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EFFECT OF TWO LEVELS FROM GINSENG AND GREEN COFFEE ON OBESE RATS

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ABSTRACT: The present study aimed to investigate the effect of two levels from (green coffee, ginseng and their combination) on nutritional and biochemical status of obese rats. Forty eight male albino rats (Sprague Dawley Strain) used in this study, the rats divided into two main groups. The first main group (6 rats) fed on basal diet (as a control negative group). The second main group (42 rats) was fed eight weeks on high fat diet HFD to induce obesity in rats. The rats in the second main group divided into seven subgroups. Subgroup (1) fed on HFD, as a control positive group. Subgroups (2 and 3) fed on HFD containing (3% and 6% ginseng), respectively. Subgroup (4 and 5) were fed on HFD containing (3% and 6% green coffee), respectively. Subgroup (6 and 7) were fed on HFD containing (3% and 6% combination of ginseng and green coffee), respectively. The experimental period lasted six weeks. Results showed that, obese rats (control positive group) recorded significant increase $p<0.5$ in (body weight gain %, (liver and kidney) weights/body weight %, glucose, leptin hormone, lipid profile "except HDL-c", Atherogenic Index", kidney functions, liver enzymes), as compared to the rats in the first main group (control negative group). Obese rats which treated with the two levels from (green coffee, ginseng and their combination) decreased body weight gain %, liver and kidney weights / body weight %, serum glucose, leptin hormone, serum cholesterol, triglycerides, LDL-c, VLDL-c, uric acid, urea nitrogen, creatinine, AST, ALT, ALP, also Lactate Dehydrogenase and γ-Glutamyl transferase, while HDL-c increased. The highest improvement in these parameters recorded for the obese group treated with 6% combination of (ginseng and green coffee). Green coffee and ginseng reduced the weight gain of obese rats and improved the side effect of obesity.

INTRODUTION: Overweight is defined by body mass index >25 that exceeds a standard body weight; however, the excess weight may also come from muscle, bone, fat, or body water [1]. While Wickelgren [2] and Achike [3] defined the obesity, as an increase in mass of adipose tissue, confers a higher risk for metabolic diseases such as non-insulin-dependent diabetes, cardiovascular disease, stroke, high blood pressure, atherosclerosis, various cancers, hyper - lipidaemia and an increased incidence of morbidity.

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On the other hand, obesity specifically refers to having a high amount of body fat, which is usually accompanied by abnormalities in leptin and insulin secretion and their action, together with defects in lipid and carbohydrate metabolism [4]. The degree of obesity is characterized by the volume and number of adipocytes, which is regulated in the so called adipocyte life cycle, several plant extracts and their respective bioactive components, are well recognized for their potential to exert anti-obesity effects [5].

Panax ginseng is an herb used in traditional medicine for thousands of years. In Mandarin the word Ginseng literally means root of man. It was so named because the root of this plant resembles the shape of a human body. Almost 2,000 years ago, the great Chinese medical directory stated that ginseng increased longevity.

The main active ingredients in ginseng are called ginsenosides. The higher the quantity of ginsenosides, the better the quality of the ginseng [6]. Ginseng has a long history of medicinal use in the oriental regions as a tonic to promote health [7]. Extensive reports point to ginseng as having many physiological and/or pharmacological effects on immune, cardiovascular, central nervous systems and endocrine glands [8]. Besides, ginseng also possesses anti aging, anti stress and anti-tumor properties [9]. In addition, several researches give evidences that ginseng possesses anti diabetic properties through lowering blood glucose effect [21] and stimulating sugar metabolism [12].

Coffee has recently received scientific attention as current epidemiologic and *in-vivo* studies have revealed its health benefits against obesity and metabolic disorders, especially type 2 diabetes [13]. These health advantages are mostly derived from chlorogenic acids contained in coffee beans [65]. Raw coffee beans are rich in chlorogenic acids and caffeine, and their contents in coffee beans are significantly decreased during the roasting and decaffeination processes [58]. Scientific studies have revealed that both coffee and caffeine play a preventive role against various degenerative diseases of modern society. Van Dam and Feskens (2002) [16] reported that moderate daily consumption of coffee helped to reduce the risk of type 2 diabetes, while Fredholm and Lindgren (1984) [17] found that caffeine promotes lipolysis in rat adipocytes.

Coffee intake has been reported to be inversely associated with weight gain [18]. Consumption of coffee has also been shown to produce changes in several glycaemic markers in older adults [19]. Similarly, other research has indicated that the consumption of caffeinated coffee can lead to some reductions in long-term weight gain, an effect which is likely to be due to the known thermogenic effects of caffeine intake [20]. Therefore, this study aimed to investigate the effect of two levels from (green coffee, ginseng and their combination) on nutritional and biochemical status of obese rats.

MATERIALS AND METHODS:

Materials: Casein, Vitamins, minerals, cellulose and choline chloride were purchased from El-Gomhoria Company, Cairo Egypt.

Corn starch, saturated fat "beef tallow", soybean oil, sucrose, ginseng and green coffee were purchased from local market, Riyadh, Saudi Arabia.

Forty eight male albino rats (Sprague Dawley Strain) (160 ± 10 g) were obtained from Animal House King Khalid Hospital, Riyadh, Saudi Arabia.

Methods: Male Albino rats (150 ± 10 g) were kept in individual stainless steel cages under hygienic conditions and fed one week on basal diet *ad libitum* for adaptation according to Reeves [21]. After a period of adaptation on basal diet, the rats were divided into two main groups.

The first main group (6 rats) fed on basal diet, as a control negative group. The second main group (42 rats) was fed 8 weeks on high fat diet HFD containing (saturated fat "beef tallow" 19%, soybean oil 1 % to provide essential fatty acids, sucrose 10%, casein 20%, cellulose 5%, Vitamin mixture 1%, salt mixture 3.5%, choline chloride 0.25% and the remainder is corn starch) to induce obesity in rats [22].

After this period, weight gain % and serum cholesterol, triglycerides, total lipids and serum lipten were determined in the first and second main groups, to ensure the induction of obesity. These parameters were (14.723 ± 4.009 %, 70.522 ± 7.095 mg/dl, 35.660 ± 6.087 mg/dl, 380.243 ± 7.550 mg/dl and 5.201 ± 0.232 ng/ml) and (40.331 ± 5.114%, 160.870 ± 8.445mg/dl, 83.662 ± 5.013 mg/dl, 520.435 ± 8.00 mg/dl and 10.326 ± 0.320 ng/ml) for the first and second main groups, respectively.

Then the rats in the second main group were divided into seven subgroups (n = 6) according to the following. Subgroup (1): fed on HFD, as a control positive group (obese group), Subgroup (2 and 3): were fed on HFDs containing 3% and 6% green coffee, respectively. Subgroup (4 and 5): were fed on HFDs containing 3 % and 6% ginseng, respectively, Subgroup (6 and 7): were fed on HFDs containing 3 % and 6% combination of green coffee and ginseng "1:1", respectively.

During the experimental period (6 week), the diets consumed and body weights were recorded every week. At the end of the experiment, the rats were fasted overnight, then the rats were anaesthetized

and sacrificed, and blood samples were collected from the aorta. The blood samples were centrifuged and serum was separated to estimate some bio-chemical parameters, *i.e*. serum glucose according to (Trinder, 1959) [23], leptin hormone [24], total lipids [25], cholesterol [26], triglycerids [27], high density lipo-protein HDL-c [28] low density lipo-protein LDL-c and VLDL-c [29].

Atherogenic Index (AI) was calculated according to this equation [AI = LDL-cholesterol / HDL-cholesterol) according to the methods described by Adeneye and Olagunju (2009) [30], Aspartate Amine Transaminase (AST) and Alanine Amine Trans-aminase (ALT) Reitman and Frankel (1957) [31] and Alkaline Phosphatase (ALP) Belfield and Goldberg (1971) [32], Lactate Dehydro-genase Howell and coll (1979) [33], γ-Glutamyl transferase was determined according to Rosalki (1975) [34], uric acid [35], urea nitrogen [36], creatinine [37].

Body weight recorded every week. Liver and kidney were separated from each rat and weighted to calculate the liver and kidney to body weight %. Results of biological evaluation of each group were statistically analyzed (mean ± standard deviation and one way ANOVA test) using SAS package and compared with each other using the suitable test (least significant differences at $P< 0.05$ [38].

RESULTS AND DISCUSSION: Effect of two levels from green coffee, ginseng and their combination on feed intake, body weight gain % and some organs weight/body weight % of obese rats.

The effect of two levels of (green coffee, ginseng and their combination) on feed intake (g/day/each rat), body weight gain % and (liver and kidney) weights/body weight % of obese rats presented in **Table 1**. The mean value of feed intake in the negative control group decreased significantly, as compared to the positive control group. Feed intake of all treated groups with the two levels of (green coffee, ginseng and their combination) showed non-significant differences in feed intake, except the groups which treated with 6 % green coffee and the mixture of 6 % (green coffee and ginseng), as compared to the positive control group.

Feeding obese rats on HFDs containing 6% green coffee or the mixture of 6 % (green coffee and ginseng) recorded the lowest mean values of feed intake, as compared to other treated groups.

The mean value of body weight gain % (BWG %) of obese group fed on high fat diet increased significantly $p<0.05$, as compared to the healthy group fed on basal diet. Feeding obese rats on high fat diet and treated with two levels of (green coffee, ginseng and their mixtures) led to significant decrease in body weight gain %, as compared to the positive control group. The lowest decrease in BWG% recorded for the group treated with 3 % ginseng, while the highest decrease in the mean value of BWG % showed in the groups which were treated with 6% green coffee and the combination of 6% (green coffee and ginseng).

The mean value of liver and kidney weights/body weight % increased significantly $P<0.05$ in the positive control group (obese rats), as compared to the negative control group. Feeding obese groups on high fat diet and treated with two levels from (green coffee, ginseng and their combination) induced significant decrease $P<0.05$ in mean values of liver and kidney weight/body weight %, as compared to the positive control group.

The high level from the combination of green coffee and ginseng (6%) recorded the best results in liver weight/ body weight %, followed by the groups which treated with the low level from the their combination and the group treated with 6% green coffee. On the other hand, groups of rats which treated with 6% green coffee, 6% (green coffee and ginseng) and 3% (green coffee and ginseng) recorded the best results in kidney weights/ body weight %.

Results in this table revealed that, feeding obese rats on HFD increased BWG %, as compared to healthy rats fed on basal diet, on the other hand treating obese groups with green coffee, ginseng and their combination led to significant decrease in BWG %, as compared to the positive control group. in this respect, Kim *et al*., (2005) [39] reported that, crude saponin CS which present in ginseng may be useful in the treatment of obesity and related disorders as anti-obesity agents.

Han *et al*., (2002) [40] reported also saponins from natural product have an antiobesity effect. CS prevented increases in the body weight, adipose

tissue weight, and liver triacylglycerol in mice fed HF diet. On the other hand, Han *et al*., (2001) [41] confirmed that, saponin suppressed increases in body, parametrial adipose tissue weights and diameter in adipose cell size induced by a HF diet through delaying the intestinal absorption of dietary fat by inhibiting pancreatic lipase activity.

TABLE 1: EFFECT OF TWO LEVELS FROM GREEN COFFEE, GINSENG AND THEIR COMBINATION ON FEED INTAKE, BODY WEIGHT GAIN % AND SOME ORGANS WEIGHT/BODY WEIGHT % OF OBESE RATS

Parameters or Groups	Feed intake (g/day)	Body weight gain % (BWG %)	Organs weight/body weight%	
			Liver	Kidney
Control (-)	12.500 ^{c} ± 0.650	28.900 ^{e} ± 1.077	2.931 ^{f} ± 0.085	0.586 ^{e} ± 0.025
Control (+)	14.243 ^{a} ± 0.732	52.303 ^{a} ± 1.613	3.833 ^{a} ± 0.083	1.238 ^{a} ± 0.076
3% green coffee.	13.501 ^{abc} ± 0.899	34.803 ^{c} ± 1.121	3.377 ^{c} ± 0.088	0.866 ^{c} ± 0.064
6% green coffee.	12.800 ^{bc} ± 0.703	30.950 ^{d} ± 1.154	3.260 ^{d} ± 0.123	0.788 ^{d} ± 0.018
3% ginseng	13.850 ^{ab} ± 0.790	39.213 ^{b} ± 1.509	3.673 ^{b} ± 0.094	1.049 ^{b} ± 0.083
6% ginseng	13.503 ^{abc} ± 0.745	34.209 ^{c} ± 1.124	3.432 ^{c} ± 0.162	0.885 ^{c} ± 0.047
3% (green coffee and ginseng) "1:1"	13.649 ^{ab} ± 1.102	34.122 ^{c} ± 1.245	3.289 ^{d} ± 0.099	0.792 ^{d} ± 0.050
6% (green coffee and ginseng) "1:1"	13.094 ^{bc} ± 0.850	29.912 ^{d} ± 1.250	3.118 ^{e} ± 0.093	0.725 ^{d} ± 0.046

All results are expressed as mean ± SD.
Values in each column which have different letters are significant different ($p<0.05$).

Concerning to green coffee, Shimoda *et al*., (2006) [42] suggested that green coffee extract GCE mediates its antiobesity effect possibly by suppressing the accumulation of hepatic triglycerides. Cho *et al*., (2010) [43] have also posited that the anti-obesity effect of GCE may be mediated *via* alteration of plasma adipokine level and body fat distribution and down regulating fatty acid and cholesterol biosynthesis, whereas up regulating fatty acid oxidation and peroxisome proliferator-activated receptor alpha (PPARα) expression in the liver.

Chlorogenic acid is also a dietary poly-phenolic compound in the coffee with anti-oxidative activity. Thus, it is suggested that caffeine, chlorogenic acid and other poly-phenolic compounds in GCBE act syner-gistically to suppress body weight gain and visceral fat accumulation in mice [100]. Effect of two levels from green coffee, ginseng and their combination on serum glucose and leptin hormone of obese rats.

Table 2 illustrates the effect of two levels (3% and 6%) of green coffee, ginseng and the mixture between them on serum glucose and liptin hormone of obese rats. The mean value of serum glucose and leptin hormone increased significantly $p<0.05$ in the positive control group fed on high fat diet, as compared to the negative control group fed on basal diet.

TABLE 2: EFFECT OF TWO LEVELS FROM GREEN COFFEE, GINSENG AND THEIR COMBINATION ON SERUM GLUCOSE AND LEPTIN OF OBESE RATS

Parameters or Groups	Glucose mg/dl	Leptin "ng/ ml"
Control (-)	73.492 ^{f} ± 4.987	5.787 ^{g} ± 0.161
Control (+)	136.737 ^{a} ± 6.741	14.905 ^{a} ± 0.304
3% green coffee.	124.100 ^{b} ± 6.595	11.405 ^{c} ± 0.216
6% green coffee.	115.157 ^{c} ± 1.447	9.342 ^{e} ± 0.694
3% ginseng	120.000 ^{bc} ± 4.410	12.277 ^{b} ± 0.611
6% ginseng	94.639 ^{d} ± 2.699	10.292 ^{d} ± 0.672
3% (green coffee and ginseng) "1:1"	98.070 ^{d} ± 2.803	9.815 ^{de} ± 0.270
6% (green coffee and ginseng) "1:1"	81.730 ^{e} ± 1.145	7.985 ^{f} ± 0.407

All results are expressed as mean ± SD.
Values in each column which have different letters are significant different ($p<0.05$).

Serum glucose and leptin hormone in the positive control group increased by about 86.056 % and 157.560 % than that of the negative control group. Using green coffee, ginseng and their combination with (3% and 6%) in treating obese rats led to a significant decrease in serum glucose and leptin hormone, as compared to the positive control group, on the other hand serum glucose and leptin hormone decreased gradually with increasing the levels of green coffee, ginseng and their combination.

The best results of serum glucose and leptin hormone recorded for the group fed on high fat diet containing 6% mixture of (green coffee and ginseng), this treatment decreased the mean value of serum glucose and leptin hormone by about 28.278% and 34.149%, than that of the positive control group.

In this respect, Sawiress 2011 [45] showed that ginseng extract (GE) resulted in reduction of the elevated blood glucose concentration in diabetic rats, an effect that was attributed in former studies to ginseng enhancement of glucose uptake through stimulating trans-location of glucose transporter GLUT4, inhibition of intracellular inflammatory molecules as Jun N- terminal kinase (JNK) which causes serine phosphorylation to insulin receptor substrate and consequently leads to interruption of signal transduction from insulin receptor to downstream molecules and insulin resistance [46] and activation of peroxisome proliferator activated receptor γ which improves insulin resistance, promotes adipocyte differentiation and induces apoptosis in large adipocytes [7]. Addionally, other investigators recorded definite insulinogenic properties of ginseng [47] or direct and indirect stimulatory on β cell secretion of insulin [48].

Vuksan *et al*., (2008) [49], who reported that ginseng reduced fasting blood glucose concentrations, HbA1C, glucose induced insulin release and improved insulin sensitivity in diabetic patients. Lim *et al*., (2009) [50] reported that, ginsam has distinct beneficial effects on glucose metabolism and body weight control in an obese animal model of insulin resistance by changing the expression of genes involved in glucose and fatty acid metabolism. Ohnishi *et al*., (1996) [11] reported that both types of ginseng may influence carbohydrate metabolism and diabetes mellitus. Numerous animal studies indicate that *P. ginseng* CA Meyer and *P. quinquefolius* L have significant hypoglyce-mic action.

Different mechanisms are involved in suppressing blood glucose levels by ginseng supplementation: modulation of glucose transport [51], glucose disposal [52] and insulin secretion [53]. Coffee has been shown to be a major contributor to the total *in-vitro* anti-oxidant capacity of the diet which may be relevant as oxidative stress can contribute to the development of type 2 diabetes [54]. Coffee is the major source of the phenol chlorogenic acid [55]. Intake of chlorogenic acid has been shown to reduce glucose concentrations in rats [56].

Coffee also contains substantial amounts of magnesium, which has been linked to better insulin sensitivity and insulin secretion [57]. α-Glucosidase inhibitors are oral hypoglycemic agents for patients with type 2 diabetes that inhibit digestion of dietary carbohydrates and thereby flatten the postprandial glucose response. Although α-glucosidase inhibitors such as acarbose and miglitol effectively alleviate both fasting and postprandial hyper-glycemia [58]. Lotus leaves could be helpful in the management of diabetes mellitus, as a lotus leaf extract has α-glucosidase inhibitory activity *in-vitro* [59].

Stricker-Krongard *et al*., (1998) [60] reported that, crude saponin (CS) of ginseng reduced levels of leptin in the HF diet group. It is more likely that decreased serum leptin was due to decreased body fat. On the other hand, leptin acts partly through interactions with neuropeptide Y (NPY) in the hypothalamus. Also Yamashita *et al*., (2012) [61] reported that, statistically significant inverse association between coffee consumption and leptin concentration

Effect of two levels from green coffee, ginseng and their combination on lipid profile of obese rats. The effect of two levels of (green coffee, ginseng and their combination) on lipid profile including total lipids, cholesterol, triglycerides, high density lipo protein-cholesterol HDL-c, low density lipo protein-cholesterol LDL-c, very low density lipoprotein-cholesterol VLDL-c and Athero-genic Index AI of obese rats presented in **Table 3** and **4**, respectively.

The mean value of serum lipids, cholesterol and triglycerides increased significantly $p<0.05$ in obese rats, as compared to the negative control group. Serum lipids, cholesterol and triglycerides increased in the positive control group by about 40.246%, 151.113% and 143.042%, than that of the negative control group, respectively **Table 3**.

All treated obese groups showed significant decrease $p<0.05$ in serum lipids, cholesterol and triglycerides, as compared to the positive control group. Treating obese rats with 3% and 6% ginseng

led to significant decrease in serum lipids, cholesterol and triglycerides, as compared to the group which treated with 3% and 6% green coffee, respectively. The highest decrease in these parameters recorded for the group treated with the combination of 6% (green coffee and ginseng), this treatment decreased serum lipid, cholesterol and triglycerides by about 13.821%, 26.053% and 35.419%, respectively.

The effect of two levels of (green coffee, ginseng and their combination) on serum lipoproteins and Atherogenic Index of obese rats presented in **Table 4**. The mean value of serum high density lipoprotein - cholesterol HDL-c decreased significantly ($p<0.05$), while low, very low density lipoprotein-cholesterol and Atherogenic Index (LDL-c, VLDL-c and AI) increased significantly ($p<0.05$) in obese group, as compared to the negative control group. Treating obese groups with 3% and 6% (green coffee, ginseng and their combination) led to significant increase in serum HDL-c, while LDL-c, VLDL-c and AI decreased significantly $p<0.05$, as compared to the positive control group.

TABLE 3: EFFECT OF TWO LEVELS FROM GREEN COFFEE, GINSENG AND THEIR COMBINATION ON SERUM LIPIDS, CHOLESTEROL AND TRIGLYCERIDES OF OBESE RATS

Parameters or Groups	Lipids mg/dl	Cholesterol	Triglycerides
Control (-)	406.250 ^{j} ± 6.238	73.390 ^{f} ± 4.320	39.607 ^{f} ± 0.951
Control (+)	569.750 ^{a} ± 4.500	184.292 ^{a} ± 4.765	96.262 ^{a} ± 3.029
3% green coffee.	552.500 ^{b} ± 5.066	173.227 ^{b} ± 3.675	88.801 ^{b} ± 3.075
6% green coffee.	532.500 ^{d} ± 6.454	161.750 ^{c} ± 4.814	77.802 ^{c} ± 4.925
3% ginseng	543.000 ^{c} ± 4.320	166.722 $^{b c}$ ± 3.450	84.226 ^{b} ± 2.068
6% ginseng	511.500 ^{e} ± 8.698	151.125 ^{d} ± 6.609	69.782 ^{d} ± 4.234
3% (green coffee and ginseng) “1:1”	503.500 ^{e} ± 2.645	146.019 ^{d} ± 4.057	68.241 ^{d} ± 3.159
6% (green coffee and ginseng) “1:1”	491.000 ^{f} ± 5.228	136.277 ^{e} ± 6.423	62.166 ^{e} ± 4.458

All results are expressed as mean ± SD.
Values in each column which have different letters are significant different ($p<0.05$).

TABLE 4: EFFECT OF TWO LEVELS FROM GREEN COFFEE, GINSENG AND THEIR COMBINATION ON SERUM LIPOPROTEINS AND AI OF OBESE RATS

Parameters or Groups	HDL-c	LDL-c	VLDL-c	AI
	mg/dl			
Control (-)	47.580 ^{a} ± 2.003	17.888 ^{f} ± 2.230	7.921 ^{f} ± 0.190	0.374 ^{f} ± 0.033
Control (+)	22.267 ^{f} ± 2.081	142.772 ^{a} ± 5.885	19.252 ^{a} ± 0.605	6.464 ^{a} ± 0.780
3% green coffee.	25.220 ^{e} ± 1.398	129.997 ^{b} ± 3.215	18.010 ^{b} ± 1.027	5.166 ^{b} ± 0.316
6% green coffee.	31.399 ^{d} ± 1.309	114.790 ^{c} ± 4.920	15.560 ^{c} ± 0.985	3.661 ^{c} ± 0.241
3% ginseng	23.936 $^{e f}$ ± 1.631	125.940 ^{b} ± 2.667	16.845 ^{b} ± 0.413	5.278 ^{b} ± 0.368
6% ginseng	37.640 ^{b} ± 1.484	99.531 ^{d} ± 4.861	13.953 ^{d} ± 0.842	2.643 ^{d} ± 0.073
3% (green coffee and ginseng) “1:1”	34.751 ^{c} ± 2.226	97.620 ^{d} ± 1.749	13.648 ^{d} ± 0.631	2.815 ^{d} ± 0.139
6% (green coffee and ginseng) “1:1”	39.989 ^{b} ± 1.364	83.854 ^{e} ± 5.513	12.433 ^{e} ± 0.891	2.095 ^{e} ± 0.081

AI: Atherogenic Index; All results are expressed as mean ± SD.
Values in each column which have different letters are significant different ($p<0.05$).

Serum HDL-c increased gradually with increasing the level of green coffee, ginseng and their combination, while LDL-c, VLDL-c and AI decreased gradually with increasing the levels of the same materials from 3% to 6%. The highest improvement of serum lipoproteins and AI recorded for the group which treated with the mixture of 6% (green coffee and ginseng) followed by the group treated with 6% ginseng, respectively.

The highest improvement of lipid profile (total lipids, cholesterol, triglycerides, HDL-c, LDL-c, VLDL-c and AI) recorded for the group which were treated with 6% (green coffee and ginseng) because this treatment decreased these parameters, except HDL-c, as compared to other treated groups. In this respect, Akiyama *et al*., (1996) [62] reported that, obesity induced by high fat intake is usually accompanied by hyperlipidemia which presents as an abnormally high concentration of lipids in blood. Generally, this abnormally high concentration of lipids in blood means elevated blood total cholesterol (TC) and/or triglyceride (TG) levels [63].

Although hyperlipidemia does not cause any symptoms by itself, these abnormally high blood

lipids levels can lead to various cardiovascular diseases (CVD) such as atherosclerosis and coronary heart disease (CHD) [64] which together are one of the most common causes of death in modern society [65].

Obesity plays a pivotal role in the pathophysiology of metabolic and cardiovascular disease [66]. These disorders include impaired glucose tolerance, Type 2 diabetes, hypertension, and dyslipidemia. Also, Must *et al*., (1999) [67] reported that, obesity is a primary risk factor for coronary heart disease (CHD) and mortality. El-Missirr *et al*., (2004) [68] supported the above mentioned results as they found development of hypercholesterolemia in serum diabetic rats.

A hypolipidemic effect of Panax ginseng extract (PGE) is associated with decrease in total cholesterol (TC), triglycerides (TGs), low-density lipoprotein (LDL), Muscular Dystrophy Association (MDA) levels and an increase in high-density lipoprotein (HDL) level. Administration of PGE increased serum superoxide dismutase (SOD) and catalase (CAT) activities while decreased MDA level indicating that antioxidant potential of PGE might induce hypolipidemic effect as one of action mechanism [69].

Dixit *et al*., (1991) [70] who mentioned that ginseng markedly reduced serum triglycerides and cholesterol in hyperlipidemic monkeys. In addition, Hwang *et al*. (2008) [71] indicated that the administration of ginseng saponins to rabbits fed high cholesterol diet decreased the serum cholesterol level. Ginseng saponin reduced the blood cholesterol concentration by increasing cholesterol secretion through bile acid synthesis. Yokozawa *et al*., (1985) [52] reported that blood cholesterol content decreased by promoting LDL receptor synthesis.

Jeon *et al*., (2000) [72] suggested that hypolipidemic effect of *Panax ginseng* extract is associated with a decrease in total cholesterol, triglyceride, LDL, malondialdehyde levels and an increase in HDL. These findings support scientific claims that ginseng has the hypolipidemic potential. Administration of *Panax ginseng* extract increased superoxide dismutase and catalase activities while decreased malondialdehyde level indicating that antioxidant potential of *Panax ginseng* extract might induce hypolipidemic effect as one of action mechanism.

The decrement in lipid profile induced by ginseng is a function of multiple integrated mechanisms including binding to peroxisome proliferator-activated receptor alpha PPARα which increases β oxidation of fatty acids and consequently reduces lipid accumulation [73]. Inhibition of pancreatic lipase activity there by reducing lipid digestion [74], inhibition of neuropeptide Y expression in hypo-thalamus [39] which is involved in stimulation of food intake, and inhibition of activity of some key enzymes involved in cholesterol and triglyceride synthesis as β methyl glutryl-CoA reductase and cholesterol 7 α hydroxylase [75].

Green Coffee Bean GCBE are un-roasted coffee and have mainly chlorogenic acid (>45% by weight). Chlorogenic acid is potent anti-oxidant. The mechanism (s) of action of GCBE on weight loss and reducing lipid are unknown. Only research in mice has demonstrated the effect of GCBE on fat metabolism, with chlorogenic acid alone having a moderate effect [42]. They were able to obtain significant data suggesting that chlorogenic acid not only retards the absorption of fats from the intestine but also activates fat metabolism in the liver. This was demonstrated by significantly lower levels of liver triglycerides after chlorogenic acid ingestion. A recent study in Japan found that coffee polyphenols enhance energy metabolism and reduce lipogenesis by down regulating sterol regulatory element-binding protein and similar molecules, which leads to the suppression of body fat accumulation [76].

Recently, intraperitoneal injection of chlorogenic acid to hamsters fed a high-fat diet caused an improvement in lipid profile, reduction in hepatic lipase, reduction in glucose and insulin and increased expression of peroxisome proliferator-activated receptor. This is one of the key regulators of lipids and glucose [77]. There have not been a human research with GCBE on fat metabolism.

Diets rich in polyphenols may help to prevent various kinds of diseases associated with oxidative stress, including coronary heart disease and some forms of cancer [78].

Green coffee extract GCE has been reported to have antioxidant activity, demonstrated by its ability to scavenge free radicals *in-vitro*, and to increase the antioxidant capacity of plasma *in-vivo* [79]. Further studies were prompted to examine the anti-obesity effect of GCBE on dietary fat absorption using olive oil-loaded mice. The elevated serum TG level was lowered by GCBE and caffeine in olive oil-loaded mice. Coffee has been reported to delay gastric emptying [80].

Effect of two levels from green coffee, ginseng and their combination on serum liver enzymes, lactate dehydrogenase and γ-Glutamyl transferase of obese rats. The effect of the two levels of (green coffee, ginseng and their mixture) on serum Aspartate Amine Transaminase (AST), Alanine Amine Transaminase (ALT), Alkaline Phosphatase (ALP), lactate dehydrogenase and γ-Glutamyl transferase of obese rats presented in **Table 5**. Feeding obese rats on high fat diet increased the mean values of serum AST, ALT, ALT, lactate dehydrogenase and γ-Glutamyl transferase significantly $p<0.05$, as compared to the negative control group. Feeding obese groups on high fat diet containing (3% and 6%) green coffee, ginseng and their combination decreased the mean value of these parameters significantly $p<0.05$, as compared to the positive control group.

The data in this table showed that, treating obese groups with high levels of green coffee, ginseng and or combination of them decreased the mean values of serum AST, ALT, ALP, lactate dehydrogenase and γ-Glutamyl transferase significantly $p<0.05$, as compared to the groups treated with low levels from the same tested materials. Feeding obese rats on HFD containing 6 % (green coffee and ginseng) recorded the best results, because this treatment showed significant decrease $p<0.05$ of all parameters, as compared to other treated groups. This treatment decreased the mean values of AST, ALT, ALP, lactate dehydrogenase and γ-Glutamyl transferase by about (43.495%, 51.024%, 36.450%, 26.569% and 45.329%), than that of the positive control group, respectively.

TABLE 5: EFFECT OF TWO LEVELS FROM GREEN COFFEE, GINSENG AND THEIR COMBINATION ON SERUM LIVER ENZYMES, LACTATE DEHYDROGENASE AND γ-GLUTAMYL TRANSFERASE OF OBESE RATS

Parameters or Groups	AST	ALT	ALP	Lactate Dehydrogenase	γ-Glutamyl transferase
	U/L				
Control (-)	45.527 ^{f} ± 3.619	12.830 ^{f} ± 1.730	83.750 ^{g} ± 4.787	92.638 ^{g} ±2.553	23.277 ^{g} ±1.808
Control (+)	145.720 ^{a} ± 7.074	58.517 ^{a} ± 3.072	146.250 ^{a} ± 4.787	220.523 ^{a} ±4.669	78.942 ^{a} ±2.144
3% green coffee.	129.714 ^{b} ± 2.924	50.562 ^{b} ± 2.097	135.000 ^{b} ± 4.082	200.590 ^{b} ±7.609	65.877 ^{b} ±4.533
6% green coffee.	113.583 ^{c} ± 1.983	40.767 ^{c} ± 2.602	119.365 ^{d} ± 2.891	180.412 ^{d} ±4.809	54.941 ^{cd} ±4.141
3% ginseng	122.943 ^{b} ± 3.581	43.627 ^{c} ± 3.401	125.250 ^{c} ± 4.112	192.062 ^{c} ±7.120	60.277 ^{c} ±3.147
6% ginseng	99.372 ^{d} ± 10.184	34.355 ^{d} ± 2.787	104.990 ^{e} ± 2.715	170.150 ^{e} ±4.466	47.882 ^{e} ±3.920
3% (green coffee and ginseng) "1:1"	95.497 ^{d} ± 3.722	33.545 ^{d} ± 2.077	108.715 ^{e} ± 3.787	185.902 ^{cd} ±4.230	55.440 ^{d} ±3.723
6% (green coffee and ginseng) "1:1"	82.339 ^{e} ± 2.865	28.659 ^{e} ± 2.296	92.941 ^{f} ± 2.190	161.931 ^{f} ±3.544	43.158 ^{f} ±2.719

All results are expressed as mean ± SD.

Values in each column which have different letters are significant different ($p<0.05$).

The results in this study revealed that, obesity induced increase liver enzymes also lactate dehydrogenase and γ-Glutamyl transferase. Green coffee and ginseng improved these parameters. In this respect, Higdon and Frei (2006) [81] found that, coffee intake reduced serum γ-glutamul transferase (GGT) activity, an indicator of liver injury. Elevated serum alanine aminotransferase (ALT) activity is a more specific marker of hepatic injury than GGT, Ruhl and Everhart (2005) [82] found that consumption of either coffee or caffeine decreased the risk of abnormally elevated alanine amino transferase (ALT) activities. Coffee intake may have beneficial effects on the liver. Increasing coffee consumption has been inversely associated with liver enzyme concentrations, including alanine amino transferase (ALT), aspartate amino transferase (AST) and gamma-glutamyltransferase [83]. In population studies, among persons with unknown diagnosis of liver disease, greater coffee intake has been associated with lower risk of cirrhosis [89] and chronic liver disease [84].

Shim *et al*., (2010) [85] suggest that ginsam effectively prevent liver injury, mainly through down regulation of oxidative stress and inflammatory response. Kim *et al*., (2013) [86] confirmed that bacterial fermentation of red ginseng could be a more effective protector against hepatic oxidative damage besides improving bioavailability of

absorption resulting from intestinal flora. Kitts and Hu (2000) [87] declared that ginsenoside compounds may be responsible for its hepatoprotective effect by scavenge and destroy lipit peroxyl radicals and reactive oxygen species.

Effect of two levels from green coffee, ginseng and their combination on kidney functions of obese rats. The data in **Table 6** illustrated the effect of green coffee, ginseng and their combination with two levels (3% and 6%) on kidney functions including (uric acid, urea nitrogen and creatinine) of obese rats. Feeding obese rats on high fat diet led to significant increase $p<0.05$ in serum uric acid, urea nitrogen and creatinine, as compared to the negative control group. These treatments increased the mean values of these parameters by about (86.245%, 166.918% and 218.359%) respectively, than that of the negative control group.

All treated groups improving kidney functions by reducing the mean values of serum uric acid, urea nitrogen and creatinine significantly ($p<0.05$), as compared to the positive control group. All kidney functions decreased gradually with increasing the levels of (green coffee, ginseng and their combination). The best results in serum uric acid, urea nitrogen and creatinine recorded for the group treated with the mixture of 6% (green coffee and ginseng), followed by the group which treated with the mixture of 3% from this mixture, respectively.

The data in this study revealed that, obesity induced increase serum kidney function. Green coffee and ginseng decreased serum uric acid, urea nitrogen and creatinine. In this respect, Henegar *et al*., (2001) [88] reported that, obesity and high-fat diets are linked with kidney dysfunction in rats and dogs. Also Jing *et al*., (2003) [89] confirm that high dietary fat worsens early disease progression in this model of renal disease.

Kang *et al*., (2008) [90] reported that, ginseng extract administration resulted in decrement of urea nitrogen and creatinine. Takako *et al*., (1995) [91] reported that, ginseng saponin protecting the kidney from oxidative stress. Ginseng's action as a free radical scavenger is important since free radical production is implicated in progressive kidney disorders. Kidney functions were greatly improved by ginseng extract as evidenced by amelioration of urea nitrogen, creatinine, total protein concentrations and serum electrolytes.

TABLE 6: EFFECT OF TWO LEVELS FROM GREEN COFFEE, GINSENG AND THEIR COMBINATION ON KIDNEY FUNCTIONS OF OBESE RATS

Parameters or Groups	Uric acid	Urea nitrogen	Creatinine
	mg/dl		
Control (-)	1.345 ^{f} ± 0.102	21.072 ^{e} ± 1.067	0.512 ^{g} ± 0.047
Control (+)	2.505 ^{a} ± 0.130	56.245 ^{a} ± 3.010	1.630 ^{a} ± 0.112
3% green coffee.	2.212 ^{b} ± 0.139	42.820 ^{b} ± 5.043	1.397 ^{b} ± 0.085
6% green coffee.	1.977 ^{c} ± 0.098	33.322 ^{c} ± 5.602	1.147 ^{c} ± 0.063
3% ginseng	2.012 ^{c} ± 0.094	38.053 $^{b\,c}$ ± 4.339	1.320 ^{b} ± 0.060
6% ginseng	1.747 ^{d} ± 0.133	26.362 ^{d} ± 3.211	0.866 ^{e} ± 0.067
3% (green coffee and ginseng) "1:1"	1.804 ^{d} ± 0.082	26.275 ^{d} ± 2.975	0.992 ^{d} ± 0.058
6% (green coffee and ginseng) "1:1"	1.562 ^{e} ± 0.056	26.084 ^{d} ± 1.424	0.717 ^{f} ± 0.072

All results are expressed as mean ± SD.
Values in each column which have different letters are significant different ($p<0.05$).

Also an increase was noted in renal tissue enzymes and antioxidants with a decrease in malondialdehyde and renal pathology. The researcher concluded that, ginseng extract may be of supportive treatment to combat diabetes complications [45].

Ginseng ameliorated the diabetic nephropathy, thus limited urinary protein excretion. This result goes hand in hand with those of Kang *et al*., (2006) [92] and Kim *et al*., (2008) [93] who reported that ginseng decreased urinary protein levels in diabetic rats.

Diets rich in polyphenols may help to prevent various kinds of diseases associated with oxidative stress, including coronary heart disease and some forms of cancer [78]. GCE has been reported to have antioxidant activity, demonstrated by its ability to scavenge free radicals *in-vitro*, and to increase the antioxidant capacity of plasma *in-vivo* [79].

Moon *et al*., (2009) [15] reported that, raw coffee beans are rich in chlorogenic acids and caffeine, and their contents in coffee beans are significantly

decreased during the roasting and decaffeination processes. Michael-Clifford (2000) [94] reported also, Chlorogenic acid (CGA) is a phenolic compound, a family of naturally occurring organic compounds found in plants. It is present in high quantity in coffee (*Coffea canephora*). Nishi *et al*., (2013) [95] suggest that, administration of CGA for 10 weeks improved the GFR in diabetic rats significantly, implicating its nephroprotective action [96].

CONCLUSION: The highest improvement in these parameters recorded for the obese group treated with 6% combination of (ginseng and green coffee). Green coffee and ginseng reduced the weight gain of obese rats and improved the side effect of obesity.

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