BIOLOGICAL EFFECT OF GINGER (*ZINGIBER OFFICINALE ROSCOE*) ON DIABETIC PREGNANT AND LACTATING RATS.

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ABSTRACT

Biochemical and histological effects of ginger as a hypoglycemic agent in diabetic albino pregnant rats were investigated.

Water extract of ginger was analyzed for phenolic acid determination by HPLC. Ginger essential oil was also analyzed for its volatile components using GC-MS.

A total of 35 pregnant albino rats were divided into 7 groups. Group 1 normal healthy control. Group 2 diabetic control which injected with Streptozotocin (STZ) (50mg/kg b.w.) to induce diabetes. Group 3 diabetic rats induced 2gm ginger powder rhizomes/100g diet. Group 4 diabetic rats injected with 3 ml water extract of ginger. Group 5 diabetic rats injected with 0.3 ml essential ginger oil. Group 6 diabetic rats injected with 0.3 ml commercial ginger oil. Group 7 diabitic rats injected with 80mg dimecron drug. Glucose, prolactin, lipids profile as well as kidney and liver function were determined in serum. The result showed that ginger water extract had several phenolic compounds. The main of compounds were sakaruntin, lutolin, rutin, querecetrin and hyperosaid, these were naturally. GC-MS identified 61 compounds in the essential oil of ginger, of which the major compounds were sesquiterpene, geraniol and farnosen. The results also showed that the ginger in forms of powder, water extract or essential oil significantly ($P<0.05$) reduced glucose, total lipids, triglycerides, total cholesterol, creatinine, urea and uric acid contents as well as the activity of transaminase (GPT and GOT), alkaline phosphates (ALP) in blood of diabetic pregnant albino rats. However, an increase in total protein and albumin/globulin ratio were found compared with the control under the same conditions.

Microscaoically, ginger administrated in diabetic pregnant albino rats showed no histopathological changes in stomach, liver, kidneys and heart compared with the control.

INTRODUCTION

Ginger (*Zingiber officinale* Rosce) is an important aromatic and medicinal plant. It has been used for the traditional Chinese and Indian pharmacopeia and medicinal purposes as well as in food as a spice (Nicoll and Henein, 2007) .More recently, many review have been devoted to specific aspects of gingers actions i.e. for its effects on the cardiovascular system (Suekawa *et al.,* 1986) ,as antimicrobial and antiviral (Mascolo *et al.,* 1989); for its efficacy on nausea and vomiting (Ernst and Pittler., 2000) , use as anti-inflammatory agent (Grzanna *et al*., 2005); and on the cancer prevention properties (Shukla and Singh, 2007) . Other general uses of ginger were its effects on the increases of relative weight of the testis, the serum testosterone level, the testicular cholesterol level and epididymal α–glucoside activity (Kamtchouing *et al.,* 2002).

Some studies have shown that ginger is effective in reducing ulcer stress-induced gastric lesions in rats and in preventing ulcer activity (Sertie *et al.,* 1991).These broad spectrum of the biological effects of ginger possible due to containing the plant various chemical compounds. The review by (Chrubasik *et al.,* 2005) have shown that crude ginger contains up to 9% lipids or glycolipids and about 5-8% oleoresin, and 3% essential oil.

Gas chromatography/mass spectrometry identified 66 compounds in the essential oil of ginger. Recently, sulfonated compounds and shogasulfonic acids A, B, C (Hori *et al.,* 2003) as well as diterpenoid galanolactone glycosides of geraniol – related compounds (Sekiwa *et al.,* 2001) were identified in the crude plant material. As ginger contains a number of coactive constituents, which perse (or after structural modification) might be potentially useful in the treatment of various diseases.

Therefore, the objective of the present study is to investigate the biological and histological effects of ginger on the pregnant rats infected with diabetes disease.

MATERIALS AND METHODS

1-Materials

1. Rhizomes ginger (*Zinigber officinale Roscoe*) from local market.
2. Water extract of ginger.
3. Essential oil of ginger.
4. Ginger oil natural from El-Haway factory for row oils.
5. Dimecron drug from pharmacy.
6. Streptozotocin (STZ) from Sigma.

2-Methods:

Preparation of studied diets:

Ginger was purchased from local market coarsely minced, air dried and pulverized with a blender to a fine powder and added as 2 gm / 100 gm diet.

Preparation of water extract of ginger:

Ginger powder (50gm) was soaked in one liter of distilled water for 12 hr, and then filtered to obtain the extract according to the method of Ozsoy-Socan *et al.* (2006). The extract was stored at -20ºC until used for separation and identification of chemical components of water extract by the method of Hertoy *et al.* (1992).

Extraction of essential oil from ginger:

The essential oil of ginger was obtained by water distillation in a glass apparatus for 6 hrs. the separated volatile oil was dried over anhydrous sodium sulphate before hold in glass bottles at -20ºC according to Guenther (1961).

Separation and identification of chemicals compounds of essential oil:

The gas chromatography/ mass spectrometry technique was used to identify the chemical compounds of ginger essential oil according to the method of Badee *et al*, (2005) .

3-Animals and experimental diets:

A total of 35 pregnant albino rats (240-250gm weight) were divided randomly into 7 groups, each group contain 5 rats

Group 1 (normal control) fed on the basal diet (casein 15%, vitamin mixture 1%, mineral mixture 4%, oil 10%, starch 65% and cellulose 5%) according to Philip *et al.* (1993).

Group 2 diabetic control fed on basal diet (diabetes was induced into the pregnant rats by injection of STZ [50mg/kg, b.w.] dissolved in 0.1 M citrate buffer, pH 7.4) according to Ozdemir *et al.* (2005).

Group 3 diabetic rats which fed on basal diet with ginger powder rhizomes (2gm/100gm diet).

Group 4 diabetic rats fed on basal diet with injection of 3 ml water extract by stomach tube daily.

Group 5 diabetic rats fed on basal diet injected with 0.3 ml essential ginger daily oil by stomach tube.

Group 6 diabetic rats fed on basal diet injected with 0.3 ml natural ginger oil daily by stomach tube.

Group 7 diabetic rats fed on basal diet injected with 80 mg dimecron drug / 100gm diet daily by stomach tube.

Table (1) showed the experimental groups and diets:

Table (1) Experimental groups and diets

Groups	Content	Casin 15%	Vitmix 1%	Min Mix 4%	Oil 10%	Starch 65%	Cellulose 5%	Ginger Powder (g)	Water extract (ml)	Essential Oil (ml)	Ginger oil natural (ml)	Drugs
1	Normal control	15	1	4	10	65	5	-	-	-	-	-
2	Diabetic control	15	1	4	10	65	5	-	-	-	-	-
3	Diabetic Rhizome	15	1	4	10	65	5	2	-	-	-	-
4	Diabetic Water extract	15	1	4	10	65	5	-	3ml/day	-	-	-
5	Diabetic Essential oil	15	1	4	10	65	5	-	-	0.3 ml/day		-
6	Diabetic commercial Ginger oil	15	1	4	10	65	5	-	-		0.3ml/day	-
7	Diabetic Drugs	15	1	4	10	65	5	-	-	-	-	80mg

4- Blood samples:

Experimental rats were taken from orbital plexus venous by using fin capillary glass tube. Blood samples were allowed to clot for one min. at 37ºC and centrifuged at 3000 rpt for 5 min. and the separated serum was kept frozen at -20ºC until analysis.

5- Biochemical measurements:

Glucose was determined by enzymatic colorimetric method according to Barham and Trined (1972).

Prolactin was determined according to Sewender, (1995).

Total lipids were determined by enzymatic colorimetric method according to Zollener and Kirsch (1962).

Triglycerides and total cholesterol were determined by enzymatic colorimetric method according to Trinder (1969).

High density lipoprotein cholesterol (HDL) and low density lipoprotein cholesterol (LDL) were determined according to Assman (1979).

Glutamic pyrovic transaminase (GPT), Glutamic oxaloacetic transaminase (GOT) activities were determined by colorimetric methods according to Reitman and Frankel (1957).

Alkaline phosphates (ALP) activity was measured at 405 nm by the method of Kind and King (1954).

Total protein (Tp) was analyzed using the method of Henry (1964).

Albumin concentration was determined by the method of Doumas *et al.* (1971). Globulin concentration was calculated by the difference between total protein and albumin.

Creatinine, urea and uric acid were determined according to Caraway's method (1975).

6- Histopathological examination:

Samples from liver, kidney, stomach and heart were collected from rats in all groups at the end of the experiment (8 weeks), fixed in 10% bufferd, formalin dehydrated in alcohol, cleared in xylol and embedded in parafin, 4M thick sections were

7- Statistical analysis:

The standard analysis of variance procedure in completely randomized design was applied for the present data according to Orkin and Drogin (1975) (LSD at 5%).

RESULTS AND DISCUSSION

The results observed that dried ginger contained 3.50% total phenolic compounds extracted by water and 1.75% total volatile essential oil. The HPLC analysis of ginger water extract showed 56 different concentration levels (Table 2). Chlorogenic lutolin, kmpferol and sakarlintin were detected and identified in ginger water extract. In connection, GC-MS analysis of essential oil compounds of ginger found 61 compounds with different concentrations also (Table 3). The analysis identified limonene as monocyclic terpens, linalyl acetate and

bornyl acetate as terpen ether, linalool, borneol, geraniol as alcohols, farnosen, trans-β-farnesene and β-bisabolene as sesquiterperne as well as neral-geraniol as aromatic hydrocarbons. Also, there were some unknown compounds.

Table (2): phenolic compounds of Ginger water extract fractionated and identified by HPLC technique.

Chemical components	Concentration mg/100 ml
Chlorogenic acid	130.27
Caffeic acid	73.31
Rutin	275.71
Hyperosaid	201.88
Querecetrin	150.11
Querecin	68.82
Lutolin	241.41
Kmpferol	53.87
Sakaruntin	87.49

Total Phenolic compounds = 3.50% D.W

Table (3) Chemical components of ginger essential oil fractionated and identified by GC/MS.

Chemical Components	mg/100g (D.W)ginger
1. Mono cyclic terpens (Limonene)	0.96
2. Terpenether	
* Linalyl acetate	14.52
* bornyl acetate	17.44
3. Alcohols	
*Linalool	19.15
*Borneol	6.31
*Geraniol	32.70
4. Farnosen	32.69
5. Sesquiterpene	
*Trans- β-farnesene	33.41
*B-bisabolene	30.11
6. Aromatic	
*hydro-carbones neral-geraniol	4.31
7. Unknown	12

Total essential oil = 1.75% ginger D.W.

In addition, these different antioxidant of phenolic and essential oil compounds which detected by HPLC and GC-MS respectively were accompanied with variations in their effectives hypoglycemic agents.

Data presented in table (4) show glucose and prolactein contents in the diabetic pregnant rats fed on the experimental diet. It was found that, at the end of the experimental period glucose content was increased significantly ($P<0.05$) in group 2 (diabetic control) than the other tested groups, followed by group-7 (dimecron drug), but group 6 (commercial oil ginger), group 5 (oil ginger and group 4 (water extract of ginger powder) had the followed contents. However, the lowest glucose content was found in group 3 (rhizomes ginger) relative to normal healthy control. There were an increase in glucose over the experimental period with distinguish increases in the period from week (1) to week (5) in all groups under study relative to group 1 (normal healthy rats) which remain almost conestant over the experimental period. For prolactein, variations among the studied groups were insignificant. Moreover, differences in prolactein over the experimental period among the examined groups were negligible.

Table (4): Determination of glucose and prolactein on diabetic pregnant rats feeding on the experimental diets.

Groups / Weeks	Glucose (mg/dl)					Prolacten(ng/ml)				
	Adapted rats	0	1	3	5	Adapted rats	0	1	3	5
1- N-control	95.13	95.27	96.12	96.13	95.18	0.95	0.93	0.92	0.92	0.79
2- Diabetic control	92.22	545.12	450.12	430.70	428.10	0.95	0.93	0.93	0.92	0.79
3- Diabetic Rhizome	95.15	450.13	210.12	195.08	187.17	0.96	1.00	1.20	1.10	0.80
4- Diabetic Water extract	95.15	390.22	215.91	198.13	190.12	0.95	1.40	1.30	1.50	0.80
5- Diabetic Essential oil	95.17	450.13	220.91	200.21	192.22	0.97	1.50	1.40	1.60	0.80
6- Diabetic commercial Ginger oil	95.17	450.18	320.99	200.55	195.23	0.95	1.30	1.40	1.50	0.80
7- Diabetic Drugs	95.17	450.91	299.19	300.15	210.22	0.95	0.88	0.82	0.85	0.80
LSD5%	Groups(G)= 17.66 Weeks(W)= 16.35 Int(GXW) = 43.26					Groups(G)= 0.04 Weeks (W)= 0.04 Int (GXW)= 0.11				

This finding reveals that powder ginger extracted with water, ginger rhizomes or oil ginger significantly lowered serum glucose

content in diabetic pregnant rats, While ginger (in all forms) had no effects on prolactein content.

The obtained results in agreement with Al-Amin *et al.* (2006). They found that ginger was significantly effective in reducing serum glucose level in the ginger-treated diabetic rats compared with the control diabetic rats. Therefore, Ali *et al.* (2008) suggested that ginger had significantly improved insulin sensitivity in treated mice.

Total lipids content was reduced significantly in diabetic pregnant rats after feeding on any of the ginger diet in comparison with group 2 (diabetic control) or group 1 (normal control) as shown in Table (5).

Table (5): Determination of total lipids and triglycerides in serum of diabetic pregnant rats feeding on the experimental diets.

Groups / Weeks	Total lipids (mg/dl)					Triglycerides (mg/dl)				
	Adapted rats	0	1	3	5	Adapted rats	0	1	3	5
1-N-control	280.15	281.91	282.17	282.10	285.33	85.21	85.22	85.17	85.50	85.23
2- Diabetic control	280.22	282.25	283.15	282.15	289.90	85.27	85.14	87.17	87.17	70.13
3-Diabetic Rhizome	280.17	282.28	250.99	253.77	240.14	85.19	85.22	62.02	65.10	67.22
4-Diabetic Water extract	280.22	282.27	227.17	220.91	215.99	85.21	85.10	80.21	79.12	75.01
5-Diabetic Essential oil	280.17	280.18	210.59	211.99	210.70	85.22	84.22	82.10	77.18	70.05
6 -Diabetic commercial Ginger oil	280.12	280.17	250.31	230.25	227.17	85.17	85.20	83.14	82.17	79.25
7-Diabetic Drugs	280.25	281.59	290.27	270.19	225.90	85.02	84.27	83.91	82.95	80.71
LSD 5%	Groups (G) = 1.69 Weeks (w) = 1.56 Int . (GXW)= 4.15					Groups (G) = 1.39 Weeks (w) = 1.29 Int . (GXW)= 3.42				

On the other hand, triglycerides content had the same trend which showed a reduction in the rats after feeding on rhizome ginger (group 3) or powder ginger extract (group 4). Whereas, minor reduction was detected after feeding on commercial oil (group 6) compared with control, where diamicron drug group observed a slightly decrease.

Similar result was found in the work of Afshari *et al.* (2007), they demonstrated that total lipids level in diabetic rats treated with

ginger were significantly ($p<0.1$) lower than the diabetic control. Diabetes induced nephropathies which were also lower in the ginger treated group.

In case of total cholesterol, it was found a significant ($P<0.05$) reduction in diabetic pregnant rats fed in the experimental diet containing extract of powder ginger (group 4) followed by oil ginger (groups 5&6) compared with group 2 (diabetic control). Such reduction however, was remarked at the end of the experimental period which found in Table (6).

Table (6): Determination of total cholesterol, low-density lipoprotein (LDL), and high-density lipoprotein (HDL) in diabetic pregnant rats feeding on the experimental diet.

Groups / Weeks	Total cholesterol(mg\dl)					LDL (mg/dl)					HDL(mg/dl)				
	Adapted rats	0	1	3	5	Adapted Rats	0	1	3	5	Adapted rats	0	1	3	5
1-Normal control	70.15	75.00	74.10	73.00	72.00	42.91	43.54	43.14	44.01	44.01	28.30	28.43	28.75	28.80	28.95
2- Diabetic control	70.21	75.00	80.00	85.00	90.00	43.10	42.70	42.70	41.20	40.20	28.51	30.21	33.15	34.00	34.11
3- Diabetic Rhizome	70.15	69.21	69.10	65.00	63.01	43.21	43.00	41.50	41.00	35.00	28.43	27.13	25.21	21.22	19.21
4- Diabetic Water extract	70.25	60.01	62.10	60.91	55.10	43.10	40.01	39.20	39.20	37.00	28.45	27.00	26.13	24.12	17.95
5- Diabetic Essential Oil	70.18	66.21	65.70	63.17	63.22	43.01	39.10	38.20	38.10	36.00	28.15	27.00	24.18	22.51	18.25
6- Diabetic Commercial Ginger Oil	70.22	66.50	65.30	64.80	62.15	43.50	38.10	38.50	27.20	17.00	28.17	22.40	21.23	20.15	19.12
7- Diabetic Drugs	70.10	70.18	70.00	72.10	69.10	43.41	45.01	45.90	46.10	46.20	28.12	27.31	27.17	26.22	25.10
LSD 5%	Groups (G)= 1.47 Weeks (W)= 1.36 Int.(GXW)= 3.60					Groups (G)= 1.10 Weeks (W)= 1.02 Int.(GXW)= 2.70					Groups (G)= 1.24 Weeks (W)= 1.15 Int.(GXW)= 3.05				

Low density lipoprotein cholesterol (LDL) content was decreased in diabetic pregnant rats fed on the experimental diets containing oil ginger (groups 5&6) followed by group 4 (powder ginger extract) and group 3 rhizome ginger. Whereas, the highest level o f (LDL) was found in group 7 (dimecron drug) relative to control group. Also, high density lipoprotein cholesterol (HDL) was decreased significantly ($P<0.05$) in the experimental diets containing the different ginger diets compared with the normal healthy control (group 1) or diabetic control (group 2).

Nevertheless, the highest reduction was detected in group 6 (commercial oil ginger).

In both (LDL) and (HDL) the reduction was marked at the end of the experimental period. Supporting evidence of the effects of ginger on reducing total cholesterol, LDL and HDL came from Badee *et al.* (2005). They found that sole ginger (powder or essential oil) or combined with cinnamon or clove decreased HDL and LDL in rats fed hyperlipidemic diet. Chrubasik *et al*. (2005) demonstrated that a high dose of ginger extract administrated over 4 weeks to rats significantly lowered fasting blood serum cholesterol. Also, Al-Amin *et al.* (2006) found that ginger-treated diabetic rats lowering cholesterol levels compared with the control diabetic rats.

Table (7) demonstrates the effect of ginger treatment of diabetic pregnant albino rats on transaminase and alkaline phosphates activities. Oil and/or powder ginger (groups 4, 5 and 6) reduced significantly transaminase (GPT and GOT) activity followed by rhizome ginger (group 3) relative to diabetic control, but dimecron drug (group 7) produced activity similar to that of diabetic animals. However, the activity reduction was obvious at the end of the experimental period.

Table (7): Determination of transaminase (GPT & GOT) and alkaline phosphates (ALP) activities in serum of diabetic pregnant rat feeding on the experimental diets.

Groups \ Weeks	GPT(μ/ml)			GOT(μ/ml)			ALP(μ/ml)		
	Adapted rats	0	5	Adapted rats	0	5	Adapted rats	0	5
1- N-control	15.00	17.00	17.00	30.0	27.0	29.0	115.0	117.0	115.0
2- Diabetic control	13.00	30.00	29.00	30.0	35.0	38.0	115.0	125.0	127.0
3-Diabetic Rhizome	15.00	16.00	17.00	30.0	32.0	33.0	117.0	118.0	121.0
4- Diabetic Water extract	15.00	20.00	18.00	30.0	27.0	25.0	115.0	117.0	115.0
5- Diabetic Essential oil	13.00	19.00	17.00	29.0	26.0	23.0	117.0	118.0	132.0
6- Diabetic commercial Ginger oil	14.00	23.00	21.0	27.0	25.0	22.0	115.0	129.0	130.0
7- Diabetic Drugs	15.00	29.00	29.00	29.0	40.0	45.0	117.0	128.0	127.0
LSD 5%	Groups (G)= 1.67 Weeks (W) = 1.09 Int. (GXW)= 2.90			Groups (G)= 1.72 Weeks (W) = 1.12 Int. (GXW)= 2.98			Groups (G)= 2.70 Weeks (W) = 1.77 Int. (GXW)= 4.69		

Similar trend was observed in alkaline phosphates (ALP) activity with different in order. Powder ginger extract (group 4) followed by rhizome ginger (group 3) and oil ginger (group 5) showed the highest reduction in (ALP) activity. This result in harmony with Sambaiah and Srinivason (1991) they found that rats fed on diet containing 2% ginger or 0.5% ginger for 4 weeks decreased significantly alkaline phosphates.

Ginger administrated into diabetic pregnant albino rats increases total protein over the diabetic control (group 2), Nevertheless, differences among ginger forms (Powder, rhizome and oil) in total protein were negligible (Table 8). The effects of ginger on albumin content in the experimented treatments (groups) was not observed, however, an increase in globulin contents in diabetic pregnant rats fed on ginger over diabetic control (group 2) or dimecron drug (group 7) was found. While, albumin/globulin ratio was increased sharply in group 5 (oil ginger) followed by group 3 (rhizome ginger) than other tested groups.

Table (8): Determination of total protein (TP), albumin (A), globulin (G) and A/G ratio in serum of diabetic pregnant rats feeding on the experimental diets.

Weeks / Groups	Total protein(TP)(g/dl)			Albumin (A) (g/dl)			Globulin			A/G %		
	Adapted rats	1	5	Adapted rats	1	5	Adapted rats	1	5	Adapted rats	1	5
1- N-control	6.1	7.8	7.3	4.3	3.2	3.5	1.8	4.6	3.8	2.3	0.6	0.9
2- Diabetic control	6.1	7.3	7.4	4.2	5.4	3.4	1.9	1.9	4.0	2.2	2.8	0.8
3- Diabetic Rhizome	6.1	8.3	9.2	5.3	4.1	3.2	0.8	4.2	6.0	6.6	0.9	0.5
4- Diabetic aWater extract	6.1	8.4	8.7	4.6	3.4	3.4	1.4	5.0	5.2	3.1	0.6	0.6
5- Diabetic Essential oil	6.1	8.1	9.3	5.7	4.4	4.2	0.3	5.1	3.1	5.4	1.2	0.8
6 - Diabetic commercial Ginger oil	6.1	7.5	7.5	4.8	2.5	4.0	1.3	5.4	3.9	3.8	0.4	1.0
7- Diabetic Drugs	6.1	8.0	7.2	4.7	4.3	4.2	1.3	3.7	3.0	3.4	1.2	1.4
LSD 5%	Groups (G) =1.23 Weeks (W) = 0.81 Int.(GXW) = 2.14			Groups (G) =0.80 Weeks (W) =0.52 Int. (GXW) =1.39			Groups (G) =0.53 Weeks (W) =0.34 Int.(GXW) =0.92			Groups (G) =0.59 Weeks (W) =0.38 Int.(GXW) =1.02		

Table (9) show creatinine, urea and uric acid in serum of the experimental pregnant rats fed on the studied diets. It was found that ginger in the form of rhizome, oil or powder reduces creatinine level compared with diabetic rats (group 2) or dimecron drug (group 7). Similar trend of the results was found in urea and uric acid level. The obtained results were in agreement with Al-Amin *et al.* (2006). They found that ginger decreased significantly both water intake and urine output in STZ- induced diabetic rats. Afshari et al (2007) found that diabetic induced nephropathies were also lower in ginger treated group.

From the present study, it can be concluded that the hypoglycemic effects of the different ginger treatment can be arranged in the following increasing order:

Rhizome ginger (group 3) > Water extract of ginger (group 4) > essential oil of ginger (group 5) > commercial ginger oil (group 6).

Table (9): Determination of creatinine, urea and uric acid in serum of diabetic pregnant rats feeding on the experimental diets.

Groups / Weeks	Creatinine (mg/dl)			Urea(mg/dl)			Uric acid(mg/dl)		
	Adapted rats	1	5	Adapted rats	1	5	Adapted rats	1	5
1- N-control	0.66	0.41	0.31	79.0	77.0	72.0	4.5	4.2	4.2
2- Diabetic control	0.59	0.66	0.67	73.0	75.0	72.0	4.4	4.7	4.4
3- Diabetic Rhizome	0.64	0.63	0.42	72.0	70.0	62.0	4.5	4.2	4.2
4- Diabetic Water extract	0.66	0.62	0.49	79.0	73.0	72.0	4.5	4.1	3.9
5- Diabetic Essential oil	0.65	0.59	0.50	79.0	73.0	69.0	4.3	4.4	4.1
6- Diabetic commercial ginger oil	0.64	0.60	0.52	72.0	74.0	67.0	4.5	3.7	3.2
7- Diabetic Drugs	0.63	0.66	0.64	70.0	74.0	73.0	4.2	4.4	4.3
LSD 5%	Groups (G)= 0.04 Weeks (W)= 0.02 Int. (GXW)= 0.07			Groups (G) =1.42 Weeks (W) =0.93 Int .(GXW) =2.47			Groups (G)= 0.21 Weeks (W)= 0.14 Int .(GXW)= 0.37		

These conclusions may be due to that rhizome ginger (group3) contains phenolic compound (which presented in water extract) and essential oil as well as other antioxidants such as vitamin C and E, where the ginger water extract (group 4) had the phenolic compounds only without any of ginger essential oil, but the essential oil treatment (group 5) had the volatile essential oil without any of phenolic

compounds, while the commercial essential oil of ginger may be adulterated with other volatile oils. It means that ginger phenolic compounds were more effective on diabetic than essential oil of ginger.

Histopathological examination revealed that rats from group 1 (normal healthy control) showed apparent normal gastric mucosa (Fig. 1). Slight atrophy of gastric mucosa was the histopathological finding observed in stomach of rats from group 2 (diabetic control) Fig. 2. No histopathological change was noticed in stomach of rats from group 3 and 4 as well as group 5 (ginger treatments) Fig. 3.

Nevertheless, stomach of rats from group 6 (commercial oil ginger) showed only slight local necrosis of lamina epithelialis (Fig.4).

On the other hand, stomach of rats from group 7 (dimecron drug) revealed necrosis of superficial layer of lamina epithelialis (Fig.5).

Examined heart of rats from group 1 (control healthy) and groups 3, 4, 5 and 6 (ginger treatments) showed no histopathological changes (Fig.6). However, heart of rats from group 2 (diabetic control) showed dilatation and congestion of myocardial vessel (Fig. 7). Heart of rats from group 7 (diamecron drug) showed marked hemorrhage (Fig. 8).No histological changes in kidney of rats of group 1 was observed, while, kidney of rats of group 2 (diabetic control) showed a vacuolation of epithelial liming renal tubules and endothelial liming glomerular tuft (Fig. 9). Kidney of rats from group 3 (rhizome ginger) showed hypertrophy of glomerular tufts (Fig. 10). Kidney of rats from group 4 (powder ginger extract) showed slight thickening of glomerular basement membrane (Fig. 11).

In groups 5 and 6 (ginger oil) no changes were observed (Fig. 12). Where, kidney of rats of group 7 (Dimecron drug) showed a hypertrophy of glomerular tufts associated with local interstitial lucocytic cells (Fig. 13).

In regard to liver, no histological changes were observed in group 1(normal healthy control), or group 5 and 6 (ginger oil), liver of rats from group 2 (diabetic control) showed ballooning degeneration of hepatocytes (Fig. 14). Liver of rats of group 4 (powder ginger extract) showed slight dilation and congestion of hepatic sinusoids as well as hepato cellular vaculization (Fig. 15). Also, liver of rats from group 7 (dimecron drug) showed congestion of control vein.

In general, most tissues of stomach, heart, kidney or liver of rats administrated with ginger remain unchanges. Also, ginger treatments protected the cells from damage. The work of Badde *et al.* (2005) revealed that all essential oils of ginger reduced the damage of liver and heart tissues of the rats. Also, Zhou *et al*. (2006) found that volatile oil of ginger significantly inhibited T lymphocytes and T helper cells, but increased the percentage of T suppressor cells to the control.

In connection of biochemical measurements and histopathological examination, these result confirmed each other. The present work showed that ginger had a large amount of antioxidants (phenolic essential oil compound), the high antioxidant value of ginger has proved highly effective with its ability to scavenge a number of free radicals and protect cell membrane lipids from oxidation (Srivastava and Mustafa, 1992; Zhou *et al.,* 2006 and Chrubasik, *et al* 2005). In diabetic animals, ginger significantly lowered serum total cholesterol, LDL, VLDL, triglyceride and phospholipids, also reduced atherosclerotic lesions and associated foam cell formation as effectively as conventional hypolipidemic drugs (Thomson *et al.,* 2002, Fuhrman *et al.,* 2000 and Verma *et al.,* 2004). This study has noticed that ginger diets significantly reduce blood glucose levels of diabetic rats and improved lipids profile and functions of liver and kidney. Also, ginger treated diabetic rats had significantly reduced nephropathy. It is likely that hypocholeterolemic effect of ginger stems from the inhibition of cellular cholesterol synthesis. Attenuation of cholesterol synthesis results in augmentation of LDL receptor activity that leads to elimination of LDL from plasma (Ness *et al,* 1996 and Afshari *et al.,* 2007). It is well established that elevation of LDL oxidation induced oxidative stress and resultant damage by diabetes. Ginger directly decreased lipid peroxidation and oxidative stress (Kota *et al.,* 2008, Shukla and Singh, 2007 and Ali *et al.,* 2008).

It is known that, impaired glucose metabolism leads to oxidative stress, proteins glycation and formation of free radicals (Ceriello *et al.,* 1992). Thus an augmentation of plasma antioxidant capacity decreased plasma free radicals (Sozmen *et al.,* 2001 and Afshari *et al.,* 2007). The reduction of lipids in the liver and plasma by ginger diets may have a role in decreasing lipid peroxidation.

In the present study, diabetes was significantly improved in rats receiving ginger. Several studies have confirmed the useful effects of antioxidants on kidney and liver function indusing renal nephopathy (Mdynneux *et al.,* 2002).

Generally, the complete normalization of oxidative stress could be obtained by glucose control so that, damage induced by oxidative stress continues (Sharma *et al.,* 2000) consumption of antioxidants such as ginger could be a useful addition to current treatment strategies e.g. with insulin.

In principle, ginger may exhibit safer therapeutic effects than conventional diabetes drug since its side effects to date are negligible in the dosages tested. Furthermore, its price relative to many conventional agents suggests that ginger could present a much more cost effective remedy for the treatment of diabetic and cardiovascular diseases, the most prevalent diseases affecting the human race.

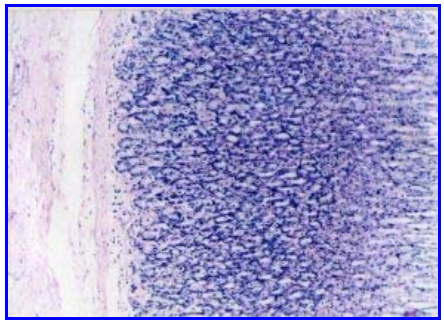
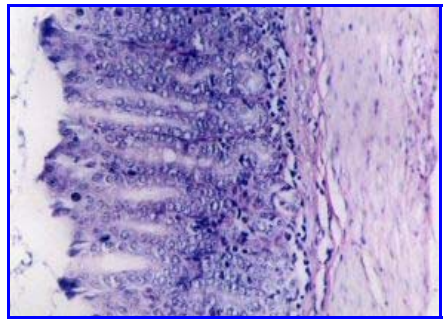


Fig. (1)



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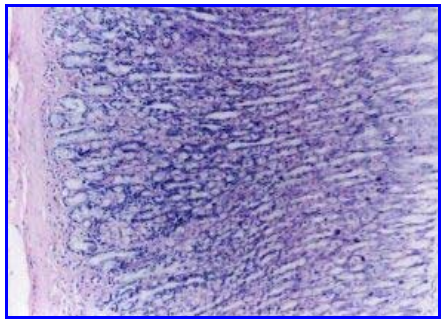

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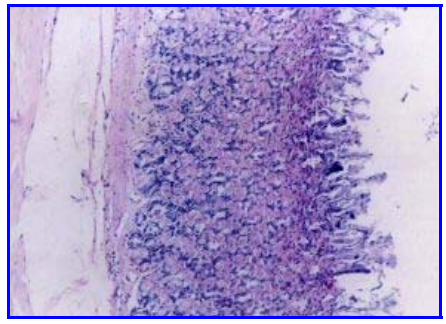

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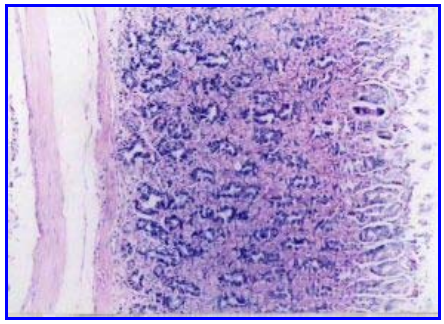

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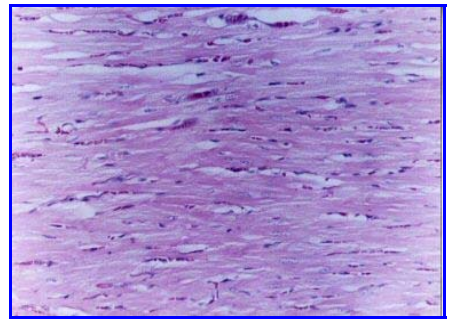

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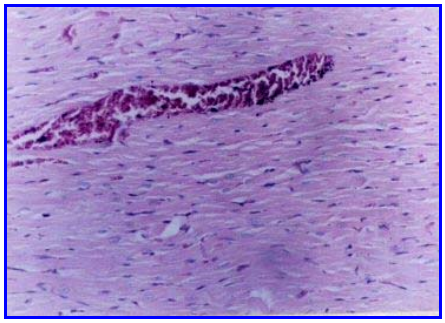

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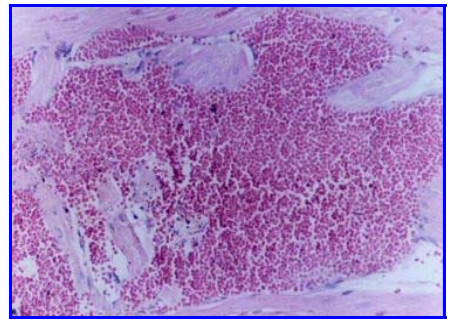

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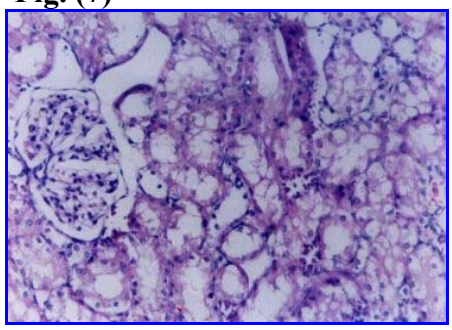

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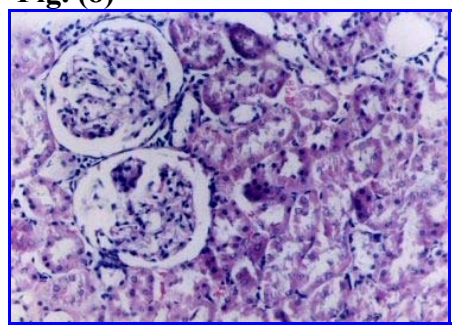

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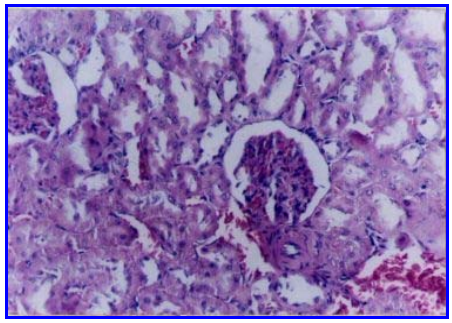

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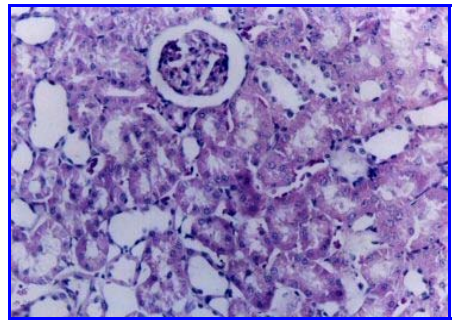

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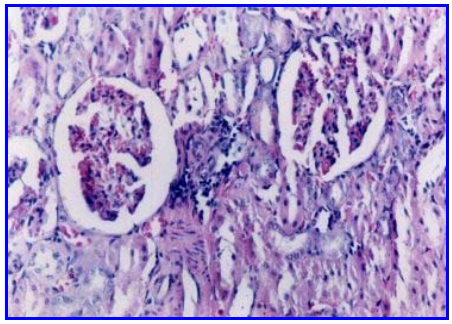

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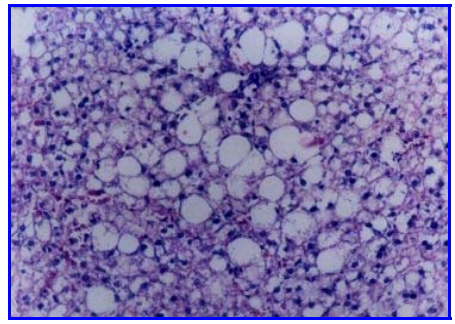

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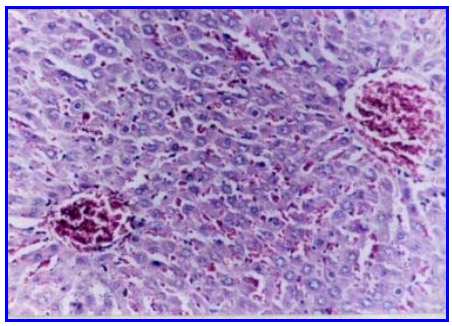

Fig. (15)

Figures (1) to (15) show the histopathological effects of ginger diabetic pregnant rats on stomash, heart, kidneys and liver tissues

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التأثير البيولوجي للجنزبيل على الفئران الحامل والمرضع المصابة بالسكر.

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الملخص العربي

تم دراسة التأثيرات البيوكيميائية والتشريحية للجنزبيل كعامل مخفض للسكر على الفئران الحوامل والمصابة بمرض البول السكري.

المستخلص المائي للجنزبيل تم تحليله للمواد الفينولية بواسطة جهاز HPLC وأيضاً تم تحليل الزيوت الأساسية للجنزبيل بواسطة جهاز GC-MS. حيث قسمت الفئران الحوامل الـ 35 إلى 7 مجموعات. المجموعة الأولي كانت من الفئران السليمة والمجموعة الثانية المصابة بالسكر تمثل مجموعة المقارنة والتي استخدم فيها STZ بتركيز 50 ملليجرام / كيلو جرام لإحداث الإصابة بالسكر، المجموعة الثالثة استخدم فيها 2 جم من مسحوق ريزوم الجنزبيل لكل 100جم من الوجبة، المجموعة الرابعة كانت الفئران المصابة بالسكر والتي تغذت بالأنبوبة المعدية على 3 مل من المستخلص المائي للجنزبيل، المجموعة الخامسة كانت الفئران المصابة بالسكروالتي تغذت تغذية معدية على 0.3 مل من الزيوت الأساسية للجنزبيل، المجموعة السادسة كانت الفئران المصابة بالسكروالتي تغذت تغذية معدية على 0.3 مل من زيت الجنزبيل التجاري ، المجموعة السابعة كانت الفئران المصابة بالسكر والتي تغذت تغذية معدية على 80 ملليجرام من دواء الداي مكرون.

تم تقدير الجلوكوز والبرولاكتين والدهون ووظائف الكبد والكلى كما تم عمل دراسة تشريحية لأنسجة المعدة والقلب والكبد والكلي.

وقد أظهرت النتائج أن المستخلص المائي للجنزبيل يحتوي على عديد من المركبات الفينولية ومن أهمها سكارنتين وليتولين ورتين وكيرسترين وهيبروسيد كمركبات طبيعية. كما وجد 61 مركب في زيت الجنزبيل والتي من أهمها مركبات سيسكوتربين وجيرانول فيرانوسين. وقد أظهرت النتائج أن الجنزبيل في صورة مسحوق أو مستخلص مائى أو زيت طيار قد خفض معنوياً على مستوي 5% كلاً من مستوي الجلوكوز والدهون الكلية والكولستيرول الكلي والكرياتنين واليوريا وحمض اليوريك وكذلك نشاط الترانس أمينيز (GOT , GPT) والألكالين فوسفاتيز (ALP) في دم الفئران الحوامل المصابة بالسكر. ومن ناحية أخري انخفض مستوي البروتين الكلي ونسبة الالبيومين إلى الجلوبيولين مقارنة بالكنترول تحت نفس الظروف.

لم تظهر أي تغيرات تشريحية في أنسجة المعدة والكبد والكلي والقلب للفئران المغذاه على الجنزبيل مقارنة بالكنترول.