Middle-East Journal of Scientific Research 21 (1): 56-62, 2014
ISSN 1990-9233

DOI: 10.5829/idosi.mejsr.2014.21.01.21154

Evaluation of Nutritional and Antidiabetic Activity of Different Forms of Ginger in Rats

Manal L.K. Anfenan

Department of Nutrition and Food Science , Collage of Home Economics
Princess Nourah Bint Abdulrahman University, Riyadh, Kingdom of Saudi Arabia

Abstract: The present study was designed to investigate the antidiabetic activity of ginger powder, extract and oil in experimental rats. 60 rats were randomly classified into normal control group and five diabetic groups induced by streptozotocin (55 mg/kg body weight). Diabetic groups were divided into non treated diabetic rats group act as control +ve group and treated groups with ginger powder, ginger aqua extract, methanolic ginger extract and ginger oil. The treatment period was 60 days. Diabetic treated groups showed reduction of increase levels of alanine and aspartate aminotransferase (ALT&AST) and alkaline phosphatise (ALP) enzymes, liver total lipid and liver cholesterol and increase levels of liver glycogen and triglyceride compared to control +ve group. Diabetic rats treated with ginger oil showed the improvement results of food intake and growth performance and normal values of serum AST and ALP enzymes, total protein, creatinine, urea and uric acid and also normal values of liver glycogen, triglyceride, total lipid and cholesterol. However, diabetic rats treated with ginger aqua extract or methanolic extract or oil showed significant increase in final weight, weight gain, Feed efficiency ratio (FER) and total protein and reduction of increased levels of serum creatinine, urea and uric acid compared to control +ve group in addition normal values of glucose, insulin, glucosalated heamoglobin (HbAc) and fructose amine (FA). It is concluded that ginger has beneficial effects on growth performance, liver and renal function because of its component and antioxidant effect. Ginger oil gives the best antidiabetic activity results followed by ginger extract in rats.

Key words: Antidiabetic Activity · Ginger (*Zingiber Officinale*) · Fructose Amine (FA) · Glucose · Glucosalated Heamoglobin (HbAc %) · Insulin · Packed Cell Volume (PCV)

INTRODUCTION

Diabetes mellitus has been known to medical sciences longer than any other hereditary metabolic diseases. It is a metabolic disorder due to relative or absolute lack of insulin and a chronic disease marked by hyperglycemia and urinary glucose excretion. Insulin is the hormone that regulates carbohydrate metabolism in the body and maintains passage of glucose across the cell membrane [1]. The major chronic complications associated with diabetes include retinopathy, neuropathy, nephropathy, atherosclerotic coronary artery disease and peripheral atherosclerotic vascular diseases. Besides hyperglycemia, several other factors like hyperlipidemia and enhanced oxidative stress play a major role in diabetic pathogenesis [2]. Several herbs have been tried in various studies with the aim to prevent or delay type 2 diabetes. Plant-derived products contain a wide range of phytochemicals, including antioxidants, which are thought to have a protective role against risk of oxidative stress-related diseases [3]. Ginger is an underground rhizome of plant Zingiber Officinale belonging to the family Zingibeaceae. Because of its pungent taste and interesting aroma, ginger has been used since the ancient times as a spice [4]. From its origin in Southeast Asia and its spread to Europe, it has a long history of use as herbal medicine. Ginger has been used historically for its medicinal value in a wide variety of diseases, especially in gastrointestinal disorders, such as constipation, diarrhea, anorexia, colic, dyspepsia, nausea, vomiting and motion sickness. In addition, ginger has medicinal properties against digestive disorders,

Corresponding Author: Manal L.K. Anfenan, Department of Nutrition and Food Science, Collage of Home Economics, Princess Nourah Bint Abdulrahman University, Riyadh, Kingdom of Saudi Arabia

rheumatism and diabetes. Ginger extract possesses antioxidative characteristic, since it can scavenge superoxide anion and hydroxyl radicals. More recently, it was reported that ginger also possessed anti-cancer, anticlotting, anti-inflammatory and analgesic activities [5-7].

This study was conducted to investigate the antidiabetic effect of ginger powder, extract and oil in experimental rats.

MATERIALS AND METHODS

Materials: Streptozotocin was procured from Sigma, St. Louis, MO, USA. Sixty white albino rats (Sprague dawley strain), weighing 156± 8g were provided from experimental animals centre in Medicine Collage of King Saud University in Riyadh. Fresh rhizomes of ginger (Zingiber Officinale) and ginger oil were purchased from local market in Riyadh. Biochemical kits were purchased from Alkan Co. for Chemicals and Biodignostics. The standard diet was performed according to NRC [8].

Methods: Preparation of ginger powder, aqueous ginger extract and methanol ginger extract: Ginger roots were peeled, cut and dry by hot air oven at 60°C then crushed to fine powder. Ginger powder was added as 7% of the standard diet. Ginger oil was given to rats at dose (4 ml/kg body weight) by stomach tube. Aqua ginger extract was prepared from 500g crushed ginger roots that homogenized in 750ml sterile 0.9% NaCl solution and 250ml ice cold water to make the volume 1000ml in blender for 12 minutes. The homogenized mixture was filtered three times through cheese cloth. The filtrate was centrifuged at 2000rpm for 10 min and the clear supernatant fraction was separated and volume made up to 1000ml with normal saline. The concentration of this aqua ginger preparation was considered to have 500mg/ml on the basis of the weight of the starting material [9]. The rat dose of aqua ginger extract was 500mg/kg by stomach tube daily. Methanolic ginger extracted prepared from crushed ginger by cold percolation in methanol for 24 hours. The extract was recovered and methanol was further added to the plant material and the extract was continued, the process was repeated three times, the three extracts were pooled together and concentrated using rotary vapor until the oleoresin was obtained. The golden brawny viscous oleoresin was maintained in dark glass-container, at (-4°C) until use [10]. The rat dose of methanolic extract of ginger was 200 mg/kg by stomach tube.

Experimental Design: After one week of adaptation, rats were randomly classified into six groups (10 rats each). The first group kept as normal control fed standard diet only. The other five groups were injected with a single intraperitoneal dose of streptozotocin (55 mg/kg body weight) in 0.1M citrate buffer of pH 4.5 then supplied with 5% glucose solution for 48h after injection in order to prevent hypoglycemia [11]. After four days, blood samples were taken from orbital plexus for estimation of glucose. The rats having persistent hyperglycemia with fasting blood sugar of more than 200mg/dL were considered as diabetic rats which were classified into:

Group 1: Non treated diabetic rats act as control +ve
Group 2: Diabetic rats treated with ginger powder.
Group 3: Diabetic rats treated with ginger aqua extract.
Group 4: Diabetic rats treated with methanolic ginger extract.
Group 5: Diabetic rats treated with ginger oil.

Food and growth performance parameters were evaluated by recording daily food intake (FI) and weekly body weight gain (WG). Feed efficiency ratio (FER) was determined by Chapman *et al.* [12].

Collection of Blood and Liver Samples: At the end of experiment (60 days), rats were anesthetized, blood sample were collected from hepatic portal vein in clean centrifuge tubes. The liver of sacrificing rats was removed by careful dissection, blotted frees of adhering blood, washed with cold saline solution and dried between two filter papers. Livers perfuse with 50 to 100 of ice cold 0.9% NaCl solution.

Blood Analysis: Blood haemoglobin, packed cell volume (PCV), glucose, insulin, glucosalated heamoglobin (HbAc%), fructose amine (FA) were estimated according to Drabkin [13], Mc Inory [14], Sasaki *et al.* [15], Hales and Randle [16], Abraham *et al.* [17] and Delpierre and Schaftingen 2003 [18] respectively. Serum alanine and aspartate aminotransferase (ALT&AST) and alkaline (ALP) activity enzymes; total protein, creatinine, urea and uric were estimated according to Reitman and Frankel [19], Kind and King [20], Bradford [21], Bonsens and Taussky [22], Patton and Crouch [23] and Fossati *et al.* [24], respectively.

Liver Analysis: Livers samples were analyzed for estimation of glycogen, triglycerides (TG), cholesterol and total lipids according to Rerup and Lundquist [25], Scheletter and Nussel [26], Abell *et al.* [27] and Folch *et al.* [28], respectively.

Statistical Analysis: Collected data were presented as mean ±SD and statistically analyzed using one way analysis of variance (ANOVA).Student "t" test was used for significance according to Artimage and Berry [29].

RESULTS AND DISSCUSION

Non treated rat diabetic (control +ve) group showed highly significant reduction in final weight (FW), weight gain (WG) and FFER at $p<0.001$ compared to normal control group. Diabetic rats treated with ginger powder or aqua extract or methanolic extract showed significant decrease in final weight, weight gain and FFER at $p<0.001$, 0.01&0.05 compared to normal control group. Diabetic rats treated with ginger oil showed the improvement results as non significant difference in final weight and weight gain but significant reduction in FFER at $p<0.05$ compared to normal control group. Diabetic rats treated with ginger aqua extract or methanolic extract or oil showed significant increase in final weight, weight gain and FFER compared to control +ve group as shown in Table 1. It was reported that diabetes mellitus is a disease in which homeostasis of carbohydrate, protein and lipid metabolism is improperly regulated by hormone insulin resulting in elevation of fasting and postprandial blood glucose levels [30]. The obtained result showed that ginger could improve the growth performance because of their nutritional constituents. It was reported that the main constituents of ginger include volatile oil (â-bisabolene, cineol, phellandrene, citral, borned, citronellol, geranial linalool, limonene, zingeberol, zingeberene, camphene), oleoresin (gingerrol, shogoal), phenol (gingerol and zingerone), proteolytic enzymes (zingibain), vitamin B6, vitamin C and calcium, magnesium, phosphorus, potassium, linoleic acid. Also, the pungency and aroma of ginger are because of the gingerol and volatile oil, respectively [31, 32].

Non treated rat diabetic (control +ve) group showed highly significant increase in glucose, FA ($p<0.001$) and HbAc ($p<0.01$) and decrease in insulin at $p<0.001$ while diabetic rats treated with ginger powder showed significant increase in glucose and decrease in insulin at $p<0.05$ compared to normal control group. Diabetic rats treated with ginger aqua extract or methanolic extract or oil showed that values of glucose, insulin, HbAc and FA were within normal control group as shown in Table 2. It is well documented that streptozotocin produced a significant increase in fasting glucose levels that was associated with a significant decrease in serum insulin levels [33]. Ginger pre-treatment inhibited the induced hyperglycemia and hypoinsulinaemia. Aqueous and ethanol extracts of Zingiber Officinale significantly reduce the blood glucose level in STZ-induced diabetic rats. Ginger produced a significant increase in insulin levels and a decrease in fasting glucose levels in diabetic rats [5]. Non treated rat diabetic (control +ve) group showed highly significant decrease in haemoglobin and packed cell volume at $p<0.01$compared to normal control group. Diabetic rats treated with ginger powder or aqua extract or methanolic extract or oil showed the values within normal control group as shown in Table 3. These results are in agreement with those obtained by Young *et al.* [34] and Yuki *et al.* [35], who reported that the antioxidant activity of ginger might be due to radical scavenging activity and their affinity to the substrates. The active compounds of ginger are 6-gingerol, tannins, polyphenolic compounds, flavonoids and triterpenoids of hypoglycemic that maintain cell function related to receptors and membrane transport.

Non treated rat diabetic (control +ve) group showed highly significant increase in serum ALT, AST and ALP enzymes at $p<0.001$ compared to normal control group. Diabetic rats treated with ginger powder showed significant increase in serum ALT, AST and ALP enzymes at $p<0.01$ but diabetic rats treated with ginger aqua extract showed significant increase in serum ALT and ALP enzymes at $p<0.01$ while diabetic rats treated with ginger methanolic extract showed significant increase in serum AST and ALP enzymes at $p<0.05$&0.01 compared to normal control group. Diabetic rats treated with ginger oil showed normal values of serum ALT, AST and ALP enzymes. Diabetic rats treated with ginger powder or aqua extract or methanolic extract or oil showed reduction of increase levels of these parameters compared to control +ve group as shown in Table 4. The protective effect of ginger was associated with decreased oxidative stress. An*in vitro*study showed that zingerone, a metabolite from ginger, inhibited lipid peroxidation in rat liver microsomes at high concentrations [36]. Ginger has a protective effect on the hepatotoxicity. The reduction in serum AST, ALT and ALP enzymes could be attributed to the fact that ginger contains high content of antioxidant that makes it a free radical scavenger [37]. Other authors have shown that ginger extract attenuates the elevated level of AST, ALT and ALP after intoxication by cisplatin, this may be attributed to that ginger component stabilize hepatocytes plasma membrane and prevent delivery of AST, ALT and ALP to the extracellular fluid [38].

Table 1: Mean values ± SD of food and growth performance parameters of the experimental rat groups.

Groups --- Variables	Normal control	Control +ve	Ginger powder	Ginger aqua extract	Ginger methanolic extract	Ginger oil
F W (g)	235.25±13.14a	190.11±9.24c***	207.67±10.66bc***	217.83±12.14b**	219.38±11.27b**	226.32±13.15ab
WG	75.64±4.33a	31.60±2.60d***	50.21±5.11c***	59.61±4.18bc**	62.61±6.61b*	65.91±6.44ab
F I(g/d)	18.70±1.39a	17.33±1.10a	17.25±1.19a	17.80±1.40a	17.78±1.21a	18.03±1.37a
FER	0.067±0.003a	0.030±0.002e***	0.048±0.005d**	0.055±0.006bc**	0.058±0.004b**	0.060±0.001b*

Significant with control (-ve) group * P<0.05 ** P<0.01 *** P<0.001.

Values with the same letters in raw indicate non- significant difference (P<0.05) and vice versa.

Table 2: Mean values ± SD of glucose, insulin, HbAc and FA of the experimental rat groups.

Groups --- Variables	Normal control Ginger oil	Control +ve	Ginger powder	Ginger aqua extract	Ginger methanolic extract	
Glucose (mg/dl)	108.77±8.23^{cd}	295.14± 5.26^{a***}	133.81±11.14^{b*}	125.19±12.17^{bc}	122.17±10.19^{bc}	12.14±8.66^{bc}
Insulin (µ/l)	18.65±1.81^{a}	7.65±1.08^{c***}	14.08±1.31^{b*}	15.21±1.42^{ab}	15.41±1.611^{ab}	15.81±1.41^{ab}
HbAc %	4.77±0.33^{b}	7.45±0.67^{a**}	5.25±0.45^{b}	5.11±0.30^{b}	4.96±0.40^{b}	4.03±0.53 ^{b}
FA (µmol/l)	175.71±15.13^{bc}	245.67±23.61^{a***}	190.20±20.21^{b}	192.14±18.19^{b}	188.30±16.15^{b}	179.31±16.71^{bc}

Significant with control (-ve) group * P<0.05 ** P<0.01 *** P<0.001.

Values with the same letters in raw indicate non- significant difference (P<0.05) and vice versa.

Table 3: Mean values ± SD of HB and PCV of the experimental rat groups.

Groups --- Variables	Normal control	Control +ve	Ginger powder	Ginger aqua extract	Ginger methanolic extract	Ginger oil
HB (g/dl)	13.96±1.61^{a}	10.21±1.32^{b**}	12.22±1.24^{a}	12.08±1.35^{a}	12.94±1.42^{a}	13.11±1.69^{a}
PCV%	38.61±2.71^{a}	29.61±2.61^{c**}	34.22±3.10^{ab}	33.66±3.05^{b*}	34.88±4.11^{ab}	34.96±3.96^{ab}

Significant with control (-ve) group * P<0.05 ** P<0.01 *** P<0.001.

Values with the same letters in raw indicate non- significant difference (P<0.05) and vice versa.

Table 4: Mean values ± SD of serum ALT, AST and ALP enzymes of the experimental rat groups.

Groups --- Variables	Normal control Ginger oil	Control +ve	Ginger powder	Ginger aqua extract	Ginger methanolic extract	
ALT(µ/ml)	19.66±1.12^{cd}	41.52±4.61^{a***}	30.21±3.25^{b**}	28.44±3.61^{b**}	24.77±2.96^{bc}	23.61±2.70^{c}
AST (µ/ml)	35.61±3.36^{d}	62.98±5.91^{a***}	48.34±4.82^{b**}	39.67±4.91^{cd}	42.711±4.59^{bc*}	38.19±4.50^{cd}
ALP (i/ml)	31.61±3.64^{d}	52.84±6.18^{a***}	45.11±4.19^{ab**}	42.81±5.08^{bc*}	44.33±4.29^{b**}	35.80±4.61^{cd}

Significant with control (-ve) group * P<0.05 ** P<0.01 *** P<0.001.

Values with the same letters in raw indicate non- significant difference (P<0.05) and vice versa.

Non treated rat diabetic (control +ve) group showed highly significant increase in serum creatinine, urea and uric acid at p<0.001 and significant decrease in serum total protein while diabetic rats treated with ginger powder or aqua extract or methanolic extract showed significant increase in serum creatinine, urea and uric acid at p<0.01&0.05 compared to normal control group. Diabetic rats treated with ginger oil showed normal values of serum total protein, creatinine, urea and uric acid. Diabetic rats treated with ginger aqua extract or methanolic extract or oil showed increase in total protein and reduction of increased levels of serum creatinine, urea and uric acid compared to control +ve group as shown in Table 5. In the diabetic rats, an increase in serum uric acid, urea and creatinine levels was observed by Abd El-Ghany [33]. The ginger treatment also resulted in a significant reduction in urine protein levels. Raw ginger is effective in reversing the diabetic proteinuria observed in the diabetic rats [39]. The administration of ethanol extract of ginger before and after cisplatin injection significantly lowered the elevated levels of serum creatinine and urea. Ginger extract has protective effect against the induced nephrotoxicity and renal failure [40]. Non treated rat diabetic (control +ve) group showed highly significant

Table 5: Mean values ± SD serum total protein, creatinine, urea and uric acid of the experimental rat groups.

Groups						
Variables	Normal control	Control +ve	Ginger powder	Ginger aqua extract	Ginger methanolic extract	Ginger oil
Total protein (g/dl))	7.27±0.74^{a}	6.01±0.56^{b*}	6.75±0.63^{a}	6.81±0.84^{a}	6.71±0.73^{a}	6.96±0.58^{a}
Creatinine (mg/dl)	0.66±0.03^{d}	1.21±0.25^{a***}	0.92±0.11^{ab**}	0.82±0.10^{bc**}	0.85±0.15^{bc**}	0.71±0.03^{d}
Urea (mg/dl)	30.61±3.14^{c}	70.21±8.16^{a***}	46.78±5.07^{b**}	48.33±6.08^{b**}	45.77±5.30^{b**}	37.71±5.17^{c}
Uric acid(mg/dl)	3.01±0.20^{c}	5.64±0.44^{a***}	4.50±0.33^{ab*}	4.03±0.42^{b*}	4.21±0.31^{b*}	3.20±0.43^{c}

Significant with control (-ve) group * P<0.05 ** P<0.01 *** P<0.001.

Mean values in each raw having different superscript (a, b, c) denote significant difference.

Table 6: Mean values ± SD of liver glycogen, triglyceride (TG), total lipid and cholesterol of the experimental rat groups.

Groups						
Variables	Normal control	Control +ve	Ginger powder	Ginger aqua extract	Ginger methanolic extract	Ginger oil
Glycogen (mg/100g)	8.44±1.03^{a}	2.88±0.24^{c***}	6.63±0.52^{b*}	6.51±0.70^{b*}	6.88±0.63^{ab}	6.95±0.50^{ab}
TG (mg/100g)	2.55±0.61^{a}	1.47±0.11^{c***}	1.98±0.23^{ab}	2.11±0.27^{a}	2.01±0.18^{a}	2.43±0.13^{a}
Total lipid (mg/100g)	34.77±5.14^{bc}	49.17±6.10^{a***}	36.21±5.41^{b}	38.80±5.64^{b}	37.66±6.03^{b}	34.11±3.25^{bc}
Cholesterol (mg/100g)	3.71±0.22^{c}	6.01±0.29^{a**}	4.25±0.43^{bc}	4.51±0.54^{b*}	4.67±0.65^{b*}	4.01±0.66^{bc}

Significant with control (-ve) group * P<0.05 ** P<0.01 *** P<0.001.

Mean values in each raw having different superscript (a, b, c) denote significant difference.

decrease in liver glycogen and triglyceride at p<0.001 and significant increase in total lipid and cholesterol at p<0.001 while diabetic rats treated with ginger powder showed significant decrease in liver glycogen at p<0.05 and insignificant difference in triglyceride total lipid and cholesterol compared to normal control group. Diabetic rats treated with ginger aqua extract showed significant decrease in liver glycogen at p<0.05 and insignificant difference in triglyceride and total lipid and significant increase in cholesterol compared to normal control group. On the other side, diabetic rats treated with ginger methanolic extract showed non significant difference in these liver parameters at p>0.05 compared to normal control group. Diabetic rats treated with ginger oil showed normal values of liver glycogen, triglyceride, total lipid and cholesterol. Diabetic rats treated with ginger powder or aqua extract or methanolic extract or oil showed increase levels of liver glycogen and triglyceride and decrease levels of liver total lipid and cholesterol compared to control +ve group as shown in Table 6.

It is well established that impaired insulin stimulated glucose metabolism is a common feature in obese and diabetic subjects. Impaired insulin stimulated glucose metabolism in peripheral tissues is tightly associated with elevated circulating lipids and tissue lipid accumulation [41]. Raw ginger was significantly effective in lowering serum glucose, cholesterol and triacylglycerol levels in the ginger treated diabetic rats compared with the control diabetic rats. Raw ginger possesses hypoglycaemic, hypocholesterolaemic and hypolipidaemic potential [39]. Ethanolic extract can protect tissues from lipid peroxidation and exhibit a significant lipid lowering activity in diabetic rats. Ethanolic extract of ginger prevent hypercholesterolemia and development of atherosclerosis in cholesterol fed rabbits [10]. Furthermore, (E)-8 beta, 17- epoxyllabed-12-ene-15, 16-dial, a compound isolated from ginger, interfered with cholesterol biosynthesis in liver homogenates of hypercholesterolaemic mice causing its reduction [42]. Feeding rats with ginger significantly elevated the activity of hepatic cholesterol 7-alpha-hydroxylase which is a rate-limiting enzyme in the biosynthesis of the bile acids and stimulates the conversion of cholesterol to bile acids leading to the excretion of cholesterol from the body [43]. In a high-fat diet fed rat model, an ethanolic extract of ginger effectively reduced triglyceride and cholesterol levels in liver. The mechanistic evidence suggested that the lipid homeostasis effect of ginger was partially due to a decrease in cholesterol biosynthesis and in enhanced hepatic uptake of circulating LDL cholesterol [44]. Finally, it is recommended to consume diets contain ginger to diabetic patient.

REFERANCES

1. Tiwari, A.K. and J.M. Rao, 2002. Diabetes mellitus and multiple therapeutic approaches of phytochemicals: Present status and future prospects. Curr. Sci., 83: 30-8.
2. American Diabetic Association, 2005. Diagnosis and classification of diabetes mellitus. Diabetic Care, 28(1): 37-42.

3. Anwar, F., U. Kalsoom, B. Sultana, M. Mushtaq, T. Mehmood and H.A. Arshad, 2013. Effect of drying method and extraction solvent on the total phenolics and antioxidant activity of cauliflower (*Brassica oleracea* L.) extracts. IFRJ, 20(2): 653-659.
4. White, B., 2007. Ginger: an Overview.American Family Physician, 75(11): 1689-1691.
5. Akhani, S.P., S.L. Vishwakarma and R.K. Goyal, 2004. Antidiabetic activity of Zingiber officinale in streptozotocin induced type I diabetic rats. J. Pharm. Pharmacol, 56(1): 101-5.
6. Wang W.H. and Z.M. Wang, 2005. Studies of commonly used traditional medicine-ginger. Zhongguo Zhongyao Zazhi, 30(20):1569-1573.
7. Ali, B.H., G. Blunden, M.O. Tanira and A. Nemmar, 2008.Some phytochemical, pharmacological and toxicological properties of ginger (*Zingiber officinale*Roscoe): a review of recent research. Food and Chemical Toxicology, 46(2): 409-420.
8. NRC, 1995. National Research Council: Nutrient Requirements of Laboratory Animals. Fourth Revised Edition, PP.29-30 National Academy Press. Washington, DC.
9. Majeed, A.A., T. Martha, K. Khaled, M. Tariq and A. Muslim, 2003. Biochemical and histopathological toxicity of aqueous ginger extract in female rats. Kuwait J. Sci. Eng., 30: 35-48.
10. Bhandari, U., R. Kanojia and K.K. Pillai, 2005. Effect of ethanolic extract of *Zingiber officinale* on dyslipidemia in diabetic rats. J. Ethnopharmacol., 97: 227-30.
11. Peschke, E., H. Ebelt, H.J. Bromme and D. Peschke, 2000. Classical and new diabetogens: Comparison of their effects on isolated rat pancreatic islets *in vitro*. Cell Mol. Life Sci., 57(1): 158-164.
12. Chapman, D.G., R. Gastilla and T.A. Campbell, 1950. Evaluation of protein in food. I. A method for the determination of protein efficiency ratio. Can. J. Biochem. Physio, 1(37): 679-686.
13. Drabkin, D.I., 1949. The standardization of hemoglobin measurements. Am. Journal Med. Sci., 217: 710-711.
14. Mc Inory, R.A., 1954. A microheamatocrit for determining the packed cell and hemoglobin concentration on capillary blood. J. Clin. Path., (7): 32-36.
15. Sasaki, T., S. Matsy and A. Sonae, 1972. Effect of acetic acid concentration on the colour reaction in the O-toluidine boric acid method for blood glucose estimation. Rinsh. Kagaku, 1: 346-353.
16. Hales, C.D. and P.J. Randle, 1963. Immuno assay of insulin with insulin antibody precipitate. J. Biochem., 88: 137-146.
17. Abraham, E.C., T.A. Huff, N.D. Cope, J.B. Wilson, E.D. Bransome and T.H. Huisman, 1978. Determination of the glycosalated heamoglobin (Hb_{A1}) with a new microcolumn procedure. Suitability of the technique for assessing the clinical management of diabetes mellitus. Diabetes, 27(9): 931-7.
18. Delpierre, G. and E.V. Schaftingen, 2003. Fructosamine3- kinase, an enzyme involved in protein glycation. Biochem. Society Trans., 31(6): 1354-1357.
19. Reitman, S. and S. Frankel, 1957. Determination of glutamate pyruvat transaminase and glutamate oxaloacetate transaminase. Am. Journal Clin. Path., 28: 56-63.
20. Kind, P.R and E.J. King, 1954. Estimation of alkaline phosphatase activity by determination of hydrolyzed phenol with aminoantipyrene. Journal Clin. Path., 7: 322-326.
21. Bradford, M.M., 1976. A rapid and sensitive method for the quantitation of microgram quantities of protein utilizing the principle of protein-dye binding analyte. Biochemistry, 27: 248-254.
22. Bonsens, K.E. and D.H. Taussky, 1984. Determination of serum creatinine. J. Chem. Inv., 27: 648-660.
23. Patton, C.J. and S.R. Crouch, 1977. Enzymatic colorimetric method to determination urea in serum. Anal. Chem., 49: 464.
24. Fossati, P., L. Prencipe and G. Berti, 1980. Use of 3, 5dichloro-2-hydroxybenzene sulfonic acid 4-amlnophenazon chromogenic system in direct enzymatic assay of uric acid in serum and urine. Clin. Chem., 26: 227-231.
25. Rerup, E. and S. Lundquist, 1967. Precipitation and purification of liver glycogen in rats. Acta Pharmmic. Tox., 25: 47-51.
26. Scheletter, G. and E. Nussel, 1975. Arbeitsmed Sozialmed Praventimed, 10: 25.
27. Abell, L.L., B.B. Levy, B.B. Brodie and R. Kendal, 1952. A simplified method for the estimation of total cholesterol in serum and demonstration of its specificity. J. Biol. Chem., 195: 357-366.
28. Folch, J., M. lees and G.H. Stanley, 1957. A simple method for isolation and purification of total lipid from animal tissue. J. Biol. Chem., 266: 497-509.
29. Artimage, G.Y. and W.G. Berry, 1987. Statistical Methods. 7th Ed. Ames, Iowa State University Press, 39-63.

30. Asha, B., K.H. Krishnamurthy and D. Siddappa, 2011.Evaluation of anti hyperglycaemic activity of *Zingiber officinale* (Ginger) in albino rats. J. Chem. Pharm. Res., 3(1): 452-456.
31. Kikuzaki, H. and N. Nakatani, 1993. Antioxidant effects of ginger constituents. Journal Food Sci., 58(6): 1407-1410.
32. Kikuzaki, H., Y. Kawasaki and N. Nakatani, 1994. Structure of antioxidative compounds of ginger. ACS Symp. Ser., 547: 237-243.
33. Abd El-Ghanny, M.A., 2007. Effect of vanadium, radish and dill on some nutritional and biochemical parameters in diabetic rats. Egyptian J. of Nutrition and Health, 2(1): 67-86.
34. Young, H.V., Y.L. Luo, H.Y. Cheng, W.C. Hsieh, J.C. Liao and W.C. Peng, 2005. Analgesic and anti-inflammatory activities of [6]-gingerol. J Ethnopharmacol, 96: 207-210.
35. Yuki, M., K. Hiroe, H. Massahi and N. Nobuji, 2008. Antioxidant properties of ginger related compounds from ginger. Bio Factors, 21(1-4): 293-296.
36. Shanmugam, K.R., K. Mallikarjuna, K. Nishanth, C. H. Kuo and K. S. Reddy, 2011. Protective effect of dietary ginger on antioxidant enzymes and oxidative damage in experimental diabetic rat tissues. Food Chemistry, 124(4): 1436-1442.
37. Ezeuko, V.C., C.R. Nwokocha and P. Mounmbegna, 2007. Effects of *Zingiber officinale* on liver function of mercuric chloride-induced hepatotoxicty in adult wistar rats. Rev Electron Biomed- Electron J. Biomed., 3: 40-45.
38. Darbar, S., A. Bose, T.K. Chattaraj and T.K. Pal, 2010. Protective role of Zingiber officinale Roscoe on Aceclofenac induced oxidative stress in rat liver. International Journal of Pharm Tech Research, 2: 495-501.
39. Al-Amin, Z.M., M. Thomson, K.K. Al-Qattan, R. Peltonen-Shalaby and M.Ali, 2006.Anti-diabetic and hypolipidaemic properties of ginger (*Zingiber officinale*) in streptozotocin-induced diabetic rats. Br. J. Nutr., 96(4): 660-6.
40. Ajith, T.A., U. Hema and M.S. Aswathy, 2007. *Zingiber officinale* Roscoe prevents acetaminophen-induced acute hepatotoxicity by enhancing hepatic antioxidant status. Food and Chemical Toxicology, 45: 2267-2272.
41. Denis-McGarry, J., 2002. Dysregulation of fatty acid metabolism in the etiology of type 2 diabetes. Diabetes, 51(1): 7-18.
42. Tanabe, M., Y.D. Chen, K. Saito and Y. Kano, 1993. Cholesterol biosynthesis inhibitory component from *Zingiber officinale* Roscoe. Chem. Pharm. Bull., 41: 710-713.
43. Srinivasan, K. and K. Sambaiah, 1991. The effect of spices on cholesterol 7-alpha hydroxylase activity and on serum and hepatic cholesterol levels in the rat. International Journal of Vitamins and Nutrition Research, 61(4): 364-369.
44. Nammi, S., M.S. Kim, N.S. Gavande, G.Q. Li and B.D. Roufogalis, 2010. Regulation of low-density lipoprotein receptor and 3-hydroxy-3- methylglutaryl coenzyme A reductase expression by *Zingiber officinale*in the liver of high fat diet fed rats. Basic and Clinical Pharmacology and Toxicology, 106(5): 389-395.