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EFFECTS OF *Nigella sativa*, *Zingiber officinale*, *Cinnamomum zeylanicum* ON SERUM LIPID PROFILE, GLUCOSE, WEIGHT, AND KIDNEY FUNCTION TESTS IN THE ANIMAL MODEL OF STZ INDUCED DIABETES MELLITUS IN MALE RATS

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ABSTRACT

This study was conducted to observe the serum biochemical changes associated with Diabetes Mellitus, in the STZ induced Diabetic rats, treated with *Nigella sativa*, Cinnamon and ginger. The study was comprised of forty adult male wistar rats, divided into eight groups of five each. Group I Untreated rats, Group II Diabetic rats (Intra-venous injection of 60mg/kg dose of Streptozotocin), the positive control group. Group III Preventive Ginger. Group IV Preventive Cinnamon: Group V Preventive *Nigella sativa*. Group VI; Therapeutic Ginger Diabetic rats; received 10000 mg/kg BW/day of the ginger extract. Group VII Cinnamon Therapeutic, Diabetic rats; received cinnamon extract 400 mg/Kg body weight and Group VIII *Nigella sativa* Therapeutic received, 200 mg/kg *Nigella sativa* extract daily. The animal were treated for 3 weeks. The diabetic rats showed increase in serum glucose levels accompanied by increase in Kidney function test parameters like Urea, Creatinine and Cysteine C levels .The animals also exhibited increase in serum Total Cholesterol (TC) and Triglycerides (TG). At the same time reductions were observed in High Density Lipoprotein Cholesterol (HDL-C) levels. Ginger effectively decreased serum glucose levels and brought the above mentioned serum assays levels near to normal value. Histological examination of the pancreas of STZ given rats, which were treated with ginger showed almost normal structure, in comparison to untreated diabetic group. The results of the study show that

treatment with aqueous extract of ginger may be efficacious in bringing down the increased serum glucose levels and dyslipidemias in diabetic rats.

Keywords: *Nigella sativa*, *Zingiber officinale*, *Cinnamomum zeylanicum*, Diabetes Mellitus, Kidney Function

INTRODUCTION

Diabetes mellitus is a group of metabolic disorders which is associated with Hyperglycemia due to defective insulin secretion, defective Insulin function or combination of these two [1]. According to estimates of IDF , 415 m global population was suffering from Diabetes mellitus in 2015 and the number of Diabetic patients is going to increase 642 m by 2040 [2, 3].

The available data shows that Diabetes prevalence, deaths attributable to diabetes, and health expenditure due to diabetes continue to rise across the globe with important social, financial and health system implications [4].

The ECDCDM (Expert Committee on the Diagnosis and Classification of DM), has revised the diagnostic criteria, based upon the data from three large cross-sectional epidemiologic studies which define the cut-off levels of serum glucose levels, which are related to augmented micro-vascular disease, like retinopathy. Minimum two repeated fasting levels that exceed 126 mg/dl (>7 mmol/L) are necessary to diagnose diabetes in the absence of clinical features. A value of 100 mg/dl or above confirms the diagnosis of impaired fasting glucose (IFG). Individuals with Impaired Fasting Glucose levels (FPG= 100-125 mg/dl (5.66.9 mmol/l) having impaired glucose tolerance test (IGT) Two hours after-load serum glucose 140-199 mg/dl (78.8 mmol/L-11.1 mmol/L) may develop diabetes . Repeated levels of two-hour glycemic responses >200 mg/dl (>11.1 mmol/L) after a standard oral glucose tolerance test (OGTT) also indicates diabetes. Raised fasting glucose levels usually precede this stage in Type 2Diabetes Mellitus [5]. Role of oxidative stress has now been well established as main causative agent at molecular level [6].Continuous exposure of human body to variety of agent's results in production of free radicals (ROS/RNS), the transfer of free unpaired electrons of free radicals lead to oxidation of cellular organelles [7].

To protect body from harmful effects of these species, body's endogenous antioxidant system comes into action or antioxidants are obtained exogenously from diet, which neutralize these species and keep the homeostatic mechanisms working. Imbalance between the RS and antioxidants creates Oxidative stress, that leads to

development of several pathologies including, Diabetes [8]. The Oxidative stress also leads to several complications associated with diabetes like micro and macrovascular complications, neuropathy, retinopathy and nephropathy [9].

Almost 40% Diabetic patients (type 1 as well as type 2) develop nephropathy ,that is main cause of chronic renal failure requiring renal replacement therapy and significantly increases morbidity as well as mortality [10]. Principal characteristic feature of diabetic nephropathy is proteinuria ranging from micro to macro albumin urea [11, 12]. Main functional abnormality seen in diabetic associated nephropathy is that the substances which are required to be retained in the body like albumin, are getting excreted and substances which are normally getting excreted via kidney ,are retained in the body like urea/BUN, at the same time Vitamin D is not getting activated therefore resulting in decrease in absorption of calcium leading to osteoporosis. At the same time decreased kidney function also affects the release of erythropoietin resulting in anemia [13].

The progressive renal failure also leads to variety of serum electrolyte disturbances and resulting symptoms [14]. The abnormality occurring in the renin-angiotensin mechanism leads to increase in blood pressure and a vicious circle starts that is characterized by more damage to kidney-diabetic nephropathy –hypertension [15].

Current approach for the prevention and treatment of diabetic nephropathy and related complications is to control glycaemia, hypertension, to delay progression of the disease mange the complications associated with chronic renal failure like anemia, Vitamin D deficiency and serum electrolytes [16, 17]. It also is necessary to control the dyslipidemias when patient is suffering from Diabetic nephropathy to reduce the cardiovascular problems.

Unfortunately at present, no single drug or proper pharmacotherapy is available to address the diabetic nephropathy as well as the complications caused by it [18].

Nigella sativa, widely known as black seeds contain wide variety of functional chemical substances [19, 20]. In many previous studies Nigella Sativa has been found effective in reducing the serum glucose levels as well as in treatment of dyslipidemias [21, 22]. It has been found to possess Nephroprotective properties as well [23].

Ginger (*Zingiber officinale*) is a spice used very widely in Asia [24]. Chemical analysis of ginger shows that it contains over 400 different compounds. The major

constituents in ginger rhizomes are carbohydrates (50–70%), lipids (3–8%), terpenes, and phenolic compounds. Ginger contains over 400 different constituents. Main constituents are carbohydrates, lipids, terpenes, and phenolic compounds. Terpene components of ginger include zingiberene, β-bisabolene, α-farnesene, β-sesquiphellandrene, and α-curcumene, phenolic compounds like gingerol, paradols, and shogaol. Ginger also contain amino acids, raw fiber, ash, protein, phytosterols, vitamins (e.g., nicotinic acid and vitamin A), and minerals [25,26].

Being rich in antioxidant components ginger has been found to possess antioxidant properties and hence reduces oxidative stress [27].

Cinnamomum zeylanicum, commonly known as Cinnamon , ia a well-used spice in Asia. It contains, Cinnamaldehyde, Eugenol, β – Caryophyllene, Linalool, Ethyl cinnamate, etc [28]. Cinnamon is known to possess serum glucose lowering effects, due to its property of increasing the insulin levels, it also has been found to decrease HbA1C and serum cholesterol levels [29].

Metformin, a biguanide is very efficacious in prevention and treatment of DM, its usefulness and safety is well documented [30]. Primarily, Metformin stimulate the activity of insulin in hepatic and skeletal muscle cell, thereby reducing the glucose levels in blood.

Metformin causes increase in anaerobic metabolism in the intestinal wall that also may be important antihyperglycaemic mechanism of action [31]. Metformin also increases circulating levels of glucagon-like peptide-1 (GLP-1) by increasing the secretion of GLP-1 itself and/or by decreasing the activity of dipeptidyl peptidase-4 (DPP4), this enzyme inactivates GLP-1 in cells and blood [32].

It also induces upregulation of the expression of GLP-1 receptors on pancreatic β-cells surface, as GLP-1 stimulates glucose-dependent insulin release from the pancreas, this mechanism provides support to the function of the β cell. Metformin also produces some action on gut microbiome [33].

MATERIALS AND METHODS

This study was conducted in the department of Clinical Pharmacy, College of Pharmacy, Northern Border University, Rafha Campus, from September 2017 to March 2018.

Animals:

Forty healthy and active adult wistar albino male rats, 90-120 days old, and weighing 200-240 gm were selected. The rats were acclimatized under environmental condition with 24 ± 3 C°, 12hr light/dark cycle and good ventilation.

Induction of Diabetes:

The rats were kept fasting one night prior to the induction of DM by a single intraperitoneal injection of 60 mg/kg STZ dissolved in distilled water [34]. DM was confirmed after 4 days of injection, by measuring the tail vein serum glucose level with accu-check sensor comfort Glucometer. The rats which were having FBG levels ≥250 mg/dl were included in the study.

Experimental Design:

After acclimatization for 1 week before the use, randomized division of the animals was done at random into 8 groups. Each group included five rats and labelling was done as A, B, C, D, E, F, G and H, according to the treatment.

Ginger, *Nigella sativa* oil and Cinnamon were obtained from the local market. The aqueous extract was prepared and was administered via oral gavage, in dose of *Nigella sativa* (80 mg/kg), *Zingiber officinale* (500 mg/kg), and *Cinnamomum zeylanicum* (50mg/kg), in two divided doses per twenty four hours.

The rats were divided in 8 groups, Group A animals were considered as control, Group B animals, made diabetic without treatment, Group C, treated with ginger before induction of DM, Group D, given *Nigella sativa* before DM induction. Group E animals, given cinnamon prior to streptozotocin (STZ) injection, Group F, G, and H rats, treated with Ginger, *Nigella sativa*, and Cinnamon respectively, after DM induction.

Statistical Analysis:

The data analysis was carried out using the Statistical Package for Social Science (SPSS software version 20, Chicago, Illinois). All numeric variables were expressed as mean ± standard deviation (SD). Statistical comparisons were performed using the one-way analysis of variance (ANOVA) test followed by post hoc least significant difference (LSD) multigroup comparison. Homogeneity of variance was assessed using the one-way ANOVA test and Levene's statistic test. For all tests, a probability ($P < 0.05$) was considered significant.

RESULTS

Serum levels of creatinine in positive control, preventive Cinnamon and therapeutic Nigella Sativa were significantly higher than normal control (P =0.0001, P =0.0001, and P =0.024); meanwhile levels in preventive Ginger, preventive Nigella Sativa, therapeutic Ginger, therapeutic Cinnamon and therapeutic Nigella Sativa were significantly lower than positive control (P =0.0001, P =0.002, P =0.0001, P =0.0001 and P =0.024, respectively) figure (1).

Serum levels of urea in positive control, preventive Cinnamon were significantly higher than normal control (P =0.0001, and P =0.0001); meanwhile levels in preventive Ginger, preventive Cinnamon, preventive Nigella Sativa, therapeutic Ginger, therapeutic Cinnamon and therapeutic Nigella Sativa were significantly lower than positive control (P =0.0001 for all). figure (2).

Serum levels of cysteine -C in positive control, preventive Cinnamon and therapeutic Nigella Sativa were significantly higher than normal control (P =0.0001, P =0.0001, and P =0.035); meanwhile levels in preventive Ginger, preventive Cinnamon, preventive Nigella Sativa, therapeutic Ginger, therapeutic Cinnamon and therapeutic Nigella Sativa were significantly lower than positive control (P =0.0001, P =0.0001, P =0.0001, P =0.0001, P =0.0001, and P =0.036, respectively) figure (3).

Serum levels of triglyceride in positive control, preventive Cinnamon, preventive Nigella Sativa and therapeutic Ginger were significantly higher than normal control (P =0.0001, P =0.0001, P =0.0001and P =0.032, respectively); meanwhile levels in preventive Ginger, preventive Cinnamon, preventive Nigella Sativa, therapeutic Ginger, therapeutic Cinnamon and therapeutic Nigella Sativa were significantly lower than positive control (P =0.0001 for all) figure (4).

Serum levels of total cholesterol in positive control, preventive Nigella Sativa, therapeutic Cinnamon and therapeutic Nigella Sativa were significantly higher than normal control (P =0.012, P =0.0001, P =0.001 and P =0.006); meanwhile levels in preventive Ginger and preventive Nigella Sativa were significantly lower than positive control (P =0.047, and P =0.001, respectively) figure (5).

Serum levels of HDL-C in positive control, preventive Ginger, preventive Cinnamon and preventive Nigella Sativa were significantly higher than normal control (P =0.0001, P =0.018, P =0.004 and P =0.018); meanwhile levels in preventive Ginger, preventive Cinnamon, preventive Nigella Sativa, therapeutic Ginger, therapeutic Cinnamon and therapeutic Nigella Sativa were significantly lower than positive control (P =0.018, P =0.0001, P =0.018, P =0.0001, P =0.0001, and P =0.0001, respectively) figure (6).

Serum levels of glucose in positive control, preventive Ginger, preventive Cinnamon, preventive Nigella Sativa, therapeutic Ginger, therapeutic Cinnamon, and therapeutic Nigella Sativa were significantly higher than normal control (P =0.0001, P =0.005, P =0.0001, P =0.0001 , P =0.0001 and P =0.0001); meanwhile

levels in preventive Ginger, preventive Cinnamon, preventive Nigella Sativa, therapeutic Ginger, therapeutic Cinnamon and therapeutic Nigella Sativa were significantly lower than positive control (P =0.0001 for all) (Table 1) figure (7).

In the first week, body weight in positive control, preventive Ginger, therapeutic Ginger were significantly higher (P =0.001, P =0.025 and P =0.001) but in therapeutic Nigella Sativa was significantly lower than normal control (P =0.022); meanwhile weights in preventive Cinnamon, preventive Nigella Sativa, therapeutic Cinnamon and therapeutic Nigella Sativa were significantly lower than positive control (P =0.005, P =0.011, P =0.017 and P =0.022, respectively). In the 2nd week, body weight in therapeutic Nigella Sativa was significantly lower than normal control (P =0.003). In the third week, body weight in positive control, preventive Ginger, preventive Cinnamon, therapeutic Ginger and therapeutic Cinnamon were significantly higher than normal control (P =0.002, P =0.0001, P =0.0001, P =0.0001 and P =0.002); meanwhile weights in preventive Ginger, preventive Nigella Sativa, therapeutic Cinnamon and therapeutic Nigella Sativa were significantly lower than positive control (P =0.034, P =0.0001, P =0.030 and P =0.0001, respectively) figure (8).

In the 1st week, food intake in preventive Nigella Sativa was significantly lower (P =0.007) but in therapeutic Ginger was significantly higher (P =0.017) than normal control; meanwhile food intake in preventive Cinnamon, preventive Nigella Sativa, therapeutic Cinnamon and therapeutic Nigella Sativa were significantly lower than positive control (P =0.040, P =0.0001, P =0.013 and P =0.006, respectively). In the 2nd week, food intake in preventive Ginger, therapeutic Ginger was significantly higher (P =0.019, P =0.0001) but in preventive Cinnamon, preventive Nigella Sativa, therapeutic Cinnamon and therapeutic Nigella Sativa was significantly lower (P =0.003, P =0.001, P =0.001 and P =0.0001, respectively) than normal control; meanwhile food intake in preventive Cinnamon, preventive Nigella Sativa, therapeutic Cinnamon and therapeutic Nigella Sativa were significantly lower than positive control (P =0.040, P =0.0001, P =0.013 and P =0.006, respectively). In the 3rd week, food intake in positive control, preventive Ginger, preventive Cinnamon, preventive Nigella Sativa, therapeutic Ginger, therapeutic Cinnamon and therapeutic Nigella Sativa were significantly higher than normal control (P =0.010, P =0.009, P =0.004, P =0.0001, P =0.0001, P =0.003, P =0.0001). Meanwhile

food intake in therapeutic Ginger, and Nigella Sativa were significantly higher than positive control (P =0.002, and P =0.018, respectively) (Table 2) figure (9).

In the 1st week, fasting blood glucose in positive control, preventive Ginger, preventive Cinnamon, preventive Nigella Sativa, therapeutic Ginger, therapeutic Cinnamon and therapeutic Nigella Sativa were significantly higher than normal control (P =0.0001, P =0.001, P =0.0001, P =0.0001, P =0.0001, P =0.0001, P =0.0001, respectively); meanwhile fasting blood glucose in preventive Ginger, preventive Cinnamon, preventive Nigella Sativa, therapeutic Cinnamon were significantly lower than positive control (P =0.0001 for all). In the 2nd week, fasting blood glucose in positive control, preventive Ginger, preventive Cinnamon, therapeutic Ginger, therapeutic Cinnamon and therapeutic Nigella Sativa were significantly higher than normal control (P =0.0001, P =0.0001, P =0.0001, P =0.0001, P =0.017, P =0.0001, respectively); meanwhile fasting blood glucose in preventive Ginger, preventive Nigella Sativa, therapeutic Cinnamon and therapeutic Nigella Sativa were significantly lower than positive control (P =0.0001 for all).

In the 3rd week, fasting blood glucose in positive control, preventive Cinnamon, preventive Nigella Sativa, therapeutic Ginger, therapeutic Cinnamon and therapeutic Nigella Sativa were significantly higher than normal control (P =0.0001, P =0.0001, P =0.0001, P =0.0001, P =0.0001, P =0.003, respectively); meanwhile fasting blood glucose in preventive Ginger, preventive Cinnamon, preventive Nigella Sativa, therapeutic Cinnamon and therapeutic Nigella Sativa were significantly lower than positive control (P =0.0001 for all) figure (10).

In the 1st week, random blood glucose in positive control, preventive Cinnamon, preventive Nigella Sativa and therapeutic Ginger were significantly higher than normal control (P =0.0001, P =0.0001, P =0.0001, P =0.023, respectively); meanwhile random blood glucose in preventive Ginger, preventive Nigella Sativa, therapeutic Ginger, therapeutic Cinnamon and therapeutic Nigella Sativa were significantly lower (P =0.0001 for all) But in preventive Ginger was significantly higher (P =0.0001) than positive control. In the 2nd week, random blood glucose in positive control, preventive Cinnamon, therapeutic Ginger, therapeutic Cinnamon, and therapeutic Nigella Sativa were significantly higher than normal control (P =0.0001for all); meanwhile random blood glucose in preventive Ginger, preventive Cinnamon, preventive Nigella Sativa, therapeutic Cinnamon and therapeutic

Nigella Sativa were significantly lower than positive control (P =0.0001 for all). In the 3rd week, random blood glucose in positive control, preventive Ginger, therapeutic Ginger, therapeutic Cinnamon, and therapeutic Nigella Sativa were significantly higher than normal control (P =0.0001for all); meanwhile random blood glucose in preventive Cinnamon, preventive Nigella Sativa, therapeutic Cinnamon and therapeutic Nigella Sativa were significantly lower than positive control (P =0.0001, P =0.0001, P =0.0001, P =0.001, respectively) (Table 3) figure (11).

DISCUSSION

In the current study, DM Type was induced in the animals with use of HFD+STZ. The current study was designed to observe the nephron-protective, nephron-curative and lipid/cholesterol reducing effects of Cinnamon, Nigella Sativa and Ginger, in comparison to Metformin. Regarding kidney function, parameters included were serum urea (end product of protein metabolism, excreted via kidney), serum creatinine (metabolite of kidney parenchymal, measured commonly to observe kidney function and cysteine c (a protein produced by body cells and excreted through kidney. Results of our study, regarding effects of Nigella Sativa related to serum urea, creatinine and body weight are in conformity with the study conducted by Dollah *et al* [35] and Serum cysteine C levels also decreased almost to normal range. Nephro-protective results in pretreated groups were almost similar as were observed by Shafiee **S** *et al* even though the nephrotoxicity was induced in that study with Cisplatin in our study it was due secondary to Diabetes mellitus ,which was induced with STZ [36]. In the study it was found that after induction of DM, levels of LDL/Cholesterol increased significantly and when treated with Nigella sativa the serum lipid profile came down, close to normal levels. These findings, tally with the previous study conducted by Dahri *et al* [37].

The study conducted by Morgan *et al* found that after induction of oxidative stress in male albino rats ,when the animals were treated with cinnamon a significant reduction in urea and creatinine was found at the same time kidney increase in kidney weight was also discovered [38]. Although the mode of induction of nephrotoxicity was different but almost similar results were found in the current study. Results of this study are also in conformity with the study conducted by Safdar *et al* [39] regarding reduction in the serum concentrations of urea and creatinine with treatment of Cinnamon after induction of nephrotoxicity. Regarding normalization of

dyslipidemias with cinnamon, our results are similar as has been seen in the study conducted by Tuzcu *et al* [40].

Regarding Ginger nephron-protective effects, results of our study are in conformity with the studies conducted by Hamed *et al* and Kopaei and Nasri [41, 42]. In which nephrotoxicity was induced with CCl4 and Gentamicin respectively. Results of current study show that after being kept on high fat diet and induction of DM, serum cholesterol levels raised market and when treated with Ginger, same came down, near to normal. Same observations were made in previous studies, even though materials and methods were bit different [43-45].

Regarding Metformin, lipid lowering effects, results of our study are in conformity with the previous studies [46]. Use of Metformin prevented kidney damage and improved kidney function significantly which was indicated by decrease in serum creatinine and urea. Results of treated group of our study regarding reduction in creatinine and urea levels are in conformity with the study conducted by Zhang *et al* [47].

CONCLUSION

This study concludes that the *Nigella sativa*, *Zingiber officinale*, *Cinnamomum zeylanicum*, possess antihyperglycemic, antihyperlipidemic, and Nephroprotective effects caused by diabetes mellitus. The lipid profile shows abnormal levels after induction of DM. It is suggested that further histochemical, phytochemical, investigations to be conducted to confirm the mechanism of action of these substances. At the same time, these substances should be studied for use as adjuvant therapeutic agents for the management of dyslipidemia, diabetes mellitus, and nephropathy associated with Diabetes mellitus.

Table (1): Kidney function tests, Cysteine –C and lipid profile in different studied groups

Groups	Creatinine (mg/dl)	Urea (mg/dl)	Cysteine- C (mg/L)	Total cholesterol (mg/dl)	Triglyceride (mg/dl)	HDL-C (mg/dl)	Glucose (mg/dl)
Normal control (NC)	0.47±0.15	33.32±5.82	0.61±0.15	91.00±8.72	70.20±4.66	23.20±1.30	60.20±5.07
Positive control Significance	1.74±0.68 ^{1}P=0.0001	101.40±11.46 ^{1}P=0.0001	1.53±0.44 ^{1}P=0.0001	119.40±9.81 ^{1}P=0.012	136.60±6.73 ^{1}P=0.0001	38.40±7.86 ^{1}P=0.0001	498.00±20.92 ^{1}P=0.0001
Preventive Ginger Significance	0.58±0.26 ^{1}P=0.655; ^{2}P=0.0001	41.60±12.36 ^{1}P=0.469; ^{2}P=0.0001	0.61±0.19 ^{1}P=0.992; ^{2}P=0.0001	97.40±13.15 ^{1}P=0.551; ^{2}P=0.047	72.20±7.36 ^{1}P=0.761; ^{2}P=0.0001	30.80±8.58 ^{1}P=0.018; ^{2}P=0.018	77.60±11.33 ^{1}P=0.105; ^{2}P=0.0001
Preventive Cinnamon Significance	1.60±0.29 ^{1}P=0.0001; ^{2}P=0.583	265.60±44.39 ^{1}P=0.0001; ^{2}P=0.0001	2.62±0.42 ^{1}P=0.0001; ^{2}P=0.0001	109.60±10.97 ^{1}P=0.090; ^{2}P=0.363	221.60±16.86 ^{1}P=0.0001; ^{2}P=0.0001	13.60±2.70 ^{1}P=0.004; ^{2}P=0.0001	91.60±14.67 ^{1}P=0.005; ^{2}P=0.0001
Preventive Nigella Sativa Significance	0.88±0.38 ^{1}P=0.111; ^{2}P=0.002	40.80±6.61 ^{1}P=0.513; ^{2}P=0.0001	0.70±0.12 ^{1}P=0.670; ^{2}P=0.0001	157.40±33.82 ^{1}P=0.0001; ^{2}P=0.001	99.00±14.90 ^{1}P=0.0001; ^{2}P=0.0001	30.80±3.11 ^{1}P=0.018; ^{2}P=0.018	100.80±22.82 ^{1}P=0.0001; ^{2}P=0.0001
Therapeutic Ginger Significance	0.68±0.28 ^{1}P=0.395; ^{2}P=0.0001	44.80±11.78 ^{1}P=0.317; ^{2}P=0.0001	0.92±0.40 ^{1}P=0.151; ^{2}P=0.0001	109.00±5.39 ^{1}P=0.100; ^{2}P=0.335	84.80±7.73 ^{1}P=0.032; ^{2}P=0.0001	24.60±1.82 ^{1}P=0.649; ^{2}P=0.0001	113.20±12.77 ^{1}P=0.0001; ^{2}P=0.0001
Therapeutic Cinnamon Significance	0.65±0.31 ^{1}P=0.418; ^{2}P=0.0001	35.40±7.27 ^{1}P=0.855; ^{2}P=0.0001	0.60±0.07 ^{1}P=0.947; ^{2}P=0.0001	128.60±22.52 ^{1}P=0.001; ^{2}P=0.393	77.40±3.29 ^{1}P=0.278; ^{2}P=0.0001	26.20±4.21 ^{1}P=0.332; ^{2}P=0.0001	106.80±19.36 ^{1}P=0.0001; ^{2}P=0.0001
Therapeutic Nigella Sativa Significance	1.14±0.57 ^{1}P=0.012; ^{2}P=0.024	31.80±5.54 ^{1}P=0.894; ^{2}P=0.0001	1.07±0.52 ^{1}P=0.035; ^{2}P=0.036	122.60±10.60 ^{1}P=0.006; ^{2}P=0.765	79.00±12.45 ^{1}P=0.197; ^{2}P=0.0001	1.80±3.27 ^{1}P=0.159; ^{2}P=0.0001	102.00±17.73 ^{1}P=0.0001; ^{2}P=0.0001

Data are expressed as mean +/- standard deviation; ^{1}P: significance versus control; ^{2}P: significance versus positive control.

Table (2): Body weight and food intake in different studied groups in different weeks

Groups	Body weight (grams)			Food intake (grams)		
	1st week	2nd week	3rd week	1st week	2nd week	3rd week
Normal control (NC)	246.80±8.96	290.00±12.53	312.00±18.26	29.42±3.48	79.00±5.34	60.20±5.07
Positive control Significance	301.20±33.00 ^{1}P=0.001	261.60±40.39 ^{1}P=0.231	506.75±62.64 ^{1}P=0.0001	37.08±4.90 ^{1}P=0.017	93.00±23.52 ^{1}P=0.253	113.00±20.07 ^{1}P=0.010
Preventive Ginger Significance	283.40±14.22 ^{1}P=0.025; ^{2}P=0.262	301.00±32.67 ^{1}P=0.639; ^{2}P=0.100	428.00±35.25 ^{1}P=0.002; ^{2}P=0.034	31.13±6.05 ^{1}P=0.575; ^{2}P=0.071	105.20±16.15 ^{1}P=0.019; ^{2}P=0.318	106.80±33.88 ^{1}P=0.009; ^{2}P=0.748
Preventive Cinnamon Significance	254.00±9.70 ^{1}P=0.647; ^{2}P=0.005	246.60±30.44 ^{1}P=0.071; ^{2}P=0.523	510.20±38.82 ^{1}P=0.0001; ^{2}P=0.923	30.25±2.63 ^{1}P=0.785; ^{2}P=0.040	32.65±0.92 ^{1}P=0.003; ^{2}P=0.001	111.80±34.98 ^{1}P=0.004; ^{2}P=0.950
Preventive Nigella Sativa Significance	259.20±31.28 ^{1}P=0.432; ^{2}P=0.011	244.20±28.23 ^{1}P=0.057; ^{2}P=0.459	352.00±74.05 ^{1}P=0.240; ^{2}P=0.0001	20.58±2.59 ^{1}P=0.007; ^{2}P=0.0001	27.43±1.03 ^{1}P=0.001; ^{2}P=0.0001	131.80±22.66 ^{1}P=0.0001; ^{2}P=0.334
Therapeutic Ginger Significance	301.20±33.00 ^{1}P=0.001; ^{2}P=1.000	261.60±40.39 ^{1}P=0.231; ^{2}P=1.000	506.75±62.64 ^{1}P=0.0001; ^{2}P=1.000	37.08±4.90 ^{1}P=0.017; ^{2}P=1.000	159.67±38.55 ^{1}P=0.0001; ^{2}P=0.0001	180.25±31.16 ^{1}P=0.0001; ^{2}P=0.002
Therapeutic Cinnamon Significance	261.80±28.60 ^{1}P=0.343; ^{2}P=0.017	278.40±45.34 ^{1}P=0.621; ^{2}P=0.475	425.80±57.01 ^{1}P=0.002; ^{2}P=0.030	28.60±2.94 ^{1}P=0.787; ^{2}P=0.013	30.95±0.25 ^{1}P=0.001; ^{2}P=0.0001	114.80±25.22 ^{1}P=0.003; ^{2}P=0.926
Therapeutic Nigella Sativa Significance	209.20±22.53 ^{1}P=0.022; ^{2}P=0.0001	214.40±50.35 ^{1}P=0.003; ^{2}P=0.051	313.40±56.66 ^{1}P=0.967; ^{2}P=0.0001	28.02±6.19 ^{1}P=0.625; ^{2}P=0.006	30.54±4.27 ^{1}P=0.0001; ^{2}P=0.0001	160.80±22.42 ^{1}P=0.0001; ^{2}P=0.018

Data are expressed as mean +/- standard deviation; ^{1}P: significance versus control; ^{2}P: significance versus positive control.

Table (3): Fasting and random blood glucose in different studied groups in different weeks

Groups	Fasting blood glucose (mg/dl)			Random blood glucose (mg/dl)		
	1st week	2nd week	3rd week	1st week	2nd week	3rd week
Normal control (NC)	81.60±9.91	135.20±6.22	80.20±6.14	104.80±8.17	72.80±2.95	80.20±11.65
Positive control Significance	418.20±33.49 [1]P=0.0001	458.00±46.54 [1]P=0.0001	478.25±27.48 [1]P=0.0001	528.80±30.56 [1]P=0.0001	514.80±42.38 [1]P=0.0001	255.00±37.52 [1]P=0.0001
Preventive Ginger Significance	155.20±35.52 [1]P=0.001; [2]P=0.0001	161.75±22.87 [1]P=0.322; [2]P=0.0001	86.60±9.50 [1]P=0.845; [2]P=0.0001	249.25±26.54 [1]P=0.0001; [2]P=0.0001	84.40±8.29 [1]P=0.284; [2]P=0.0001	250.00±24.44 [1]P=0.0001; [2]P=0.816
Preventive Cinnamon Significance	155.80±43.73 [1]P=0.0001; [2]P=0.0001	514.50±36.71 [1]P=0.0001; [2]P=0.052	216.80±22.71 [1]P=0.0001; [2]P=0.0001	484.20±47.42 [1]P=0.0001; [2]P=0.117	219.00±10.79 [1]P=0.0001; [2]P=0.0001	121.00±12.71 [1]P=0.065; [2]P=0.0001
Preventive Nigella Sativa Significance	161.00±23.52 [1]P=0.0001; [2]P=0.0001	139.50±20.02 [1]P=0.871; [2]P=0.0001	220.60±41.12 [1]P=0.0001; [2]P=0.0001	470.00±78.81 [1]P=0.0001; [2]P=0.054	99.20±22.10 [1]P=0.115; [2]P=0.0001	108.20±31.52 [1]P=0.198; [2]P=0.0001
Therapeutic Ginger Significance	418.20±33.49 [1]P=0.0001; [2]P=1.000	479.75±41.92 [1]P=0.0001; [2]P=0.440	428.25±122.70 [1]P=0.0001; [2]P=0.179	470.20±23.00 [1]P=0.0001; [2]P=0.042	514.80±42.38 [1]P=0.0001; [2]P=1.000	215.00±18.92 [1]P=0.0001; [2]P=0.070
Therapeutic Cinnamon Significance	234.80±23.69 [1]P=0.0001; [2]P=0.0001	202.00±78.74 [1]P=0.017; [2]P=0.0001	252.00±64.59 [1]P=0.0001; [2]P=0.0001	500.60±70.45 [1]P=0.0001; [2]P=0.316	395.40±20.70 [1]P=0.0001; [2]P=0.0001	422.20±31.90 [1]P=0.0001; [2]P=0.0001
Therapeutic Nigella Sativa Significance	451.00±5.90 [1]P=0.0001; [2]P=0.096	251.00±25.90 [1]P=0.0001; [2]P=0.0001	186.20±38.52 [1]P=0.003; [2]P=0.0001	545.00±19.96 [1]P=0.0001; [2]P=0.562	366.80±24.81 [1]P=0.0001; [2]P=0.0001	337.20±66.46 [1]P=0.0001; [2]P=0.001

Data are expressed as mean +/- standard deviation; [1]P: significance versus control; [2]P: significance versus positive control.

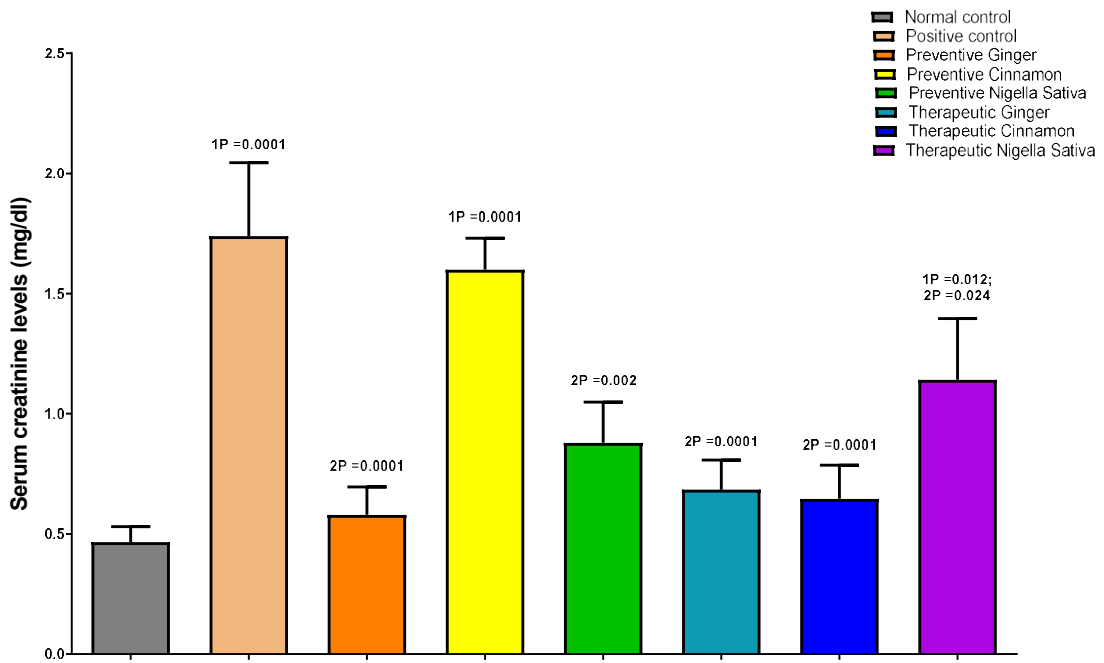

Figure 1: Serum Creatinine Levels of different groups

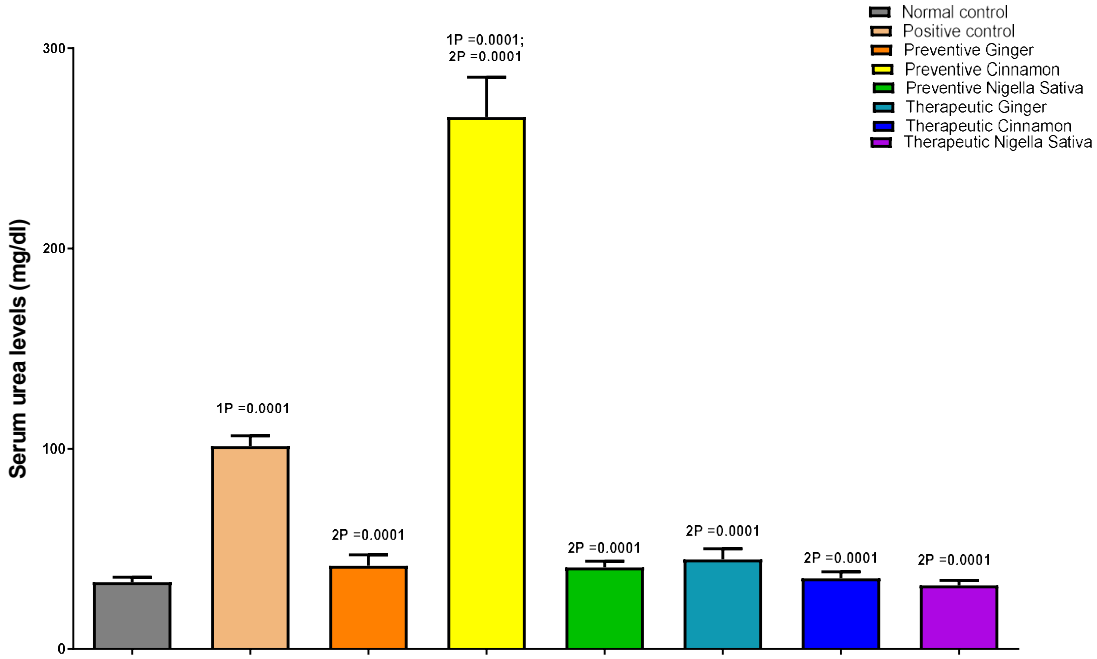

Figure 2: Serum Urea Levels of different groups

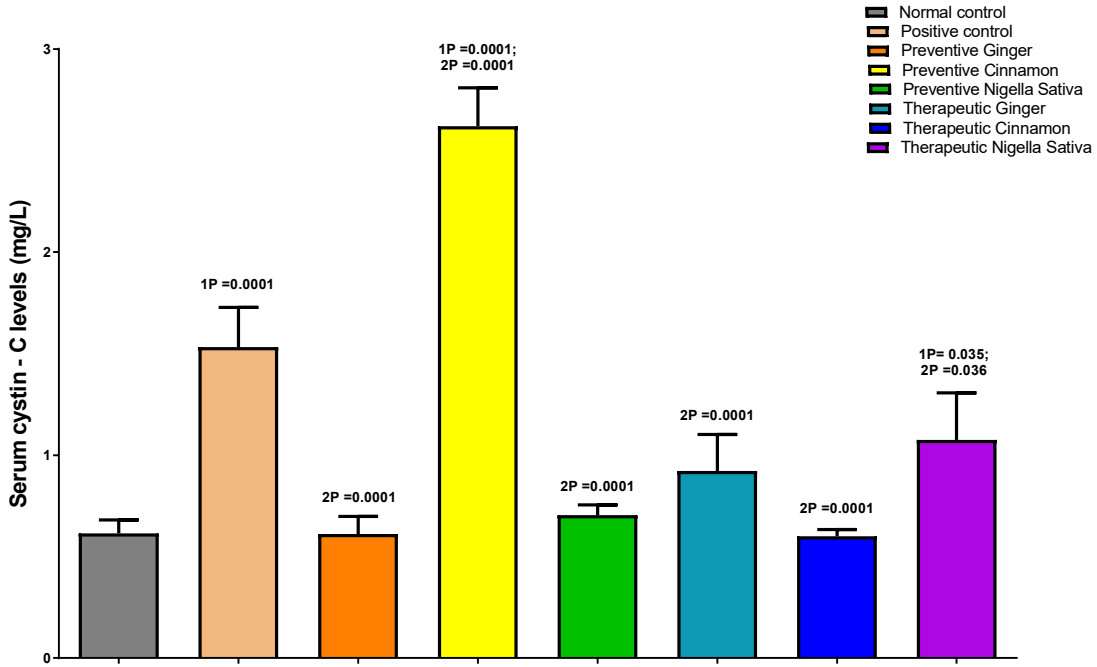

Figure 3: Serum Cysteine –C Levels of different groups

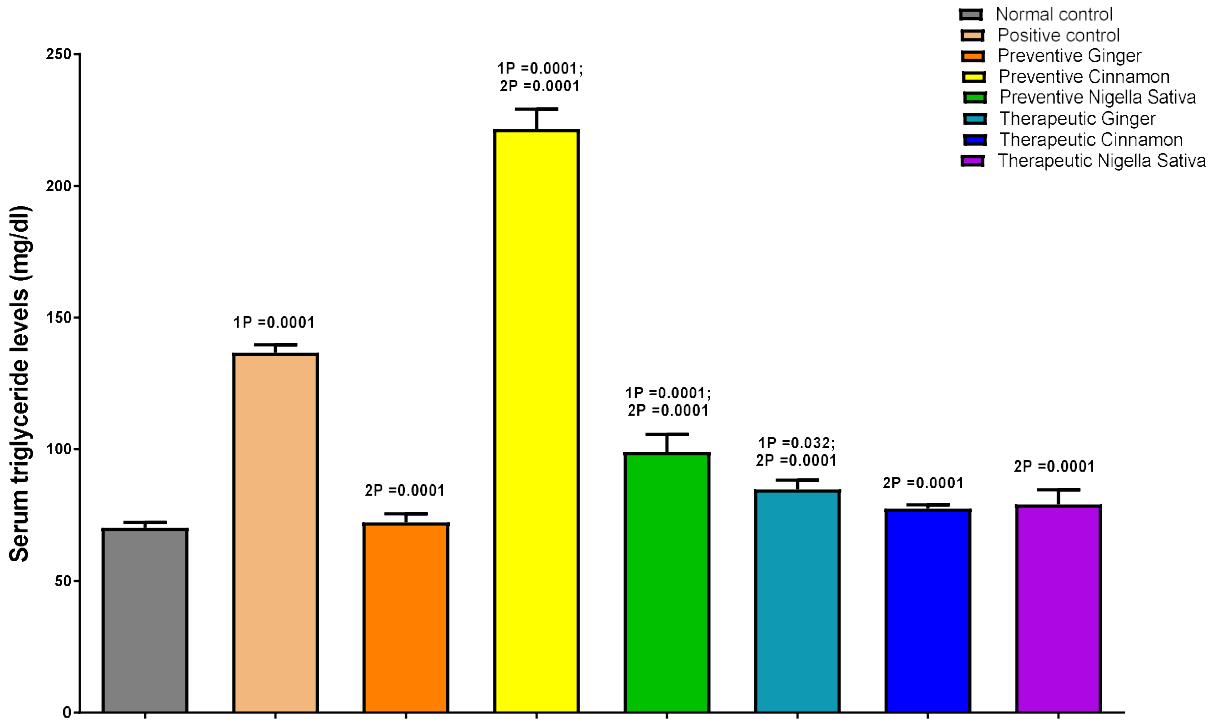

Figure 4: Serum Triglycerides Levels of different groups

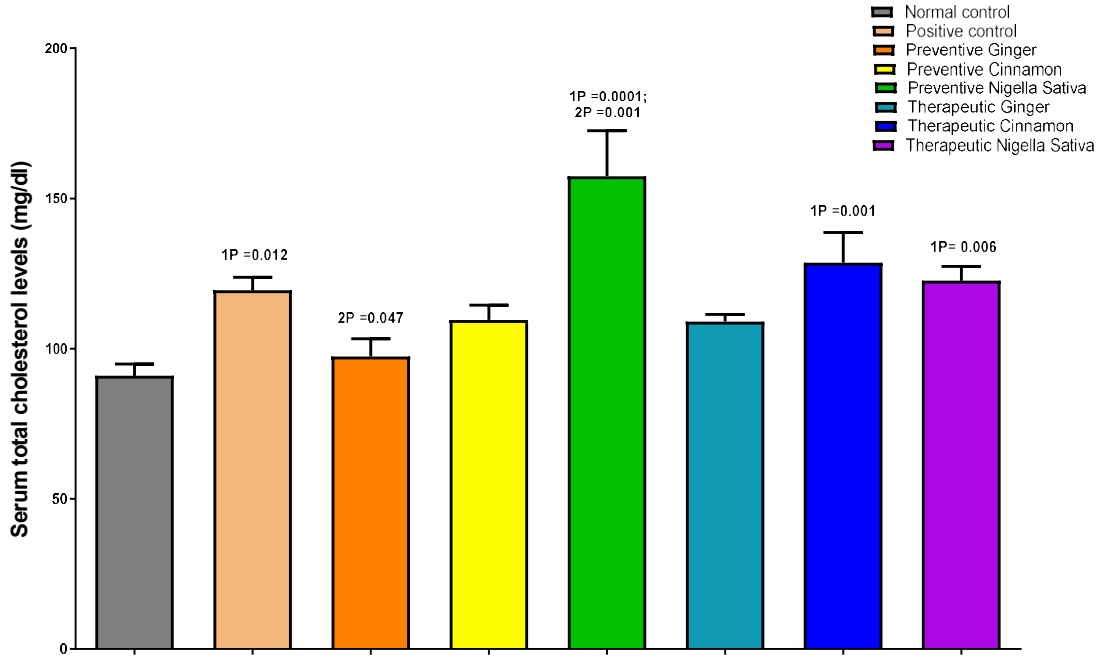

Figure 5: Serum Total Cholesterol Levels of different groups.

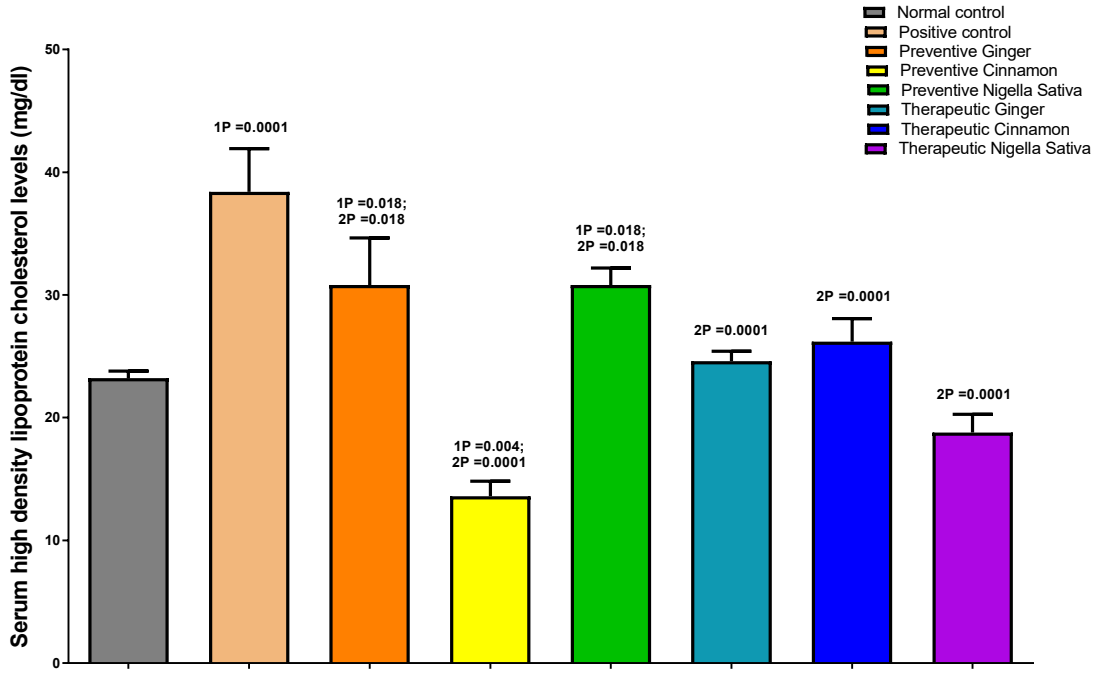

Figure 6: Serum HDL Levels of different groups

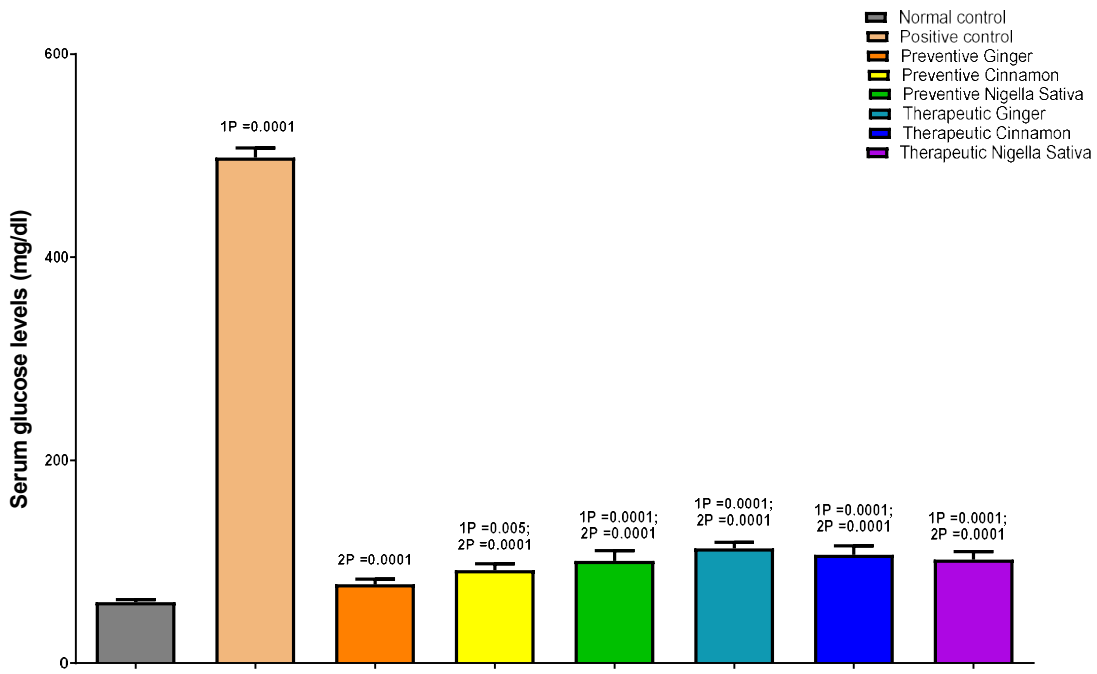

Figure 7: Serum Glucose Levels of different groups

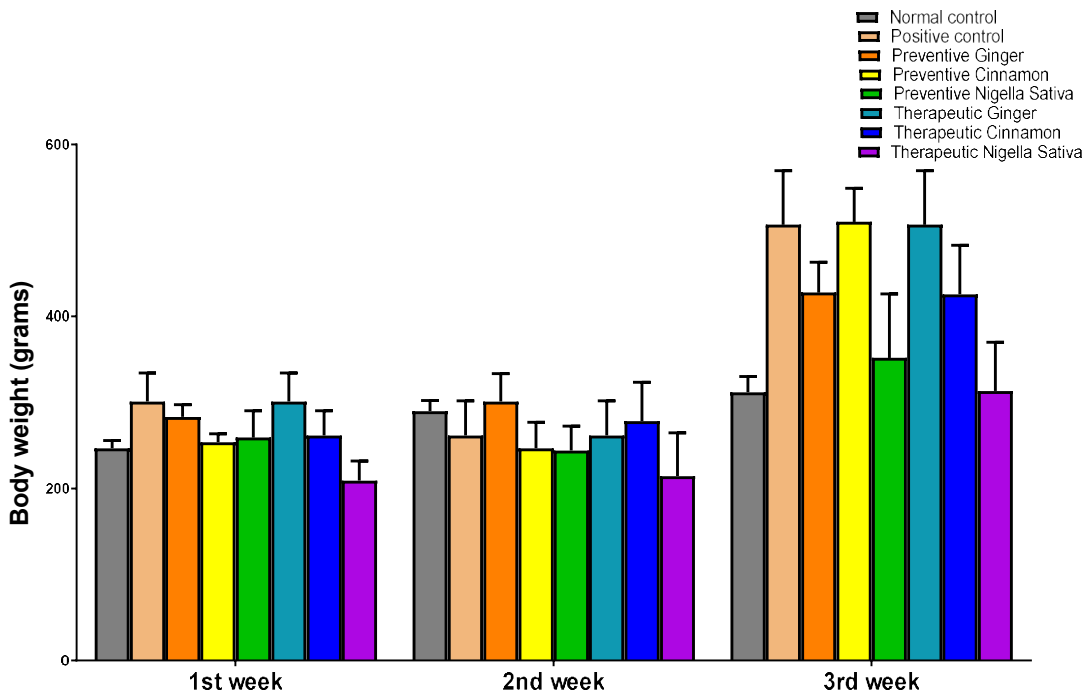

Figure 8: Body weight of different groups

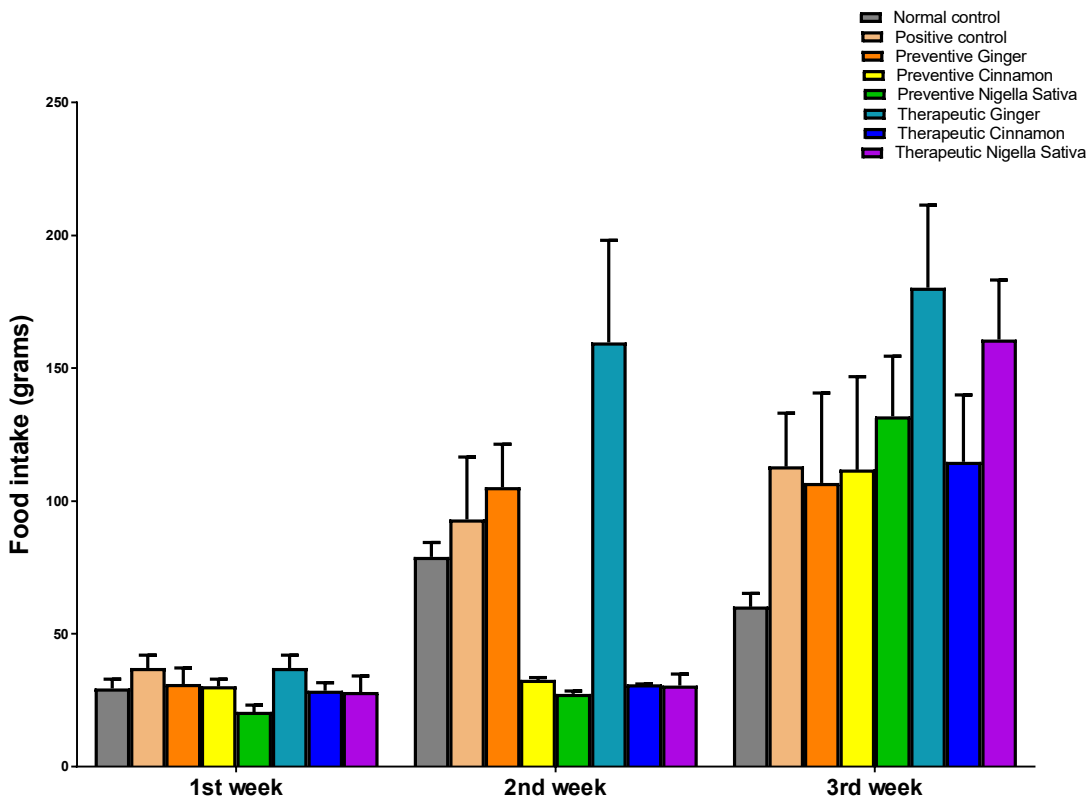

Figure 9: Food Intake Levels of different groups

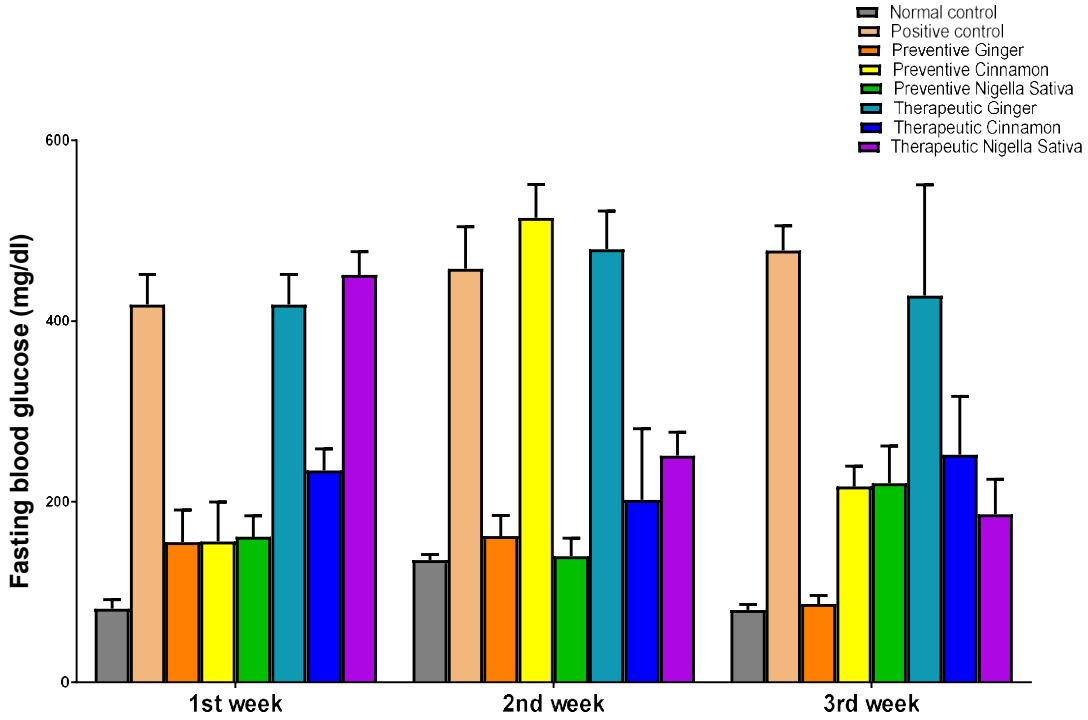

Figure 10: Serum Fasting Blood Glucose Levels of different groups

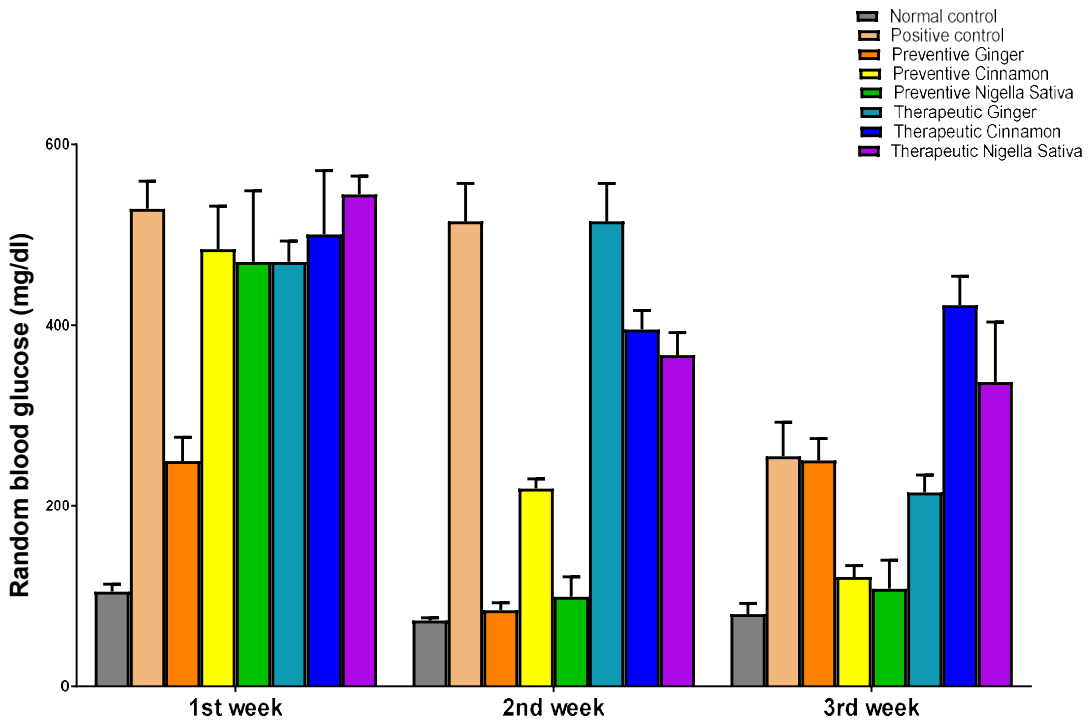

Figure 11: Random Blood Glucose of different groups

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