, our results agree with Hadrami and Al-Khayri (2012) who published that with improving diabetic diet may help to prevent a variety of diseases. In addition, individuals with type 2 diabetes have a higher incidence of liver function test abnormalities than individuals who do not have diabetes. Mild chronic elevations of transaminases often reflect underlying insulin resistance (Salih 2013).

Table 9: Liver function in diabetic rats fed on Damsissa dried leaves.

	Groups		AST (IU/L)	ALT (IU/L)
1	**Negative Control**		29.33^{e} ±9.18	11.00^{d} ±2.61
2	**Positive Control**		73.67^{a} ±8.94	26.50^{a} ±3.54
3	**Dry**	**5 %**	62.00^{b} ±7.52	18.00^{b} ±1.71
4		**10 %**	49.50^{c} ±6.40	14.75^{c} ±1.44
5		**15 %**	32.33^{d} ±2.90	12.75^{d} ±2.83

Histopathological examination of liver:

Liver of rat from group 1 revealed the normal histological structure of hepatic lobule (Photo 1). Meanwhile, liver of rats from group 2 (positive control group) revealed cytoplasmic vacuolation of hepatocytes, dilatation of hepatic sinusoids (Photo 2) and mononuclear cells infiltration in the portal triad (Photo 3). However, liver of rats from group 3 (fed on *DLP* at 5%) showed sinusoidal leukocytosis (Photo 4) and binucleation of hepatocytes (Photo 5). Slight activation of Kupffer cells was the only histopathological findings observed in liver of rats from groups 4 & 5 (fed on *DLP* at 10% & `5%) (Photos 6 & 7).

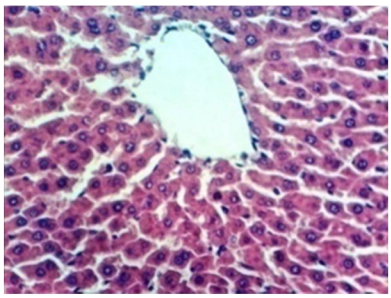
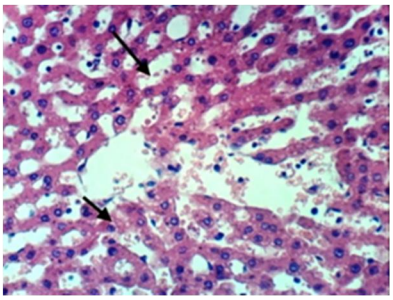


Photo 1: Control (-ve)



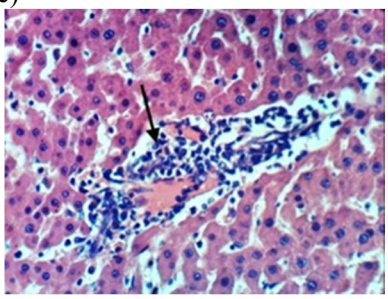
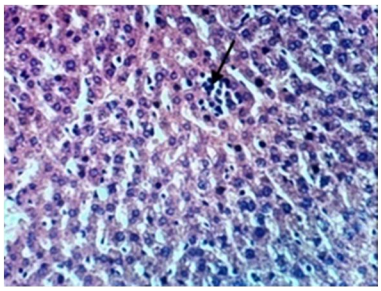


Photo 2 &3: Control (+ ve)



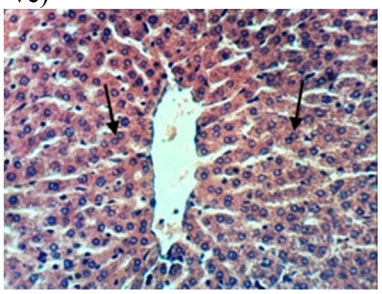


Photo 4 &5: 5% DLP

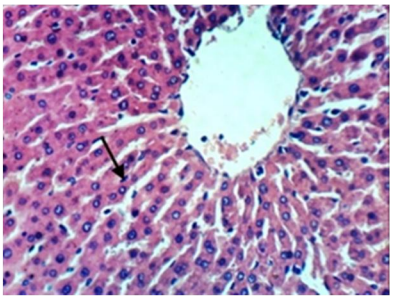


Photo 6: 10% DLP

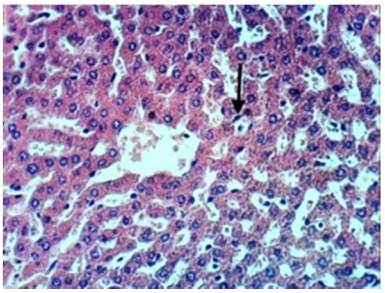
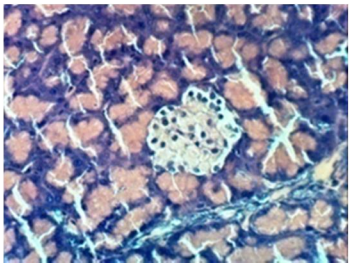


Photo 7:15% DLP

Histopathological examination of pancreas:

Microscopically, pancreas of rats from group 1 showed no histopathological changes (Photos. 1 & 2). In contrary, pancreas of rats from group 2 revealed vacuolations of acinar epithelium (Photos. 3 & 4) and vacuolations of cells of islets of Langerhan's (Photo 4). However, pancreas of rats from groups 3, 4 & 5 revealed no histopathological changes (Photos. 5, 6 & 7).



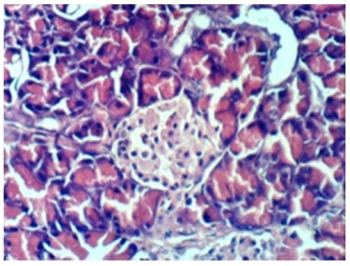


Photo 1 &2: Control (-ve)

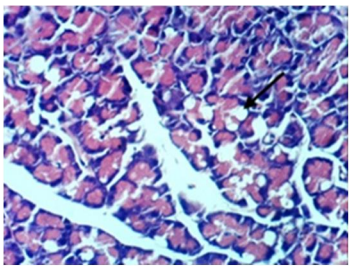
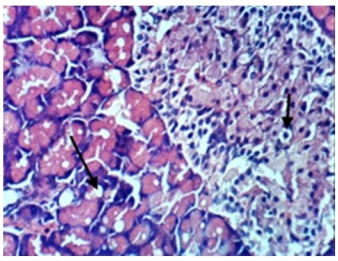



Photo 3 &4: Control (+ ve)

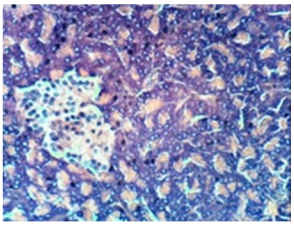


Photo 5: 5% DLP

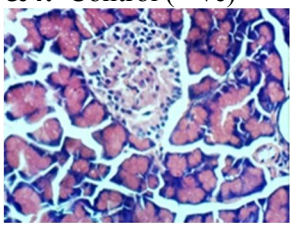


Photo 6: 10% DLP

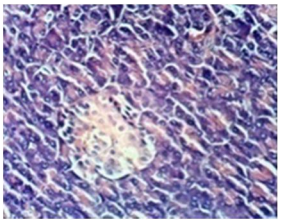


Photo 7: 15% DLP

Recommendation

Medicinal plants industries should be encouraged to use *Damsissa* leaves for fortification to be included in wide scale in the Egyptian meal, factories and medicines; such leaves have the capability to give more protection against hyperglycemia disease and to improve blood lipid levels as well as reducing hazards on liver and kidney functions.

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