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Effect of Raw and Cooked Ginger (*Zingiber officinale* Roscoe) Extracts on Insulin Sensitivity in Normal and High-fat Diet-induced Diabetic Rats

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Abstract Few studies have determined the effect of different ginger extracts on insulin sensitivity, very few have explored the effect of raw extract of this spice on this parameter while the effect of cooked ginger extract (the form in which the spice is commonly consumed) is yet to be ascertained. This experimental study was therefore designed to determine the effect of raw and cooked ginger extracts on insulin sensitivity in normal and high-fat diet-induced diabetic rats. Ginger rhizomes were washed, peeled, wet-milled and sieved without adding water to obtain the raw extract. The raw extract was boiled for 1 hour to obtain the cooked extract. Seventy male albino rats of weight range 120-160g were divided into seven groups (n=10) and designated thus: ND_2C-non-diabetic control; ND_2R-non-diabetic rats given raw ginger extract (2ml/kg body weight); ND_2Co- non-diabetic rats given cooked (boiled) ginger extracts; D_2C-diabetic control; D_2R- diabetic rats given raw ginger extract; D_2Co- diabetic rats given cooked ginger extract; and D_2D-diabetic rats given metformin (anti-diabetic drug)-200mg/kg body weight. Diabetes was induced in the diabetic groups by feeding the animals with high-fat diet (HFD) for 12 weeks to mimic Type 2 diabetes. Ginger extracts and the drug were administered as a daily oral dose for 4 weeks after diabetes induction. Insulin sensitivity (Insulin Tolerance Test) was determined before and after diabetes induction and at the end of the 4 weeks extracts administration using standard analytical method. Mean data were analyzed using ANOVA at $p \leq 0.05$. Baseline Insulin Sensitivity (IS-%/min) in all the groups ranged from 2.2 to 2.4. After 12 weeks feeding, the IS in the three groups fed normal diet ranged from 1.9 to 2.1 while in the four groups fed HFD Insulin Sensitivity ranged from 0.1 to 0.3. Four weeks administration of raw and cooked ginger extracts did not significantly alter IS in normal rats while in diabetic rats raw, cooked ginger extracts and metformin significantly increased IS (%/min) to 2.1, 1.2 and 1.7 respectively relative to control which was 0.1. Insulin Sensitivity was maintained within the normal level in normal rats that were given raw and cooked ginger extracts while the raw extract was more effective than the cooked extract in increasing insulin sensitivity to normal level in diabetic rats. Both raw and cooked ginger extracts improved insulin sensitivity in high-fat diet-induced diabetic rats but the raw extract was more effective, hence, ginger in both forms may be applicable in the management of Type 2 diabetes. Human trial is hereby recommended.

Keywords: *ginger extracts, insulin sensitivity, high-fat-induced diabetes*

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1. Introduction

Diabetes mellitus (DM) is a group of metabolic disorders characterized by chronic hyperglycemia resulting from defects in insulin secretion, insulin action or both. There are two major types of DM. These are Type 1 DM also known as Insulin Dependent Diabetes Mellitus (IDDM) and Type 2 DM also known as Non Insulin Dependent Diabetes Mellitus (NIDDM). Type 1 DM is caused by autoimmune destruction of pancreatic β islet cells leading to absolute insulin deficiency while Type 2 DM is precipitated by obesity, inactivity, chronic high-fat diet or chronic high-fructose diet consumption leading to insulin resistance [1]. Chronic hyperglycemia which is a consequence of diabetes mellitus results to various micro vascular and macro vascular complications. Micro vascular complications account for diabetes morbidity and these include: retinopathy, nephropathy, neuropathy, peripheral neuropathy which leads to foot ulcers and may necessitate limb amputation. Macro vascular diabetic complications mostly attribute to the mortality of the disease and these include; stroke, cardiovascular diseases and hypertension [2].

The prevalence of diabetes mellitus has been witnessing a notable increase in trend especially towards the end of the twentieth century. This may be as a result of lifestyle changes related to modernization, civilization and computerization which witnessed a rapid advancement at this period [3]. For instance in the United States of

America the prevalence of DM among adults ≥ 20 years was 5.1% in 1988-1994 [4] while in 2003-2006 this was 9.6% among the same age group [5]. In China prevalence of DM in 1994 among Chinese adults (25-84 years) was 2.5% [6] but this was 9.7% among the adult Chinese in 2008 [7] and 11.6 % in 2013 among the same age group [8]. The prevalence has followed similar trend in Nigeria. The prevalence of Type 2 DM among adults 25-74 years in 1998 was 1% [9] and 2% among Nigerians in Diaspora (all age groups) in 1997 [10] but in 2011 the prevalence of DM was 4.1% among all age groups [11]. Even Type 2 which was commonly referred to as maturity-onset DM has started gaining incidence among children and adolescents. Among Piman Indian children the prevalence was 0% in 1967-1976, 1.4% in 1987-1996 among boys (10-14 years); 0.7% in 1967-1976 and 2.9% in 1987-1996 among girls of the same age group. In the age group 15-19 years the prevalence was 2.4% in 1967-1976 and 3.8% in 1987-1996 among boys while among girls this was 2.7% in 1967-1976 and 5.3% in 1987-1996 [12].

Globally the people with diabetes mellitus was estimated to increase in year 2000 to 2010 from 14.2 million to 17.5 million in North America, 15.6 million to 22.5 million in South America, 26.5 million to 32.9 million in Europe, 9.4 million to 14.1 million in Africa, 84.5 million to 132.2 million in Asia and 1.0 million to 1.3 million in Australia giving a total global estimated increase from 151 million people in 2000 to 221 million people in 2010 [13]. This was projected to increase to 324 million by 2025 [14] and 366 million 2030 [15]. In 2013, 382 million people had diabetes mellitus worldwide and this is expected to rise to 592 million by 2035 [16]. This shows clearly that the prevalence is increasing more than it was projected or expected, hence, the need to address this disease cannot be over emphasized.

Several reports have established the development of insulin resistance and Type 2 diabetes mellitus as a result of chronic high-fat diet consumption and obesity while the possible mechanisms have also been identified. Activation of serine kinases (e.g. protein kinase C-Θ) by the increased intracellular accumulation of fatty acid metabolic derivatives (such as ceramide, fatty acyl-CoAs, diacylglycerol), which is commonly associated with obese and chronic high-fat diet consumption states, has been identified as the most potent mechanism of the diabetogenic effect of obesity and chronic high-fat diet consumption [17,18]. Another possible mechanism is the alteration of adipocyte production by resistin and adiponectin which has been observed to be associated with insulin resistance and impairment of glucose metabolism in obese subjects [19,20].

More still, the increased intramuscular accumulation of triglyceride in high-fat diet-induced insulin resistance in skeletal muscle of mice was reported to be associated with the insulin resistant state [21]. Insulin resistance results from reduced sensitivity of insulin receptors to insulin. Insulin receptor belongs to receptor tyrosine kinase which consists of insulin-like growth factors (IGF-1) receptor and the insulin receptor-related receptor (IRR) [22].

In insulin resistant state which commonly results from hyperlipidemia and hyper- uricaemia that results from obesity/chronic high-fat and high fructose-diets respectively, unesterified lipids and uric acid interfere with the insulin receptors by reducing the affinity of insulin receptors for insulin thus reducing glucose uptake by the body cells consequently leading to hyperglycemia and hyperinsulinemia. Hyperlipidemia has also been reported to increase the expression and activity of protein tyrosine phosphatase-1B (PTP-1B) which forms a physical complex with insulin receptor (IR) and insulin receptor substrate-1 (IRS-1) via dephosphorylation [1,22,23,24]. This results in deactivation of phosphoinositide 3 kinase (PI3K), reduced tyrosine kinase activity and GLUT4 expression thus rendering the insulin receptors in muscles and adipose tissues insensitive to insulin [1,22]. This commonly occurs in Type 2 diabetes mellitus. In Type 1 diabetes there exists absolute deficiency of insulin which leads to chronic uncontrolled hyperglycemia.

Ginger (*Zingiber officinale*) is a rhizome that has been in use as a spice since ancient times and in alternative medicine for different ailments. The versatility of its culinary uses is unrivalled because it is suitable for all dishes; both sweet and savoury. This was one of the reasons that informed the choice of this spice coupled with the blood glucose lowering effect of its different extracts as reported by different research findings [25,26]. The continual increase in the global prevalence of diabetes mellitus coupled with the possible use of ginger in the management of this diseases demands that the concept be deeply explored for a better understanding towards proper dietary application. This study was therefore designed to determine the effect of raw and cooked (the form in which the spice is most commonly consumed) ginger extracts on insulin sensitivity in normal and high-fat diet-induced diabetic rats.

2. Materials and Method

Preparation of ginger extracts: The method of Akhani et al., [27] which was used by Elshater et al., [28] was used with slight modification.

Raw extract: Fresh ginger rhizomes (Roscoe variety) were purchased from Bodija market in Ibadan, Nigeria. This was identified and authenticated in the Herbarium Unit of the Department of Botany, University of Ibadan. The rhizomes were washed, peeled, washed and wet-milled (without the addition of water) with a plate attrition mill (Amuda Plate mill, India). This was then sieved with a cheese or muslin cloth and the extract was stored in tightly closed plastic jars at 2°C (at the closest part to the freezer in a refrigerator) until use.

Cooked extract: Raw extract was boiled at the medium heat of a 2-burner Thermo cool gas cooker (India) for 1 hour. This was then cooled and stored in plastic jars at 2°C until use.

Formulation of High-fat diet: The method of Martinello *et al.*, [29] was used with slight modification. The composition was as follows: 45% normal rat pellets (Lanko feeds, Nigeria), 30% beef tallow, 20% full cream milk powder (Real Milk, Chellarams) and 5% table sugar. This was formulated weekly to prevent deterioration due to rancidity.

Collection of rats: Four weeks old male albino rats (140) of weight range 50-55g were purchased from the Experimental Animal Unit of the Department of Veterinary Physiology, University of Ibadan, Nigeria. These were raised

to desired weight range before experimentation commenced. Animals were fed normal rat pellets and tap water ad libitum and were treated according to the research protocol as approved by the U.I/U.C.H. Ethics Review Committee (Ethical Approval Number- NHREC,05/01/2008a).

Induction of diabetes: Seventy rats of weight range 120-160g were used. Hyperglycemia was induced in forty of the rats by feeding them with the High-Fat Diet (HFD) for 12 weeks while the remaining 30 rats were fed normal rat pellets (Lanko feeds, Nigeria). After 12 weeks HFD consumption animals with FBG ≥170mg/dl were used for further experimentation. The rats in this group were divided into seven groups and designated thus:

ND_2C: non-diabetic control
ND_2R: non-diabetic rats given raw ginger extract
ND_2Co: non-diabetic rats given cooked ginger extract
D_2C: diabetic control
D_2R: diabetic rats given raw ginger extract
D_2Co: diabetic rats given cooked ginger extract
D_2D: diabetic rats given antidiabetic drug

Extracts' administration: Raw and cooked ginger extracts (2ml/kg body weight containing 6.8mg of gingerol/kg body weight for raw extract and 9.4mg of gingerol/kg body weight for cooked extract) and the anti-diabetic drug (Metformin- 200mg/kg body weight) were administered once daily for 4 weeks with gastric canula according to the designation of the groups above. Gingerol is the active anti-diabetic component of fresh ginger.

Insulin Tolerance Test: This measures insulin sensitivity in large number of samples. The method of Buettner *et al.*, [30] was used with slight modification. Animals were fasted for 20 hours after which 0.15U/kg body weight of insulin (Humulin, Eli Lilly, Indiana, U.S.A) was administered intraperitonealy and the blood glucose was determined at 0, 10, 20, and 30 minutes. The animals were given glucose solution ad libitum immediately after the test to prevent hypoglycaemic shock. This test was performed before HFD consumption, at 12 weeks HFD consumption, and at end of the 4 weeks of extracts administration.

Insulin sensitivity can be expressed in K_{ITT} which is the rate constant for ITT (Insulin Tolerance Test). This can be calculated from the ITT data using the following equation:

$$K_{ITT}(\%/\min) = \frac{0.693}{t_{0.5}} \times 100$$

Where $t_{0.5}$ is the time required for blood glucose to reach half of its initial value or the blood glucose half time. Normal K_{ITT} is ≥ 2.0%/min while values less ≤ 1.5%/min is considered abnormal and depicts a state of insulin resistance or insensitivity.

Statistical analysis: Descriptive statistics (mean, standard deviation) and inferential statistics (Analysis of Variance-Least Significant Difference) were used to analyse the data using Statistical Package for Social Science (SPSS) version 17.

3. Result

Insulin Tolerance Test result before the introduction of HFD is expressed in Table 1. Glucose was disappearing from the blood at a normal rate.

After a 12 week consumption of HFD by the diabetic groups insulin tolerance was greatly reduced because glucose disappearance from the blood was very slow and the rate low as can be seen in Table 2. On the other hand the three groups of rats that were maintained on the normal diet maintained a normal insulin tolerance (Table 2).

At 4 weeks of the ginger extracts administration, insulin tolerance among the non-diabetic groups of rat was not altered (Table 3) while in the diabetic groups (D_2R, D_2Co, and D_2D) insulin tolerance was greatly enhanced relative to the diabetic control group (D_2C).

Table 1. Insulin Tolerance Test (Insulin sensitivity) before the introduction of HFD

Groups	FBG (mg/dl) 0min	FBG (mg/dl) 10min	FBG (mg/dl) 20min	FBG (mg/dl) 30min
ND_2C	70.3± 0.87	63.6±1.01	50.3±0.71	36.2±1.05
ND_2R	79.0±1.22	71.7±1.58	52.9±1.36	39.0±1.41
ND_2Co	74.3±1.73	67.8±1.20	52.9±1.69	38.1±1.67
D_2C	74.6±1.42	67.4±1.67	47.7±1.22	36.0±1.12
D_2R	75.3±1.87	70.7±1.00	50.2±0.97	38.7±1.12
D_2Co	77.0±3.94	67.2±1.87	49.2±2.77	37.0±3.04
D_2D	68.6±3.54	61.8±4.49	47.7±2.83	32.4±2.30

FBG –Fasting blood glucose
ND_2C: Non-diabetic control; ND_2R: Non-diabetic rats given raw ginger extract; ND_2Co:Non-diabetic rats given cooked ginger extract; D_2C: Diabetic control; D_2R: Diabetic rats given raw ginger extract; D_2Co Diabetic rats given cooked ginger extract; D_2D: Diabetic rats given metformn.

Table 2. Insulin Tolerance Test at 12 weeks HFD consumption

Groups	FBG (mg/dl) 0min	FBG (mg/dl) 10min	FBG (mg/dl) 20min	FBG (mg/dl) 30min
ND_2C	71.9±5.58	67.6±2.74	57.0±1.58	42.1±2.42
ND_2R	71.7±1.73	68.2±1.32	58.6±1.94	40.4±2.18
ND_2Co	69.9±2.67	64.9±3.02	49.9±2.47	37.7±2.74
D_2C	172.2±4.29	170.9±2.14	169.1±3.22	165.9±2.62
D_2R	172.1±3.36	172.2±3.15	172.9±3.52	174.9±3.44
D_2Co	172.8±3.24	169.6±3.89	166.9±3.56	162.1±4.35
D_2D	172.0±2.00	170.6±5.01	168.2±2.47	163.1±3.52

FBG Fasting Blood Glucose
ND_2C: Non-diabetic control; ND_2R: Non-diabetic rats given raw ginger extract; ND_2Co:Non-diabetic rats given cooked ginger extract; D_2C: Diabetic control; D_2R: Diabetic rats given raw ginger extract; D_2Co Diabetic rats given cooked ginger extract; D_2D: Diabetic rats given metformn.

Table 3. Insulin Tolerance Test at 4 weeks raw and cooked ginger extracts and Metformin administration

Groups	FBG (mg/dl) 0min	FBG (mg/dl) 10min	FBG (mg/dl) 20min	FBG (mg/dl) 30min
ND_2C	70.8±1.30	67.7±2.83	55.3±2.87	40.3±3.67
ND_2R	68.3±4.21	64.1±3.69	52.3±2.45	35.8±3.96
ND_2Co	67.1±3.95	63.6±2.40	51.7±2.69	35.0±2.35
D_2C	178.4±3.50	177.0±3.39	175.3±2.74	174.4±2.74
D_2R	86.7±1.59	80.6±1.85	68.0±2.20	47.3±2.33
D_2Co	83.0±1.31	82.9±1.36	69.3±1.49	60.9±2.17
D_2D	77.2±1.58	78.0±2.14	64.0±2.20	49.0±1.31

FBG Fasting Blood Glucose
ND_2C: Non-diabetic control; ND_2R: Non-diabetic rats given raw ginger extract; ND_2Co:Non-diabetic rats given cooked ginger extract; D_2C: Diabetic control; D_2R: Diabetic rats given raw ginger extract; D_2Co Diabetic rats given cooked ginger extract; D_2D: Diabetic rats given metformn.

Table 4. K_{ITT} (%/min) of the Insulin Tolerance Tests

Groups	K_{ITT} before HFD	K_{ITT} at 12 weeks HFD	K_{ITT} at 4 weeks ginger
ND_2C	2.2±0.76	1.9±0.23	2.0±0.25
ND_2R	2.3±0.09α	2.0±0.20α	2.2±0.18α
ND_2Co	2.3±0.08α	2.1±0.25α	2.2±0.14α
D_2C	2.4±0.07	0.2±0.14	0.1±0.06
D_2R	2.3±0.10α	0.1±0.07α	2.1±0.12*
D_2Co	2.4±0.24α	0.3±0.09α	1.2±0.13*
D_2D	2.4±0.21α	0.2±0.09α	1.7±0.09*

* significantly different from diabetic control; α – not significantly different from ND_2C and D_2C
ND_2C: Non-diabetic control; ND_2R: Non-diabetic rats given raw ginger extract; ND_2Co:Non-diabetic rats given cooked ginger extract; D_2C: Diabetic control; D_2R: Diabetic rats given raw ginger extract; D_2Co Diabetic rats given cooked ginger extract; D_2D: Diabetic rats given metformn.

Table 4 shows the constant for ITT as computed from the results of Insulin Tolerance Test before HFD introduction, after 12weeks HFD consumption and at the end of the 4 weeks ginger extracts administration. $K_{ITT} \geq 2.0$ is normal. At baseline (before HFD introduction) K_{ITT} in all the groups was normal while at 12 weeks of HFD consumption by the diabetic groups K_{ITT} has reduced drastically (Table 4). The 4 weeks raw and cooked ginger extracts administration as well as the drug had a beneficial effect in increasing the K_{ITT} in the diabetic groups (D_2R, D_2Co and D_2D).

4. Discussion

The glucose disappearance rate at 10, 20 and 30 minutes was similar in all the groups before the introduction of the HFD because this was 9.53%, 20.91% 28.05% respectively in the non-diabetic control group (ND_2C) and 9.65%, 29.22% and 24.52% in the diabetic control group (D_2C) as can be deduced from Table 1 and the trend in other groups was similar to these. This is the case in a normal and non insulin resistant state showing that the exogenous insulin was effectively responsive in enhancing glucose uptake by body cells and well tolerated, hence, a normal glucose disappearance rate was recorded. This was in line with the report of Okita *et al.*, [31] who observed similar glucose disappearance rate in non-diabetic human subjects. This shows that insulin was well tolerated before the introduction of the HFD.

However, after a 12 week HFD consumption the glucose disappearance rate among the non-diabetic groups that were not given the experimental diet maintained a normal trend while that of the rats fed experimental diet have reduced glaringly. For instance, in the diabetic control group the glucose disappearing rate was 0.75%, 1.05% and 1.89% at 10, 20 and 30 minutes respectively and this was similar in all other diabetic groups as can be estimated from Table 2. This clearly shows that the 12 week HFD was able to induce an insulin resistant state. The glucose disappearing rate observed among Type 2 diabetic patients was comparatively lower than that of normal subjects as reported by Okita *et al.*, [31] but not as low as that observed after a 12 week HFD consumption by rats in this study. The report of this study was in line with the observation of Croze *et al*, [32] in Type 2 diabetic mice fed HFD.

The 4 weeks raw and cooked ginger extracts administration enhanced glucose disappearance rate in the non-diabetic rats relative to the non-diabetic control group that was not treated (Table 3) while the efficacy of these extracts and metformin in ameliorating the induced insulin resistant state was clearly evidenced among the diabetic groups (Table 3). In the diabetic control group glucose disappearing rate at 10, 20 and 30 minutes were: 0.07%, 0.96% and 0.34% respectively while in the diabetic rats given raw ginger juice these rate were: 7.03%, 15.63% and 30.44% at 10, 20 and 30 minutes respectively. Similar trend was observed in the drug-treated diabetic group while in he cooked extract-treated group the glucose disappearance rate was not as high as in the other groups as can be deduced from Table 3. This shows clearly that the induced insulin resistant state was ameliorated by the raw and cooked as well as drug administration. The glucose disappearing rate observed in this study before the introduction of the HFD (Table 1) as well as that of Pereira *et al.*, [33] in non-insulin resistant states was similar to that of the treated groups inn this study (Table 3), hence, raw and cooked ginger extracts could be beneficial in the treatment/management of Type 2 diabetes mellitus.

There was no significant difference ($p<0.05$) in K_{ITT} in all the groups before the introduction of the HFD with the evidence of normal insulin sensitivity because the K_{ITT} values in all the groups were greater than 2%/min (Table 4). Even though the K_{ITT} values tend to reduce slightly in the groups of rats that were fed normal diet at 12 weeks ($K_{ITT\ at}$ 12 weeks HFD) compared to the values at the beginning of this study the values still depicted a normal insulin sensitivity state with an mean value of 2.01 in these three groups of rats as can be deduced from Table 4. On the other hand in the groups that were fed HFD for 12 weeks there existed a marked significant ($p<0.05$) reduction in insulin sensitivity compared to the rats groups that were fed normal diet affirming the induction of insulin resistance by chronic HFD consumption [34]. Raw, cooked ginger extracts and metformin significantly increased insulin sensitivity from 0.10 in the diabetic control group to 2.09, 1.23 and 1.69%/min respectively at 4 weeks administration (Table 4) while in the groups fed normal diet raw and cooked extracts also increased insulin sensitivity by 10.55 and 11.06% respectively as can be deduced from Table 4 thus establishing the evidence of past scientific reports that ginger improves insulin sensitivity [35,36,37,38].

5. Conclusion and Recommendation

Raw and cooked ginger extracts enhanced insulin sensitivity in normal and high-fat diet-induced diabetic rats. The efficacy of the raw extract in bringing insulin sensitivity back to normal in the diabetic state was clearly evident while cooked ginger extract also improved the insulin sensitivity but not to the normal level within the four weeks of administration.. Dietary ginger may therefore be beneficial in the prevention and management of Type 2 diabetes mellitus. Human trial is hereby recommended.

References

[1] Xu E., Schwah M. and Marette A. (2014). Role of protein tyrosine phosphatase in the modulation of insulin signaling and their implication in the pathogenesis of obesity-linked insulin resistance. *Review on Endocrine and Metabolic Disorders;* 15(1): 79-97.

[2] Fukami K., Yamgishi S. and Okuda S. (2014). Role of Advanced Glycation Endproducts-Receptor for dvanced Glycation Endproduct system in cardiovascular disease. *Home/Current Pharmaceutical Design*; 20(14): 2395-2402.

[3] Ramachandran A,, Snchalatha C., Latha E., Manoharan M. and Vijay V (1999). Impart of urbanization on the lifestyle on the prevalence of diabetes in Native Asian Indian population. *Diabetes Research and Clinical Practice;* 44(3): 207-213.

[4] Harris M.J., Flegal K.M., Cowie C.C., Eberharddt M.S., Goldstein D.E., Little R.R. Weidmeyer H-M and Holt D.D.B. (1998). Prevalence of diabetes impaired fasting glucose and impaired glucose tolerance in U.S. adults: The third National Health and Nutrition Examination Survey, 1988-1994. *Diabetes Care*; 21(4): 518-5.

[5] Cowie C.C., Rust K.F., Byrd-Holt D.D., Gregg E.W., Ford E.S., Geiss L.S., Banbridge K.E. and Fradkin J.E. (2010). Prevalence of diabetes and high risk for diabetes using A1C criteria in the U.S. population in 1988-2006. *Diabetes Care*; 33(3): 362-268.

[6] Pan X-R., Yang W-Y., Li G-W., Liu J. and National Diabetes Prevention and Control Co-operative Group (1997). Prevalence of diabetes and its risk factors in China. *Diabetes Care*; 20(11): 1664-1669.

[7] Yang W., Lu J., Weng J., Jia W., Ji L., Xiao J., Shan Z., Liu J., Tian H., Ji Q., Zhu D., Ge J., Lin L., Chen L., Guo X., Zhao Z., Li Q., Zhou Z., Shan G. and He J. (2010). Prevalence of Diabetes among men and women in China. *The New England Journal of Medicine*; 362: 1090-1101.

[8] Xu Y., Wang L., He J., Bi Y., Li M., Lu J., Xu M., Li Y., Hu N., Li J., Mi S., Chen C-S., Li G., Mu Y., Zhao J., Kong L., Chen J., Lai S., Wang W., Zhao W. and Ning G. (2013). Prevalence and control of diabetes in Chinese adults. *The Journal of the American Medical Association*; 310(9): 948-959.

[9] Rotimi C.N., Cooper R.S., Okosun I.S., Olatubosum S.T., Bella A.F., Wilks R., Bennett F., Cruickshank J.K. and Korrester T.E, (1999). Prevalence of diabetes and impaired glucose tolerance in Nigerians, Jamaicans and U.S. Blacks. *Ethnicity and Disease*; 9(2): 190-200.

[10] Cooper R.S., Rotimi C.N., Kaufman J.S., Owoaje E.E., Fraser H., Forrester T., Wilks R., Riste L.K. and Cruickshank J.K. (1997). Prevalence of NIDDM among populations of the African Diaspora. *Diabetes Care*; 20(3): 343-348.

[11] Whiting D.R., Guarigata L., Weil C. and Shaw J. (2011). IDF Diabetes Atlas: Global estimates of the prevalence of diabetes for 2011 and 2030. *Diabetes Research and Clinical Practice*; 94(3): 311-321.

[12] Dabelea D., Hanson R.L., Bennett P.H., Roumain J., Knowler W.C. and Pettitt D.J. (1998). Increasing prevalence of Type 2 diabetes in American Indian children. *Diabetologia*; 41(8): 904-910.

[13] Amos A., McCarty D. and Zimmet P. (1997). The rising global burden of diabetes and its complications: estimates and projections to the year 2010. *Diabetic Medicine*; 14: S1-S85

[14] Zimmet P. (2003). The burden of type 2 diabetes, are we doing enough? *Diabetes and Metabolism*; Vol. 29, Issue 4 part 2: 659-668.

[15] Wild S., Roglic G., Green A., Sicree R. and King H. (2004). Global prevalence of diabetes: Estimates for the year 2000 and projections for 2030. *Diabetes Care;* 27(5): 1047-1053.

[16] Guariguata L., Whiting D.R., Humbleton I., Beagley J., Linnenkamp U. and Shaw J.E. (2014). Global estimates of diabetes prevalence for 2013 and projections for 2035. *Diabetes Research and Clinical Practice*; 103(2): 137-149.

[17] Boden G. and Shulman G.I. (2002). Free fatty acids in obesity and Type 2 diabetes: Defining their role in the development of insulin resistance and beta cell dysfunction.*European Journal of Clinical Invesigation*; 32: 14-23.

[18] Kraegen E.W., Cooney G.T., Ye J. and Thompson A.L. (2001). Triglycerides, fatty acids and insulin resistance, hyperinsulinemia. *Experimental and Clinical Endocrinology and Diabetes;* 109: 516-526.

[19] Steppan C.M. and Lazar M.A. (2004). The current biology of resistin. *Journal of Internal Medicine;* 255: 439-447.

[20] Yamauchi T., Kamon J., Waki H., Terauchi Y., Kubota N., Hara K., Mori Y., Ide T., Murakami K. and Tsuboyama-Kasaoka N. (2001). The fat-derived hormone adiponectin reverses insulin resistance associated with both lipoatrophy and obesity. *Nature Medicine;* 7: 941-946.

[21] Park S-Y., Cho Y-R., Kim H-J., Higashimori T., Danton C., Lee M-K., Dey A., Rothermel B., Kim Y-B., Kalinowski A., Russel K.S. and Kim J.K. (2005). Unravelling the temporal pattern of diet-induced insulin resistance in individual organs and cardiac dysfunction in C57BL/6 mice. *Diabetes*; 54: 3530-3540.

[22] White M.F. (1998). The IRS-1 signaling system: a network of docking proteins that mediate insulin and cytokines action. *Recent Progress in Hormone Research;* 53: 119-138.

[23] Le Roith D. and Zick Y. (2001). Recent advances in our understanding of insulin action and insulin resistance. *Diabetes Care*; 24: 588-97.

[24] Goldstein B.J., Bittner-Kowalczyk A., White M.F. and Harbeck M. (2000). Tyrosine dephosphorylation and deactivation of insulin receptor substrate-1 by protein tyrosine phosphatase 1B, possible facilitation by the formation of a ternary complex with the grb2 adaptor protein. *Journal of Biological Chem*istry; 275: 4283-4289.

[25] Ojewole J.A.O (2006). Analgesic, Antiinflammatory and Hypoglycemic effects of ethanol extract of Zingiber officinale (Roscoe) rhizomes in mice and rats. *Phytotherapy Research*: 20: 764-772.

[26] Al-Amin Z.M., Thomson M., Al-Qattan K.K., Peltonen-Shalaby R. and Ali M. (2006). Antidiabetic and hypolipidemic properties of ginger (Zingiber officinale) in streptozotocin-induced diabetic rats. *British Journal of Nutrition*; 96(4): 660-666.

[27] Akhani S.P., Vishwakarma S.L and Goyal R.K. (2005). Antidiabetic activity of *Zingiber officinale* Roscoe in streptozotocin-induced non-insulin dependent diabetic rats. *Indian Journal of Pharmaceutical Science*; 65(5): 553-557.

[28] Elshater A.A., Salman M.M.A. and Moussa M.M.A. (2009). Effect of Ginger extract consumption on levels of blood glucose, lipid profile and kidney functions in alloxan-induced diabetic rats. *Egyptian Academic Journal of Biological Sciences*; 2(1): 153-162.

[29] Martinello F., Soares S.M. and Franco J.J. (2006). Hypolipidemic and antioxidant sctivates from Tamarindus indica pulp fruit extract in hypercholesterolemic hamsters. *Food and Chemical Toxicology*; 44(6): 810-818.

[30] Buettner R., Parhofer K.G., Woenckhaus M., Wrede C.E., Kunz-Schughart L.A., Scholmerich J. and Bollheimer L.C. (2006). Defining high-fat diet rat models: metabolic and molecular effects of different fat types. *Journal of Molecular Endocrinology*; 36: 485-501.

[31] Okita K., Iwahashi H., Kozawa J., Okauchi Y., Funahashi T., Imagawa A. and Shimomura I. (2013). Usefulness of the insulin tolerance test in patients with Type 2 diabetes receiving insulin therapy. Journal of Diabetes Investigation; 5(3): 30-312.

[32] Croze M.L., Geleon A. and Soulage C.O. (2015). Abnormalities in myo-inositol metabolism associated with type 2 diabetes in mice fed a high-fat diet: benefits of a dietary myo-inositol supplementation. British Journal of Nutrition; 113: 1862-1875.

[33] Pereira M.P., Buzelle S.L., Batistela E., Doneda D.L., De Franca S.A., dos Sandos M.P., Andrade C.M.B., Ganofalo M.A.R. and Kawashita N.H. (2014). High glucose uptake in growing rats adapted to a low-protein high-carbohydrate diet determines low fasting glycemia even with high hepatic gluconeogenesis. Canadian Journal of Physiology and Pharmacology; 92(6): 460-466.

[34] Li Y., Tran V.H., Kota B.P., Nammi S., Duke C.C. and Roufogalis B.D. (2014). Preventive effect of Zingiber offinale on insulin resistance in a high-fat high-carbohydrate diet-fed rat model and its mechanism of action. *Basic Clinical Pharmacology and Toxicology*; 115(2): 209-215.

[35] Arablou T., Aryaeian N., Valizadeh M., Shariffi F., Hosseini A. and Djalali M. (2014). The effect of ginger consumption on glycemic status, lipid profile and some inflammatory markers in patients with Type 2 diabetes mellitus. *InternationalJournal of Food Sciences and Nutrition*; 65(4): 515-520.

[36] Mozaffari-Khosravi H., Talaei B., Jalali B-A., Najarzadeh A. and Mozayan M.R. (2014). The effect of ginger powder supplementation on insulin resistance and glycemic indices in patients with Type 2 diabetes: A randomized double-blind placebo-controlled trial. *Complementary Therapies in Medicine*; 22(1): 9-16.

[37] Mahluji S., Attari V.E., Mabassori M., Payahoo L., Ostadrahimi A. and Golzari S.E.J. (2013). Effect of ginger (Zingiber officinale) on plasma glucose level, HbA1c and insulin sensitivity in type 2 diabetic patients. *International Journal of Food Sciences and Nutrition*; 64(6): 682-686.

[38] Iranloye B.O., Arikawe A.P., Rotimi G and Sobade A.O. (2011). Anti diabetic and antioxidant effects of *Zingiber officinale* on alloxan-induced and insulin resistant diabetic male rats. *Nigerian Journal of Physiological Sciences*; 26(1): 89-96.