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Comparative hypoglycemic effect of acetone extract of banana (*Musa paradisiaca)*, kiwi (*Actinidia deliciosa planch*) and olive (*Olea europaea* L.), byproducts

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The effect of acetone extraction of peels and leaves of banana and peels of kiwi as well as olive leaves on streptozotocin (STZ)-induced diabetic rates. Oral ingestion of their extracts for 60 days reversed the adverse effects of diabetes as compared to control rats. Olive leaves showed the highest percentage of improvement in diabetic rats, while banana leaves showed the lowest percentage of improvement compared to standard anti-diabetic-drug. Higher percentages of improvement were demonstrated in olive leaves extract for total cholesterol (TC) and HDL-C, while low in banana leaves compared to standard drug. Hepatic ALT, AST and ALP activities were increased significantly in diabetic rats compared to controls. However, treatment of diabetic rats with byproducts showed fluctuated percentages of improvement compared to drug. The level of serum total bilirubin was significantly increased in diabetic rats, which was improved by treatments High levels of both intercellular adhesion molecule (ICAMs) and vascular adhesion molecule (VCAMs) in diabetic rats were detected. Treatment with kiwi peels extract exhibited the highest percentage of improvement as compared to standard drug. Further, significant increase in tumor necrosis factor-α (TNF-α) and C-reactive protein (CRP), was detected in diabetic rats. Treatment of diabetic-rats with extracts ameliorated their levels. Histopathological investigation of hepatic tissue in diabetic rats demonstrated focal necrosis, while by treatment with extracts revealed their regenerative effect on β-cells and hepatic parenchyma. Hence, it could be concluded that, the anti-hyperglycemic properties of extracts may offer a potential therapeutic source against diabetes.

Keywords: anti-diabetic, *streptozotocin,* Kiwi, banana, olive wastes

INTRODUCTION

Type II diabetes: it is non-insulin-dependent diabetes mellitus (NIDDM), or adult-onset diabetes (Schulze and Hu, 2005). Insulin is hormone needed to convert sugar, starch and other food into energy needed for daily life. The cause of diabetes continues to be mystery; although both genetic and environmental factors such as obesity and lack of exercise appear to play a part. Plants have always been an important source of drugs and many of currently available drugs have been derived directly or indirectly from

them. Ethno botanical reports indicate about 1200 plants in the world with anti-diabetic potential (Perez et al., 1984 and Alarcon-Aguilara et al., 2002).Streptozotocin (STZ) causes selective degeneration of pancreatic β cells thereby inhibiting insulin secretion. The morphology and physiology of the liver also may be affected by changes in the levels of insulin (Das et al., 2011).In our recent studies, different fruits wastes like banana (*Musa paradisiaca*) & kiwi (*Actinidiadeliciosa*) peels and banana as well as olive leaves were tested for anti-diabetic potential

MATERIALS AND METHODS

Plant materials:

Peels of kiwi (*Actinidiadeliciosa*) and banana variety maghrbiy (*Musa SP.*) were obtained from the local market at Giza, Egypt. Leaves of banana variety maghrbiy and leaves of olive variety kalamata (*Oleaeuropea L*.) were obtained from the *Nubaria* farm (National research centre, Giza, Egypt).

Chemicals and reagents:

All solvents and kits were of analytical grade (from Sigma-Aldrich and Bio-diagnostic Company, Egypt)**.**

Experimental animals

Animal experiments were carried out to investigate the effect of kiwi and banana peels, banana and olive leaves 80% acetone extract treatments on STZ- induced type 2 diabetes in rats. The basal diet is consisting of corn starch 65%, casein 15% , corn oil 10%(Table 1), and salt mixture 4%, in addition to vitamins mixture 1% and cellulose 5% as described in AOAC. (2005).

Experimental design

One hundred and thirty two male albino rats weighted from 200 ± 50 g were selected for this study and divided into eleven groups **(**twelve rats for each group)

Group 1:

Normal healthy control rats.

Groups 2-5:

Normal healthy rat's orally administrated with 80% acetone extracts of different tested samples (kiwi peels, banana peels, banana leaves and olive leaves) extracted with 80% acetone (500 mg/kg body weight daily for 30 days (Castillo et al., 2010 and Wainstein et al., 2012).

Groups 6-11:

Considered as diabetic groups; where type 2 diabetes was induced by streptozotocin, each rat was injected intra peritoneally with a single dose of streptozotocin (45mg/Kg body weight), dissolved in 0.01M citrate buffer immediately before use (Emerick et al., 2005; Milani et al., 2005). After injection, animals had free access to food and water. After two hours each rat was orally administered with 2.5 ml 40% glucose solution as well as 5% glucose solution to drink overnight to counter hypoglycemic shock (Bhandari et al., 2005). Hyperglycemic rats (blood glucose level ≥ 250) were used for the experiment and classified as follows:

Group 6:

Diabetic group sacrificed after three days of STZ injection.

Group 7-10:

Diabetic animals treated orally with 80% acetone extracts of different tested by product at dose 500 mg/kg body weight for 30 days, each rat received 55 mg/0.5 ml distilled water (Sundaram and Subramanian, 2012).

Group 11:

Diabetic animals treated with glibenclamide (Glucophage) 10 mg/kg body weight (each rat received 1.5 mg/0.5 ml distilled water) and considered as reference drug (Dachicourt et al., 1998). All groups fed on the basal diet during the experimented period (30 days), water and diet gave *ad libitium*, then animals were sacrificed by decapitation at the end of experimental period.

Ethical Consideration:

The study was conducted in accordance with the ethical committee guidelines of the Institution on the use of animals for research.

Biological analysis:

Plasma lipids were determined spectro photometrically according to the method of Zollner and Kirsch (1962). The triglycerides in plasma were estimated spectro photometrically according to the method of Fossati and Prencipe (1982). The method of Allian et al. (1974) was used to determine total cholesterol. Plasma HDL cholesterol was determined according to the study of Burstein (1970).The activities of plasma alanine aminotransferase (ALT) and (AST) were measured as described by Reitman and Frankel (1957).

Table 1. Composition of basal diet

Ingredients	Amount (g/kg)
Corn Starch	650
Casein	150
Corn oil	100
Cellulose	50
Salt mixture	40
Vitamin mixture	10

The activity of ALP was determined according to the method described by Belfield and Goldberg (1971).Total bilirubin was determined according to the method described by Walter and Gerade (1970).

Immunosorbent assay:

Adhesion molecules (VCAM-1 and ICAM-1), were estimated in serum by ELISA; a sandwich enzyme immunoassay (Uotila et al., 1981).

Histopathological examination:

Liver of the sacrificed rats were taken and immersed in 10 % formalin solution. The specimens were then trimmed, washed and dehydrated in ascending grades of alcohol. Dehydrated specimens were cleared in xylem, embedded in paraffin, sectioned at 4-6 microns thickness and stained with Heamtoxylin and Eosin for histopathological examination according to the method described by Drury et al., (1980). The histopathological examination was done by Dr. KawkabAbd El Aziz Ahmed, Department of Pathology, Faculty of Veterinary Medicine, and Cairo University.

Statistical analysis:

The ANOVA test was performed for statistical analysis using SPSS computer program version (8) combined with Co-state computer program, where unshared letters are significant at $p \leq 0.05$(Silva et al., 2006).

RESULTSAND DISCUSSION

Effect of 80% acetone extracts of tested plant by-products on pancreatic function

Determination of glucose levels and α-amylase activity

The blood glucose levels andα-amylase activity of different experimental groups are given in Table (1). There was a significant elevation in blood glucose level (368.80 mg/dl) after a single dose of streptozotocin (STZ) injection as compared to normal control group (100.60 mg/dl). The high level of glucose was lowered towards the control level gradually after treatments with acetone extracts of all samples of bypropduct tested. Remarkable improvement in glucose levels was noticed by after the treatments with the four extracts tested which was ranged from 261.43 to 283.10% by leaves of banana and olive, respectively compared to drug 272.96%.

Results are in a good agreement with Wu et al., (2015); Murthy and Felicia (2015); Kappelet al., (2013) and Jemaiet al. (2009) for kiwi fruit, banana peels, banana leaves and olive leaves, respectively, the results recorded significant decreases in the serum glucose level post treatments of diabetic rats with the plant extracts.

On the other hand, in diabetic condition, significant increase in α- amylase enzyme activity was recorded reached to 318.74 U/L compared to normal control rats. The improvement of α-amylase in diabetic groups after the treatments with the tested by-products extracts was ranged from 24.88 to 28.81% for leaves of banana and olive, respectively.

From these data it was noticed significant reductions in blood glucose level and α-amylases activity in diabetic rats by extracts treatments. This may be due to presence of polyphenol and flavonoid as declared by Jemai et al.,(2009) who mentioned that ole uropein and hydroxyl tyrosol in olive leaves extracts have this action. Also, rutin in banana peels and leaves (Kappel et al., 2013 and Passo-Tsamo et al., 2015), and quercetin-3-rhamnoside in kiwi fruit (Lee et al., 2011). These compounds may be achieved by two mechanisms. Firstly, the extracts may cause more glucose to be utilized by the body and secondly, it may stimulate the release of insulin (Eidi et al., 2009) or may be due to stimulate insulin sensitivity (Ble-Castillo et al., 2010). On the other hand, the hypoglycemic effect is presumably due to an increase in glucose consumption by the peripheral tissues (Chattopadhyay, 1996). Extracts may cause inhibition of intestinal absorption of glucose (Pari and Saravanan, 2002).

Table 2.Effect of 80% acetone extracts of tested plant by-products on glucose level and α-amylase activity

Glucose level			
Groups	**Level (mg/dl)**	**Changes relative to normal control %**	**Improvement%**
Nor. Contol	$100.60^{b} \pm 7.30$	100.00	----
Dia. +VeControl	$368.80^{a} \pm 30.82$	366.60	----
Nor. KPE	$88.40^{b} \pm 8.38$	87.87	----
Nor. BPE	$93.20^{b} \pm 12.15$	92.64	----
Nor. BLE	$97.40^{b} \pm 10.09$	96.82	----
Nor. OLE	$78.60^{b} \pm 4.67$	78.13	----
Dia. KPE	$92.00^{b} \pm 17.35$	91.45	275.15
Dia. BPE	$99.40^{b} \pm 8.96$	98.81	267.97
Dia. BLE	$105.80^{b} \pm 10.35$	105.17	261.43
Dia. OLE	$84.00^{b} \pm 8.94$	83.50	283.10
Dia. Drug	$94.20^{b} \pm 12.64$	93.64	272.96
α-Amylase activity	**activity (U/L)**		
Nor. Control	$246.62^{b} \pm 30.78$	100.00	----
Dia. +VeControl	$318.74^{a} \pm 15.97$	129.24	----
Nor. KPE	$244.47^{b} \pm 7.02$	99.13	----
Nor. BPE	$247.70^{b} \pm 23.64$	100.44	----
Nor. BLE	$252.00^{b} \pm 42.44$	102.18	----
Nor. OLE	$248.77^{b} \pm 18.09$	100.87	----
Dia. KPE	$249.85^{b} \pm 22.96$	101.31	27.93
Dia. BPE	$253.08^{b} \pm 12.39$	102.62	26.62
Dia. BLE	$257.39^{b} \pm 21.99$	104.36	24.88
Dia. OLE	$247.70^{b} \pm 9.78$	100.44	28.81
Dia. Drug	$255.23^{b} \pm 18.41$	103.49	25.75

All values represented as mean ± S.D.
Means with different letters are significantly different ($p<0.05$).
(Nor.): normal, (Dia.): diabetic, (Con.) control, (KPE): kiwi peels extract, (BPE): banana peels extract, (BLE): banana leaves extract and (OLE): olive leaves

Furthermore, olive leaves extract was found to inhibit the activities of α-amylases from human saliva and pancreas. In animal models the hypoglycemic effect of olive leaves may be facilitated through the reduction of starch digestion and absorption (Wainstein et al., 2012).

Effect of 80% acetone extracts of tested plantby-products on lipid profile

Diabetes is associated with hyperlipidemia (Maiti et al., 2005). Hyperlipidemia is a condition excess of fatty substances, lipids, largely cholesterol and triglycerides, in blood. It is also called "hyper lipoproteinemia" because these fatty substances travel in the blood after attachment to proteins such as the best-known lipoproteins are LDL (low-density lipoprotein) and HDL (high-density lipoprotein). This is the only way that these fatty substances can remain dissolved in blood circulation (Harikumar et al., 2013).

The data in Table (2) showed high level of total lipid (970.37 mg/dl) and triglycerides (176.92 mg/dl) in diabetic rats compared to normal control one (574.07 and 110.26 mg/dl, respectively).Olive leaves showed the highest percentage of improvement in total lipid (62.58%) and triglycerides (48.37%), while banana leaves showed the lowest percentage of improvement in total lipid (35.48%) and triglycerides (42.33%), compared to anti-diabetic standard drug (50.97 and 44.20%, respectively).Data in Table (3) showed highest level of total cholesterol (208.46mg/dl) and lowest HDL-C (39.40 mg/dl) in diabetic rats, compared to normal control onewhichrecorded143.85 and 55.16mg/dl, respectively ($p\leq0.005$). No significant difference was noticed between normal control rats and normal rats treated with the four different treatments.

Table 3.Effect of 80% acetone extracts of tested plant by-products on total lipid (TL) and triglyceride (TG).

Total lipid level			
Groups	**Level (mg/dl)**	**Changes relative to normal control %**	**Improvement%**
Nor. Con	$574.07^{c} \pm 79.65$	100.00	----
Dia. +VeCon	$970.37^{a} \pm 21.11$	169.03	----
Nor. KPE	$585.19^{c} \pm 82.40$	101.94	----
Nor. BPE	$607.41^{bc} \pm 27.47$	105.81	----
Nor. BLE	$625.93^{bc} \pm 63.34$	109.03	----
Nor. OLE	$588.89^{c} \pm 69.78$	102.58	----
Dia. KPE	$633.33^{bc} \pm 33.12$	110.32	58.71
Dia. BPE	$648.15^{bc} \pm 34.64$	112.90	56.13
Dia. BLE	$766.67^{b} \pm 95.87$	133.55	35.48
Dia. OLE	$611.11^{bc} \pm 39.28$	106.45	62.58
Dia. Drug	$677.78^{bc} \pm 89.39$	118.06	50.97
Triglycerides level			
Nor. Con	$110.26^{c} \pm 12.16$	100.00	----
Dia.+Ve Con	$176.92^{a} \pm 4.05$	160.47	----
Nor. KPE	$112.82^{bc} \pm 10.57$	102.33	----
Nor. BPE	$115.38^{bc} \pm 14.39$	104.65	----
Nor. BLE	$117.44^{bc} \pm 4.93$	106.51	----
Nor. OLE	$114.36^{bc} \pm 6.93$	103.72	----
Dia. KPE	$124.10^{bc} \pm 10.32$	112.56	47.91
Dia. BPE	$126.67^{bc} \pm 3.34$	114.88	45.58
Dia. BLE	$130.26^{b} \pm 9.14$	118.14	42.33
Dia. OLE	$123.59^{bc} \pm 8.99$	112.09	48.37
Dia. Drug	$128.21^{bc} \pm 8.11$	116.28	44.20

All values represented as mean ± S.D.
Means with different letters are significantly different ($p<0.05$).
(Nor.): normal, (Dia.): diabetic, (+VeCon.) control, (KPE): kiwi peels extract, (BPE): banana peels extract, (BLE): banana leaves extract and (OLE): olive leaves extract

The improvement percentages were high in olive leaves extract (41.18% for TC and 24.40% for HDL-C) and low in banana leaves (31.02% for TC and 18.45% for HDL-C) compared to standard drug which showed 38.50 and 25.00%, respectively. Olive leaves showed the highest improvement for lipid profile followed by banana peels > kiwi peels > banana leaves.

The changed values of lipid profile from normal rats to diabetic rats may be due to low activity of cholesterol biosynthesis enzymes or low level of lipolysis that are under the control of insulin (Sharma et al., 2003). The results are in a good agreement with Shehata and Soltan (2013); Kumar et al., (2012) and Husni (2015) for kiwi, banana and olive leaves, respectively, they reported that the dietary fiber component in samples was responsible for its hyperlipidemia lowering effect. The fiber reduced the gastric emptying rate and makes it possible for rats to feel full, which delaying the absorption and digestion of nutrients and reduced feed intake. On the other hand, reduction in the level of total cholesterol may be due to inhibit cholesterol synthesis paralleled with the inhibition of 3-Hydroxy-3-methylglutary1 (HMG)COA reduced activity or degradation of cholesterol in the intestine by certain bacterial metabolites (Champe et al., 2005).

Effect of 80% acetone extracts of tested plant by-products on liver functions of diabetic and treated groups

Determination of ALT, AST and ALP activities

The role of liver in developing type 2 diabetes has attracted much interest. Furthermore, it is thought that abnormal function of liver attributed to insulin-resistance syndrome may lead to development of type 2 diabetes (Marchesini et al., 2001). The excess in free fatty acids found in the insulin resistance state is known to be precisely toxic to hepatocytes. Putative mechanisms include cell membrane disruption at high concentration, mitochondrial dysfunction, toxin formation and activation and inhibition of key steps in the regulation of metabolism (Neuschwander and Caldwell, 2003).

Liver function test is assessed through using liver enzymes aspartate aminotransferase (AST), alanine aminotransferase (ALT), and alkaline phosphatase (ALP). Both AST and ALT are considered markers of hepatocellular health. ALT is considered the most specific biomarker of liver pathology and is found mainly in liver (Lee et al., 2004). Because AST and ALP can be found in other tissues, they are thought to be less specific biomarkers of liver function (Lee et al., 2003).

Hepatic ALT, AST (U/ml) and ALP (U/L) activities were increased significantly in diabetic rats (176.00, 231.58 U/ml and 163.44 U/L, respectively) compared to normal control rats (81.70, 141.21 U/ml and 94.71 U/L, respectively) as presented in Tables (4,5) . These enzymes were restored towards the control level after the treatments with acetone extracts of the four byproducts. Liver biomarkers showed the highest improvement in diabetic rats by treatments with olive leaves for ALT (103.74%), kiwi peels for AST (62.18%) and banana leaves for ALP (71.49%) compared to drug 111.82, 60.54 and 71.18 %, respectively.The present results have the same trend with those reported by Shehata and Soltan (2013); Kaimal et al., (2010) and Mousa et al.,(2014) for kiwi, banana and olive leaves, respectively. They suggested that the various compounds such as flavonoids and other polyphenols, terpenoids, glycosides and phytosterols present in the extracts might have exerted synergistic effect. This in turn protected hepatic tissue from oxidative injury associated with diabetes mellitus. The authors observed decreases in AST and ALT activities and increases in the serum insulin for diabetic rats but not for normal rats.

Total bilirubin

Table (6) demonstrated the level of bilirubin and total protein content in the serum of the experimental groups. Bilirubin is used as a marker of cholestasis and is believed to be a toxic waste metabolite of heme catabolism (Foresti and Motterlini, 2014). However, several studies have reported that bilirubin plays a protective role in cardiovascular and metabolic diseases (Lin et al., 2004 and Vitek, 2012). On the other hand, hyperglycemia induced oxidative stress which is known to be a component of molecular and cellular tissue damage (Nalini et al., 2011). Indeed, bilirubin has been shown to be more effective at protecting lipids from oxidation than the water soluble antioxidants such as glutathione, which primarily protect proteins from oxidation (Sedlak et al., 2009).However, bilirubin has also been demonstrated to be almost 30 times more potent toward the prevention of LDL-C oxidation compared to vitamin E (Yesilova et al., 2008).The level of bilirubin in serum was significantly increased in diabetic control rats (1.16 mg/dl) compared to normal control rats (0.64 mg/dl) and normal rats by treatment with the four extracts. The values were ranged from 0.63 to 0.69 mg/dl. After acetone extract treatments of diabetic rats, hence the percentage improvements were ranged from 71.21 to 83.16% compared to drug 80.53%.While, significant reduction in the serum total protein content was recorded (3.67 g/dl), when compared with normal control group (5.59 g/dl) or normal rats groups treated with the extracts (4.92 to 5.32 g/dl). The highest improvements in both total bilirubin and protein values (83.16 and 30.25%) were observed after treatment with olive leaves extract. These results are in a good agreement with Mahboob et, al. (2005), who found a relation between protein content and elevated lipid peroxidation process and decreased antioxidant defensive system in serum of diabetic patients. Insulin generally has an anabolic effect on protein by stimulation of protein synthesis and retards protein degradation (Murray et al., 2000). Protein synthesis was found to be decreased in all tissues due to decreased production of ATP in absolute or relative deficiency of insulin (Chatterjee et al., 1994).These results indicated the effectiveness of the tested extracts in ameliorating STZ -induced toxicity. The possible mechanism may be attributed to their antioxidant properties of byproduct extracts. Moreover, most of bioactive compounds (especially flavonoids and triterpenoids such as ursolicacid) showed a mechanism to improve hepatic and pancreas cells functions and hence normalized liver enzymes as reported by Zheng et al., (2007) and Gilani et al., (2009).

Effect of 80% acetone extract of the tested plant by-products on VCAM and ICAM1 levels

Cell Adhesion Molecules (CAMs) are proteins, with a molecular weight of 95–110 kDa, located on the cell surface involved in binding with other cells or with the extracellular matrix (ECM) in the process called cell adhesion. In essence, cell adhesion molecules help cells stick to each other and to their surroundings (Shimaoka et al., 2003).

Table 4.Effect of 80% acetone extracts of tested plant by-products on TC and HDL-C.

Total cholesterol level			
Groups	**level (mg/dl)**	**Changes relative to normal control%**	**Improvement%**
Nor. Con	$143.85^{b} \pm 22.85$	100.00	----
Dia. +VeCon	$208.46^{a} \pm 9.18$	144.92	----
Nor. KPE	$142.31^{b} \pm 8.16$	98.93	----
Nor. BPE	$146.15^{b} \pm 16.09$	101.60	----
Nor. BLE	$152.31^{b} \pm 7.98$	105.88	----
Nor. OLE	$146.15^{b} \pm 11.21$	101.60	----
Dia. KPE	$154.62^{b} \pm 16.41$	107.49	37.43
Dia. BPE	$158.46^{b} \pm 5.01$	110.16	34.76
Dia. BLE	$163.85^{b} \pm 8.43$	113.90	31.02
Dia. OLE	$149.23^{b} \pm 15.72$	103.74	41.18
Dia. Drug	$153.08^{b} \pm 5.70$	106.42	38.50
HDL-C level			
Nor. Con	$55.16^{a} \pm 3.20$	100.00	----
Dia.+Ve Con	$39.40^{b} \pm 1.30$	71.43	----
Nor. KPE	$53.36^{a} \pm 3.48$	96.73	----
Nor. BPE	$52.37^{a} \pm 3.82^{a}$	94.94	----
Nor. BLE	$50.57^{a} \pm 1.16$	91.67	----
Nor. OLE	$54.67^{a} \pm 2.90$	99.11	----
Dia. KPE	$51.88^{a} \pm 2.75$	94.05	22.62
Dia. BPE	$50.07^{a} \pm 2.09$	90.77	19.35
Dia. BLE	$49.58^{a} \pm 8.36$	89.88	18.45
Dia. OLE	$52.87^{a} \pm 3.10$	95.83	24.40
Dia. Drug	$53.19^{a} \pm 3.20$	96.43	25.00

All values represented as mean ± S.D.Means with different letters are significantly different ($p<0.05$).
(Nor.): normal, (Dia.): diabetic, (Con.) control, (KPE): kiwi peels extract, (BPE): banana peels extract, (BLE): banana leaves extract and (OLE): olive leaves extract.

Table 5.Effect of 80% acetone extracts of plant by-products tested on ALT and AST enzyme activities

ALT activity			
Groups	**activity (U/ml)**	**Changes relative to normal control %**	**Improvement %**
Nor. Con	81.70c ± 7.46	100.00	----
Dia. +VeCon	176a ± 18.15	215.43	----
Nor. KPE	86.38bc ± 3.79	105.73	----
Nor. BPE	88.26bc ± 2.62	108.04	----
Nor. BLE	92.87bc ± 7.86	113.67	----
Nor. OLE	84.94b ± 5.64	103.97	----
Dia. KPE	102.42b ± 12.41	125.36	90.07
Dia. BPE	91.96bc ± 4.39	112.56	102.86
Dia. BLE	96.91bc ± 7.89	118.61	96.81
Dia. OLE	91.25bc ± 6.33	111.69	103.74
Dia. Drug	84.64bc ± 10.73	103.60	111.82
ASTactivity			
Nor. Con	141.21b ± 10.55	100.00	----
Dia. +VeCon	231.58a ± 23.25	164.00	----
Nor. KPE	147.21b ± 3.49	104.25	----
Nor. BPE	150.00b ± 4.97	106.23	----
Nor. BLE	150.79b ± 3.04	106.79	----
Nor. OLE	142.51b ± 7.17	100.92	----
Dia. KPE	142.88b ± 10.37	101.19	62.81
Dia. BPE	153.72 b ± 15.94	108.86	55.14
Dia. BLE	158.84b ± 6.41	112.48	51.52
Dia. OLE	149.86b ± 3.44	106.13	57.87
Dia. Drug	146.09 b ± 10.86	103.46	60.54

All values represented as mean ± S.D.Means with different letters are significantly different ($p<0.05$).
(Nor.): normal, (Dia.): diabetic, (+VeCon.) control, (KPE): kiwi peels extract, (BPE): banana peels extract, (BLE): banana leaves extract and (OLE): olive leaves extract.

Table 6.Effect of 80% acetone extracts of plant by-products tested on ALP enzyme activity

Groups	**ALP activity (1U/L)**	**Changes relative to normal control %**	**Improvement %**
Nor. Con	94.71^{b} ± 1.91	100.00	----
Dia. +VeCon	163.44^{a} ± 15.44	172.57	----
Nor. KPE	98.61^{b} ± 2.96	104.12	----
Nor. BPE	100.17^{b} ± 6.44	105.76	----
Nor. BLE	97.11^{b} ± 1.68	102.53	----
Nor. OLE	95.88^{b} ± 4.61	101.24	----
Dia. KPE	99.48^{b} ± 6.60	105.04	67.53
Dia. BPE	103.47^{b} ± 12.52	109.25	63.32
Dia. BLE	98.74^{b} ± 9.90	101.08	71.49
Dia. OLE	97.65^{b} ± 9.03	103.67	68.89
Dia. Drug	96.03^{b} ± 11.50	101.39	71.18

All values represented as mean ± S.D.Means with different letters are significantly different ($p<0.05$).
(Nor.): normal, (Dia.): diabetic, (+VeCon.) control, (KPE): kiwi peels extract, (BPE): banana peels extract, (BLE): banana leaves extract and (OLE): olive leaves extract.

Table 7. Effect of 80% acetone extracts of tested plant by-products on serum total bilirubin level

Bilirubin level			
Groups	**Level (mg/dl)**	**Changes relative to normal control %**	**Improvement %**
Nor. Con	$0.64^{b} \pm 0.06$	100.00	----
Dia.+Ve Con	$1.16^{a} \pm 0.11$	182.07	----
Nor. KPE	$0.65^{b} \pm 0.06$	102.77	----
Nor. BPE	$0.67^{b} \pm 0.03$	105.05	----
Nor. BLE	$0.69^{b} \pm 0.08$	108.57	----
Nor. OLE	$0.63^{b} \pm 0.05$	98.86	----
Dia. KPE	$0.67^{b} \pm 0.02$	105.89	76.18
Dia. BPE	$0.70^{b} \pm 0.07$	109.63	72.44
Dia. BLE	$0.71^{b} \pm 0.05$	110.86	71.21
Dia. OLE	$0.63^{b} \pm 0.05$	98.90	83.16
Dia. Drug	$0.65^{b} \pm 0.05$	101.54	80.53

All values represented as mean ± S.D.Means with different letters are significantly different ($p<0.05$).
(Nor.): normal, (Dia.): diabetic, (+Ve Con.) control, (KPE): kiwi peels extract, (BPE): banana peels extract, (BLE): banana leaves extract and (OLE): olive leaves extract

Table 8.Effect of 80% acetone extracts of tested plant by-products on VCAM and ICAM-1 levels

VCAM level			
Groups	**(ηg/ml)**	**Changes relative to normal control %**	**Improvement%**
Nor. Con	$9.10^{e} \pm 0.14$	100.00	----
Dia. +VeCon	$21.87^{a} \pm 0.29$	240.24	----
Nor. KPE	$9.51^{e} \pm 0.57$	104.43	----
Nor. BPE	$10.29^{de} \pm 0.52$	113.07	----
Nor. BLE	$10.77^{de} \pm 0.72$	118.31	----
Nor. OLE	$9.40^{e} \pm 0.49$	103.26	----
Dia. KPE	$10.71^{de} \pm 0.53$	117.61	122.63
Dia. BPE	$13.70^{bc} \pm 0.46$	150.46	89.78
Dia. BLE	$13.94^{b} \pm 0.48$	153.09	87.15
Dia. OLE	$11.72^{d} \pm 1.51$	128.78	111.46
Dia. Drug	$11.99^{cd} \pm 0.10$	131.67	108.57
ICAM-1 level			
Nor. Con	$4.80^{f} \pm 0.41$	100.00	----
Dia.+VeCon	$24.01^{a} \pm 1.62$	499.93	----
Nor. KPE	$6.99^{ef} \pm 0.77$	145.52	----
Nor. BPE	$6.92^{ef} \pm 0.46$	144.07	----
Nor. BLE	$8.74^{e} \pm 0.52$	182.03	----
Nor. OLE	$5.18^{f} \pm 0.77$	107.84	----
Dia. KPE	$18.89^{bc} \pm 0.79$	393.20	106.73
Dia. BPE	$20.90^{b} \pm 0.67$	435.05	64.89
Dia. BLE	$20.13^{bc} \pm 0.49$	419.15	80.78
Dia. OLE	$18.09^{c} \pm 0.49$	376.54	123.39
Dia. Drug	$14.37^{d} \pm 1.00$	299.24	200.69

All values represented as mean ± S.D.Means with different letters are significantly different ($p<0.05$).
(Nor.): normal, (Dia.): diabetic, (+VeCon.) control, (KPE): kiwi peels extract, (BPE): banana peels extract, (BLE): banana leaves extract and (OLE): olive leaves extract**.**

These proteins are typically trans membrane receptors and composed of three domains: 1- intracellular domain that interacts with the cytoskeleton, 2- trans membrane domain, and 3- extracellular domain that interacts either with other CAMs of the same kind (hemophilic binding) or with other CAMs of the extracellular matrix (hetrophilic binding) (Brackenbury et al., 1981). ICAM-1 (intercellular adhesion molecules) also known as CD54 (Cluster of Differentiation 54) is a protein that in humans is encoded by the ICAM1 gene (Katz *et al.*, 1985 and Carlson et al., 1988), which is a type of intercellular adhesion molecule continuously present in low concentrations in the membranes of leukocytes and endothelial cells. Vascular cell adhesion protein 1 also known as vascular cell adhesion molecule 1 (VCAM-1) or cluster of differentiation 106 (CD106) is a protein that in humans is encoded by the VCAM1 gene which contains six or seven immunoglobulin domains, and is expressed on both large and small blood vessels only after the endothelial cells are stimulated by cytokines (Cybulsky et al., 1991). The VCAM-1 protein mediates the adhesion of lymphocytes, monocytes, eosinophils, and basophils to vascular endothelium. It also functions in leukocyte-endothelial cell signal transduction, and it may play a role in the development of atherosclerosis (Myron et al., 2001), and rheumatoid arthritis (Fougerolles et al., 2000). Certain melanoma cells can use VCAM-1 to adhere to the endothelium, and VCAM-1 may participate in monocyte recruitment to atherosclerotic sites. As a result, VCAM-1 is a potential drug target (Yonekawa and Harlan, 2005).

Table (7) shows the effect of four tested acetone extracts on levels of VCAM and I-CAM and their levels in diabetic rats were 21.87 and 24.01ηg/ml, respectively compared to control group which showed values of 9.10 and 4.80 ηg/ml, respectively. Normal rats groups after the extracts administration had values ranged from 9.40 to 10.77 ηg/ml for V-CAM and from 5.18 to 8.74 ηg/ml for I-CAM1. These high levels of both CAMs in diabetic rats declared the initiation of inflammatory process; hence inflammation emerges to be independent risk factor for the development of atherosclerosis (Borai et al., 2015). Large evidence has shown strong associations of circulating levels of endothelial adhesion molecules with insulin resistance in non-diabetic individuals or with type 2 diabetic patients (Cui and Song, 2009). Insulin resistance might be related to endothelial dysfunction (Targher et al., 2000). This is may be due to insulin enhances nitric oxide production within the endothelial cells hence nitric oxide modulates a number of endothelial functions, including the expression of adhesion molecules (Moncada et al., 2002).

Diabetic groups under treatment with kiwi peels extract exhibited the highest percentage of improvement (122.63%) compared to drug treated animals which showed 108.57% for V-CAM and also showed 123.39% with olive leaves extract for ICAM-1 compared to drug treated which showed 200.69%(Table 8).

These results could be contributed to polyphenols and flavonoids components of the samples, which have therapeuticanti-inflammatory tools in inflammatory diseases including obesity and type II diabetes, cardiovascular diseases, neurodegenerative diseases, cancer and aging (Santangelo et al., 2007).

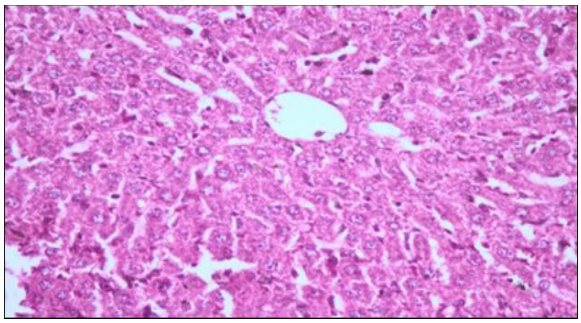
Histopathological examination of hepatic rats

Histopathological examination of liver sections of rats from normal control rats (Photomicrograph 1) showed healthy hepatic cords and blood sinusoids. The treatments with the four plants extract on normal rat groups showed nohistopathological changes except for slightly congested central vein with kiwi peels extract (Photomicrograph 2)

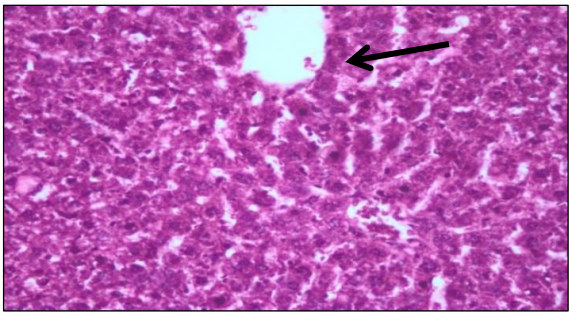
,**banana peels showing apparently healthy hepatic cords and blood sinusoids (H&E X 400**)(Photomicrographs 3 &4),and slight congested blood sinusoids with olive leaves extract (Photomicrograph 5). Diabetic control group (Photomicrograph 6) showed focal aggregation of mononuclear cells and congestion of hepatic sinusoids.

On the other hand, diabetic rat after treatments showed no histopathological changes except for slightly focal congested blood sinusoids with kiwi peels extract (Photomicrograph7) ,

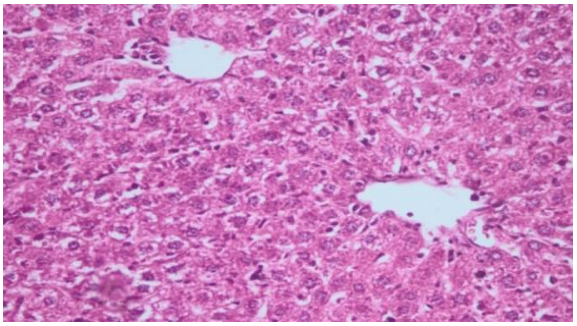
banana peels and leaves showing apparently healthy hepatic cords and blood sinusoids (H&E X 400) (Photomicrographs 8,9**),** severely congested hepatoportal blood vessels with olive leaves extract (Photomicrograph10). Diabetic rats treated with drug demonstrated severe congested central vein and blood sinusoids (Photomicrograph11).



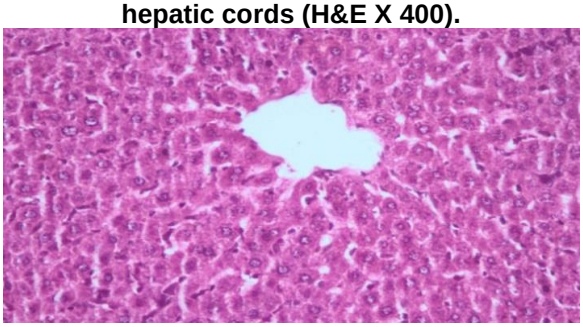
Photomicrograph 1.Liver of normal control rats showing apparently healthy hepatic cords and blood sinusoids (H&E X 400).



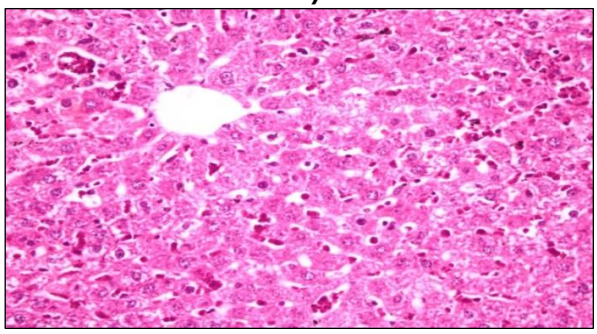
Photomicrograph 2.Liver of normal rats treated with kiwi peels extract showing slightly congested central vein (arrow) with normal hepatic cords (H&E X 400).



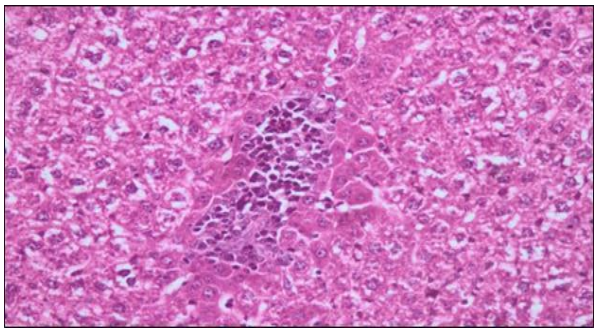
Photomicrograph 3 Liver of normal control rats of banana peels showing apparently healthy hepatic cords and blood sinusoids (H&E X 400).



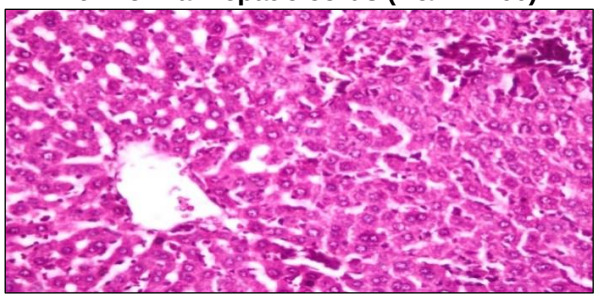
Photomicrograph 4 Liver of normal control rats of banana leaves showing apparently healthy hepatic cords and blood sinusoids (H&E X 400).



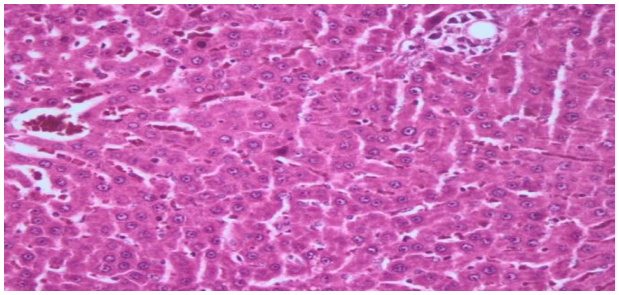
Photomicrograph 5. Liver of normal rats treated with olive leaves extract showing slightly congested blood sinusoids (arrow) with normal hepatic cords (H&E X 400).



Photomicrograph 6. Liver of diabetic rats showing focal aggregation of mononuclear cells (arrow) (H&E X 400).

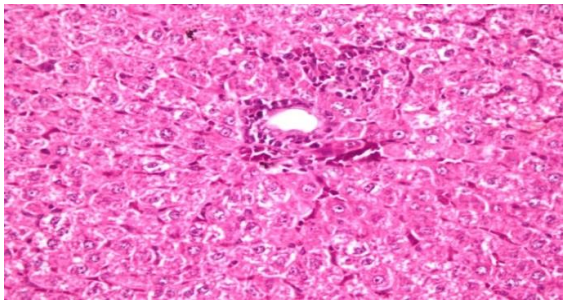


Photomicrograph 7. Liver of diabetic rats treated with kiwi peels extract showing



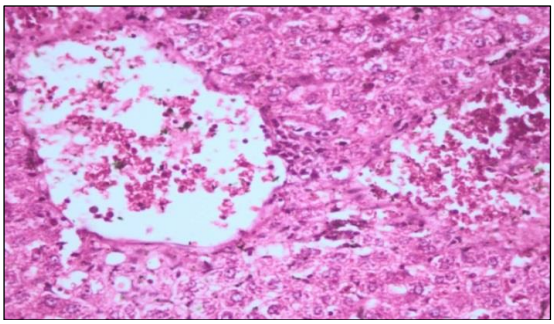
Photomicrograph 8. Liver of diabetic rats of banana peels showing apparently healthy

apparently healthy hepatic cords with slightly focal congested blood sinusoids (arrow), (H&X400)

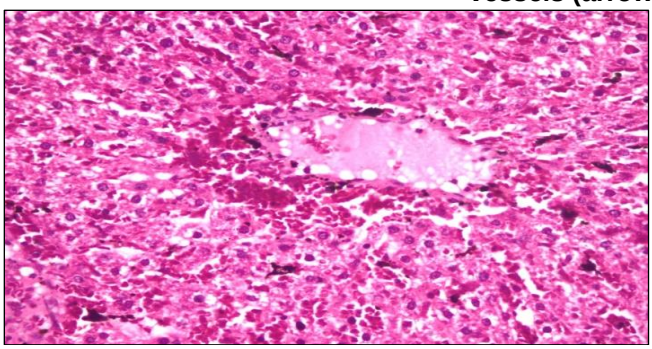


Photomicrograph 9. Liver of diabetic rats of banana leaves showing apparently healthy hepatic cords and blood sinusoids (H&E X 400).

hepatic cords and blood sinusoids (H&E X 400).



Photomicrograph 10. Liver of diabetic rats treated with olive leaves extract showing severely congested hepatoportal blood vessels (arrows) (H&E X 400).



Photomicrograph 11. Liver of diabetic rats treated with drug showing Severely congested central vein (arrow head), and blood sinusoids (arrows) (H&E X 400).

The present focal aggregation of mononuclear cells and congestion of hepatic sinusoids liver in diabetic rats may be due to STZ is diabetogenic, hepatotoxic, nephrotoxic and also causes gastric ulceration (Piyachaturawat et al., 1988 and Piyachaturawat et al., 1990). Also, attention has long centered on the liver in diabetes mellitus because of the importance of this organ in carbohydrate metabolism and regulation of blood sugar (Salih et al., 2009). Nanji et al., 1986) and Hamilton (1987) revealed the occurrence of hepatic changes in some cases of diabetic patients. Liver biopsy showed an accumulation of fats into the hepatocytes, lead to a significant increase in liver weight. Also, liver enlargement has been indicated in experimental diabetic rats (Cefalu et al., 1991).

CONCLUSION

From the previous results it could be concluded that supplementation diet with fresh or dried banana, kiwi peels and banana and olive leaves may be useful for acute liver failure patients, and it could be develop the retarded liver function and lipid profile of them.

CONFLICT OF INTEREST

The authors declared that present study was performed in absence of any conflict of interest.

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