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The Influence of Catechin on Adiponectin and Insulin Resistance in Obese Rats

Rasha Hadi Talib **Noaman Ibadi Mohammad**

Department of Physiology, Biochemistry, and Pharmacology; Faculty of Veterinary Medicine, University of Kufa; Kufa, Iraq.

Corresponding author: RHT, e-mail: rashah.alnasrallah@student.uokufa.edu.iq
Co-author: NIM, e-mail: noamani.alabedi@uokufa.edu.iq

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Abstract:

Obesity represented as an abnormal accumulation of visceral fat. The synthesis of adiponectin has been linked to visceral fat accumulation. Obesity, and cardiovascular disease have all been linked to decreased levels of adiponectin. This study included the effect of catechin administration for 30 days on lipid profile, glucose, adiponectin and insulin serum levels as well as IR of obese female rats. Twenty female rats were conducted to the experiment where divide to four equal groups as; negative normal group received normal diet for all experiment time (60 days); positive obese control group received high fat diet (HFD) for (60 days); GTC-fed group fed HFD; ATV-fed group this group received ATV as cholesterol lowering drug. The significant differences considered at ($p < 0.05$ with 95% CI). The study revealed that the levels of Total-Ch, triglycerides and glucose were significantly higher in positive than negative control group. Additionally, a significant decreased Total-Ch, triglycerides and glucose level of Catechin treatment group than positive control group. Moreover, a significant reduction of adiponectin means levels obtained in positive control group compared to negative control and Catechin treatment groups. Furthermore, a significant difference of IR obtained between means of positive control group with Catechin treatment group. HDL-C levels were also differed significantly between positive control groups and Catechin treatment group. In conclusion this study exposed a positive influence of catechin administration on obesity lethal factors such as cholesterol, hyperglycemia, IR and the serum concentration of adiponectin in obese female rats.

Keywords: Catechin, Atorvastatin, Adiponectin, Cholesterol, Triglyceride and HDL.

Introduction:

Obesity is disparity involving energy expenditure and caloric ingestion [1]. The variations are thought to broaden the prospect of preliminary metabolic syndrome, diabetes, atherosclerosis and vascular disease [2]. Additionally, enduring overweight deteriorates the severity of antecedent renal injury [3]. Obesity's deleterious consequences are typically caused by a combine of excessive adipose tissue development and an advanced production of pathogenic factors from larger adipocytes [4]. Obesity complications are a result of various factors cooperating, comprising genetic as well as environmental causes [1].

Adiponectin (Adipo-Q) single-chain encompassed of 244 amino acids and a molecular weight of 26 kDa distributed via white adipose tissue (WAT), which is reside in chromosome 3q27, determines the AdipoQ protein [5]. The production of AdipoQ has been concomitant to visceral fat enlargement. Insulin resistance (IR), Obesity, and cardiovascular disease have all been linked to decreased levels of AdipoQ. Obesity prevention becomes essential for public health. It might be safer to address the issue of obesity by using dietary supplements to prevent or treat the condition [6].

A number of recent investigations in Iraq have studied the effects of certain plant extracts and compounds on models of animals. Among these studies are Flavonoids of Black Grape on insulin by Alol et al [7], the oxidative and hyperglycemic effect of fructose and H_2O_2 that can be ameliorating by oral administration of Oleuropein of olive leaves [8]. Soybean lecithin has a protective role in reduction of hypercholesterolemia in rats was presented by Alshammary et al [9]. In addition, Abd Al-Ameer et al concluded that isolated compound of onion oil improved diabetes status but the most potent was observed as anti-diabetic & antioxidant effect [10]. Furthermore, some chemical preparations play a hormonal role in diabetic induced rats such as serotonin was investigated and revealed that serotonin plays a protective role against diabetes-induced rats [11]. Treatment with Green Tea Catechin (GTC) increased the levels of PPAR-γ inside brown adipose tissue (BAT), visceral WAT, subcutaneous WAT, as well as expression of genes implicated in fatty acid metabolism. These results show that Catechin has an opposing obesity effect by shifting the PPAR-signaling route. YAN, JingQi et al. and SUN, Jiahong et al. [12,13] mentioned that heart disease is the primary source of disability, morbidity and death globally. Coronary heart disease with atherosclerosis can be reduced by GTC due to (LDL)-cholesterol-lowering action [14]. Notably, GTC reduce cholesterol absorption and its level in the liver that promotes LDL-receptor activation and its expression. However, some study discovered that GTC ensues a discriminating and powerful reductor of squalene epoxidase, that controlling production of cholesterol. GTC dramatically decreases the amount of serum LDL [15]. Furthermore, GTC has varied implications on cancer prevention triggered apoptosis because of ROS generation and activating caspase-9 and 3, usually resulting in obstruction of cell-cycle during gape one phase by modulating cyclin D1 expression, p21, and cdk4 [16]. Tea and its components can exhibit antibacterial effects by blocking intracellular enzymes and nucleic acid synthesis, damaging cell walls and membranes [17]. Anti-diabetes mellitus effect has been shown to sustain β-cell by decreasing radicals and inflammation-factors in vitro or decreasing Nitric oxide synthesis. Green tea was also able to reduce blood sugar levels in diabetic rats by stimulating β-cells to secrete more insulin [18]. Catechin-based anti-inflammatory therapy decreased responses to inflammation in adipocytes, normalized AdipoQ levels, protected the liver's cells from obesity-induced damage, and recovered normal functioning of the liver [19].

Atorvastatin (ATV) is lipid soluble, can enter cells via penetrating the lipid bilayer and rapidly absorbed following oral administration, commonly used Cholesterol lowering drug to treat hypercholesterolemia [20]. It inhibits 3-hydroxy-3 methylglutary-coenzyme a reductase (HMG-CoA), the enzyme that catalyzes the rate – limiting step of Cholesterol synthesis, have beneficial effect of ATV include reduce systemic LDL cholesterol level. [21].

The present study was aimed to use GTC in comparison to ATV as standard lipid lowering factor both are orally administered to white female rats, to investigate its effect on improving IR and hypoadiponectinemia in these rats.

Material and Methods:

Experimental design

Twenty female white rats were conducted to the experiment healthy female white adult rats weighing 135–147 g was used in this investigation. Earlier to the trial commenced, rats finished one week attainment used to their new environs. They were retained at ambient temperature, maintained for 12-hour light/dark phase, and abandoned access to water. Rats were habituated to their new surrounds for one week proceeding to the experimentation. The they were divide to for equivalent number rats group (5 rats each group) as; normal negative group received normal diet for all experiment time (60 days); positive obese control group received high fat diet (HFD) for (60 days); GTC-fed group, after they reaching obesity this group fed HFD with daily GTC dosage (1.7) mg per (kg/day) for 30 days [19]; the last ATV-fed group after they reaching obesity this group received ATV dissolved in distal water and supplied everyday of dosage (40) mg per (kg/day) [21].

The HFD has 4.14 kcal/g comprises carbohydrates 43%, fats 40%, and proteins 17%. Whereas, the normal food diet includes 3.06 kcal/g comprises carbohydrates 48.8%, fats 3%, and proteins 21%. All ingredients of high fat diet were thoroughly mixed and baked in the oven at 65∘C overnight [22].

Blood samples

Following overnight fasting, physicochemical and endocrine markers were evaluated using serum samples obtained from the animal's heart blood via sterile syringe. Animal anesthesia by Ketamine 10 milligram per Kg of body wight and Xylazine 90 milligram per Kg of body weight (0.2 ml per animal) and collecting 5 ml of blood. The serum was obtained from blood used for laboratory analysis. The kits used from Bio research for diagnosis – Germany to determine Glucose, Triglyceride, Total-C, and HDL-C spectrophotometrically. In addition, AdipoQ and Insulin determined by ELISA technique using Rat (AdipoQ and insulin) Elisa kits SUNLONG–Chin respectively. The HOMA-IR measurement index was calculated using the formula: [glucose (mg/dL) x insulin (mU/L)]/405 [23].

Statistical analysis

Statistical data analysis was conducted according to SPSS version 25, where T-test and ANOVA (a one- way) were employed to determine significant differences among and within groups. Data were provided as mean ± SD, with P values < 0.05 indicating statistical significance for biochemical parameters.

Ethical approval

Every experiment was authorized by the Animal Ethics Committee at University of Kufa named Institutional Animal Care and Use Committee (IACUC) according to its agreement document, University of Kufa, No1686 for the Data 10-3-2024.

Result:

Table (1) elucidates the mean ± SD comparisons of negative with positive group, positive with GTC-fed group and positive with ATV-fed group. Rats' weights elucidated at initial, after 30 days, gain weights, and final periods of experiment. All biochemical and hormonal levels expressed as Glucose, Cholesterol, Triglyceride, HDL-C, Insulin and AdipoQ as well as HOMA-IR. Glucose elevated in obese group after 30 days significantly above normal with $p<0.001$ but its levels returned to near normal value of negative control group after 30 days administration of GTC. Triglyceride level were also differed significantly (obtained $p<0.001$) between means of negative and positive control groups, and between means of positive control group with ATV and GTC treatment groups. Total-cholesterol level were also differed significantly (obtained $p = 0.002$) between means of negative and positive control groups, and obtained $p = 0.001$ between means of positive control group with ATV and GTC treatment groups. HDL-C level were decreased significantly (obtained $p<0.001$) between means of negative and positive control groups, but it increased significantly in ATV and GTC treatment groups. The results exposed that the levels of AdipoQ, insulin and calculated HOMA-IR were significantly different (obtained $p < 0.001$) between means of negative and positive control groups, and negative control group with ATV and GTC treatment groups. The differences of triglycerides, total-cholesterol and HDL-C among experiment groups explained in figure (1) below. The effect of GTC and ATV on AdipoQ, Insulin and HOMA-IR were explained in figure (2) below.

Table 1: Weight, biochemical parameters, adiponectin and insulin levels for all experimental groups.

Biochemistry	Groups represented as (Mean ± SD)						
	Negative Control	**Positive Control**	**P-value* (Neg. vs. Pos.)**	**Cat. Group**	**P-value* (Cat. Vs. Pos.)**	**ATV. Group**	**P-value* (ATV. Vs. Pos.)**
Initial BW (g)	140.6 ± 3.78	143.2 ± 2.59	0.59	143.8 ± 2.86	0.99	142.6 ± 3.58	0.94
BW (g) 30 d	150.2 ± 2.86	217.6 ± 4.28	< 0.001	212.8 ± 4.44	0.44	210.8 ± 7.12	0.17
BWG (g) 30 d	9.6 ± 3.21	66 ± 10.2	< 0.001	69 ± 5	0.92	68.2 ± 9.12	0.97
BW (g) 60 d	158.4 ± 9.4	205.4 ± 5.55	< 0.001	185.4 ± 4.22	0.001	191.2 ± 6.46	0.019
Glucose (mg/dL)	122.72 ± 14.4	225.51 ± 24.47	< 0.001	135.68 ± 4.72	< 0.001	131.88 ± 3.9	< 0.001
Triglyceride (mg/dL)	35.66 ± 6.45	108.75 ± 7.35	< 0.001	68.93 ± 2.67	< 0.001	50.83 ± 4.59	< 0.001
Total-C (mg/dL)	64.49 ± 3.18	81.47 ± 6.56	0.002	66.05 ± 7.33	0.004	62.36 ± 6.02	0.001
HDL-C (mg/dL)	33.69 ± 2.83	24.02 ± 1.74	< 0.001	29.14 ± 1.36	0.005	37.51 ± 1.91	< 0.001
Adiponectin (ng/mL)	25.59 ± 2.81	14.06 ± 0.73	< 0.001	20.48 ± 1.39	< 0.001	17.48 ± 1.39	< 0.001
Insulin (mU/L)	1.84 ± 0.16	3.59 ± 0.39	< 0.001	2.54 ± 0.37	< 0.001	2.27 ± 0.13	< 0.001
HOMA-IR**	0.56 ± 0.08	2.01 ± 0.41	< 0.001	0.85 ± 0.11	< 0.001	0.74 ± 0.06	< 0.001

***** *Indicate Significant p-value is <0.05. ** The value of HOMA-IR greater than 2 indicates insulin resistance*

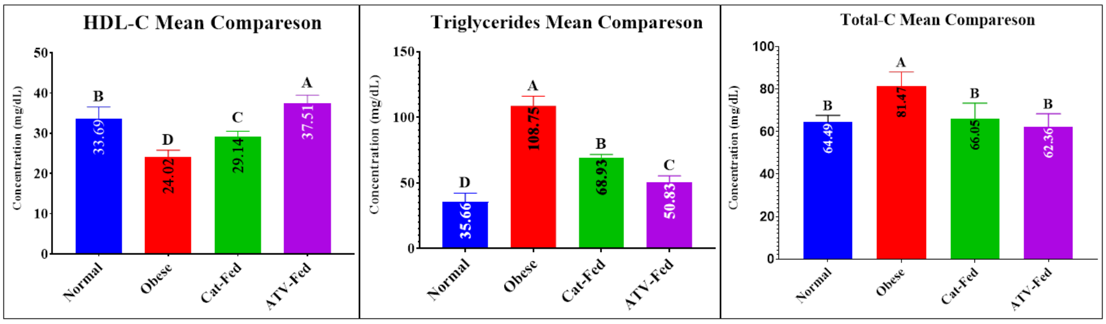

Figure 1: Role of orally intubated 1.7mg (Kg/day) of GTC and 40mg (Kg/day) of ATV on Cholesterol, Triglyceride and DHL level for all groups.

Dissuasion:

Glucose and insulin resistance

The data of our study indicate to hyperglycemia in obese rats with insulin resistance, but decreased in catechin-fed group after 30 days treatment. A study explain that blood glucose level was significantly low in rats after the administration of green tea and green tea a dose powder catechin suspension, whereas the level of blood glucose level remained high in diabetic rats [24].

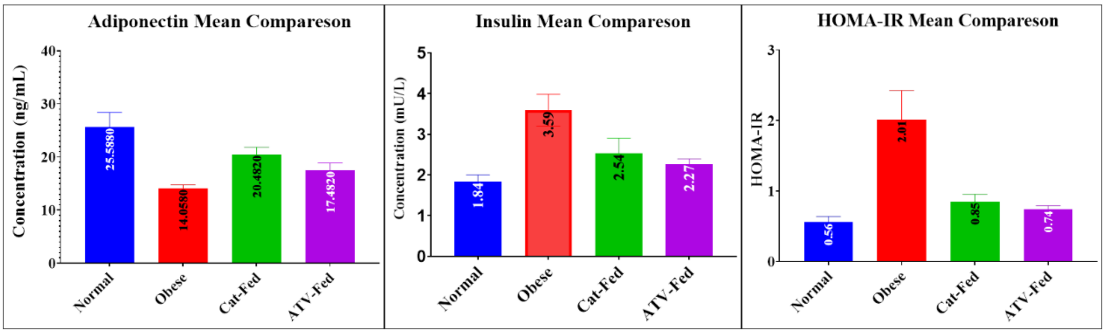

Figure 2: Role of orally intubated 1.7mg (Kg/day) of GTC and 40mg (Kg/day) of ATV on Adiponectin, Insulin and HOMA-IR levels compared to other groups.

Numerous beneficial effects of green tea and its catechins, particularly epigallocatechin-3-gallate (EGCG), make this natural product an attractive pharmacological agent that can be further developed to treat diabetes and its complications [25]. A cell model confirmed that adipose-derived stem cells (ADSC) incubated with GTC increase cell viability under high-glucose stress. This is due to survival marker p-Akt expression. In an animal model, type 1 diabetes induced the activation of several pathological signals, including islet size reduction, extracellular fibrotic collagen deposition, oxidative stress elevation, survival pathway suppression, apoptosis signaling induction, and Sirt1 antioxidant pathway downregulation. Ordinary ADSC transplantation slightly improved the above pathological signals. Further, EGCG-pretreated ADSC transplantation significantly improved the above pathological conditions. Taken together, GTC-pretreated ADSCs show clinical potential in the treatment of patients with type 1 diabetes through the regeneration of damaged pancreatic tissues [26].

Treatment by GTC attenuated weight gain and visceral fat accumulation, and significantly reduced fasting serum glucose and insulin levels. Homoeostasis model assessment of insulin resistance (HOMA-IR), a measure of insulin resistance, was lower in GTP-treated animals compared with normal control rats. Moreover, insulin-stimulated glucose uptake by isolated soleus muscle was increased in GTC-fed rats compared with obese control rats. GTC treatment attenuated the accumulation of ectopic lipids (triacyl- and diacyl-glycerol), enhanced the expression and translocation of glucose transporter-4, and decreased pSer612IRS-1 and increased pSer473Akt2 expression in skeletal muscle. These molecular changes were also associated with significantly decreased activation of the inhibitory (muscle-specific) protein kinase (PKC) isoform, PKC-θ. Additionally, regular ingestion of GTC exerts a number of favorable metabolic and molecular effects in an established animal model of obesity and insulin resistance. The benefits of GTC are mediated in part by inhibiting PKC-θ and improving muscle insulin sensitivity [27].

Adiponectin

The AdipoQ levels decreased in obese rats while improved in Cat.-fed and ATV-fed groups after 30 days treatments of Catechin and ATV respectively in this study. Supplement of GTC mentioned to improved protein expression and plasma levels of AdipoQ in adipose tissue of HFD rats. Also, treatment with GTC was able to increase AdipoQ secretion in a dose-dependent manner. In addition, GTC supplement was also shown to suppress inflammation and improve metabolic factors associated with insulin sensitivity [28].

Studies of rat models showed HFD intake resulted in circulating lipid disorder, HOMA-IR, decreased circulating AdipoQ, and obesity. GTC supplement improved all of these measures. GTC in 3T3-L1 adipocytes reduced TNF-α provoked protein carbonylation, pro-inflammatory cytokine production MCP-1, plus AdipoQ concentrations. Catechin's ability to reduce JNK and p38 activation and prevent PPAR-γ downregulation contributes to its preventive effects on adipose inflammation [29].

Lipid Profile

This study showed that triglycerides and total cholesterol were increased in obese rats and decreased in Cat-fed and ATV-fed groups after 30 days treatment with catechin and ATV respectively. In contrast HDL-C decreased in obese group and return to near normal value in cat-fed and ATV-fed groups after treatments.

Catechin most abundantly present in brewed green tea, investigated to enhance energy expenditure, increase fatty acid oxidation and thermogenesis, and reduce fat absorption. Scientists also propose that tea polyphenols may counteract the decrease in resting metabolic rate associated with weight loss [30].

Studies show that GTC along with caffeine can reduce body weight and waist circumference by having a synergistic effect on adipose tissue thermogenesis [30,31], GTC also reportedly prevent adipogenesis in mature adipocytes, prevent the differentiation of pre-adipocytes to adipocytes, and therefore, reduce fat accumulation in adipose tissues. Catechins are also positively associated with improvements in biomarkers like insulin, glucose, high-density lipoproteins (HDL), low-density lipoproteins (LDL), and total cholesterol. Studies indicate the consumption of GTC correlate to increased endurance capacity and exercise tolerance which may possibly boost EE [32].

The results of this study in accordance with Nakadate et.al [18], where serum biochemical analysis revealed that feeding a high-calorie diet affected serum parameters associated with obesity, including total cholesterol, and triglyceride. Treatment with GTC significantly improved the serum parameters indicating that GTC improved serum parameters in mice with obesity [18].

Consuming GTCs with meals, particularly gallated Catechins, has been demonstrated to reduce pancreatic lipase activity in the small intestine, which inhibits fat absorption and encourages fat excretion in the feces, leading to weight loss. Furthermore, gallated Catechins bind to bile acid micelles in the small intestine and release the cholesterol from the micelles, thus decreasing cholesterol absorption and serum cholesterol levels [18]. It is believed that GTCs are absorbed by the body and transported to target cells, where they act similarly to other bioactive substances [33], GTCs can boost the expression and activity of lipolytic enzymes in fat cells, thus augmenting the release of fat-derived glycerol [34]. Furthermore, GTCs have been demonstrated to enhance the activity of hepatic β-oxidation-related enzymes, augment skeletal muscle β-oxidation-related enzymes and fatty acid transport enzymes, and increase β-oxidation activity when combined with exercise [18]. It is thought that increased fat burning and increased energy expenditure during everyday activities can help to balance energy and lipids and reduce visceral fat. Recent discoveries indicated that GTCs can improve energy metabolism in brown adipocytes, potentially alleviating chronic obesity [35].

Green tea-Catechin dose-dependently inhibited pancreatic lipase activity, thereby inhibiting triglyceride absorption and postprandial hypertriglyceridemia. In addition, GTCs have been shown to increase cholesterol 7α-hydroxylase gene expression in HepG2 cells which may stimulate bile acid production and reduce cholesterol levels in hepatocytes the decrease of TG level is beneficial to the blood lipid of overweight and obese people [36].

Limitations

One of the difficulties that the researcher faced was the difficulty of obtaining the experimental materials, as they took a long time to arrive. In addition, there is a lack of financial support to carry out important steps that include an in-depth study of other genetic influences within the tissues under study.

Conclusions:

We found that GTC has positive effect on AdipoQ in obese female rats where increased AdipoQ after 30 days administration. Additionally, after GTC administration Lipid profile improved significantly in these rats, where it is evidently due to minimizing serum Cholesterol and Triglyceride concentrations in obese rats and increase Serum HDL concentration in obsess rat. The other most important effects of GTC were observed by increase insulin sensitivity and improving glucose levels in rats.

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