GREEN TEA; BEST WAY TO STRUGGLE LIPID
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Abstract:
Introduction: Tea is one of the most common famous drink used daily in many countries in the world. Green tea contains polyphenolic compounds as catechins, that contains epigallocatechin gallate (EGCG). The lowering of plasma cholesterol levels and blood pressure as well as improvement of insulin sensitivity and endothelial function by green tea.

Aim of the work: Study the effect of green tea on obesity, blood lipid level and its effect on fatty liver.

Materials and Methods: All animal procedures were approved by the ethical committee of Faculty of Medicine, Tanta University. Thirty male Albino rats in the range of 230–280 g body weight was used in this study. All subjects were kept in an animal room of Physiology Department of Faculty of Medicine, Tanta University, in a controlled temperature and 12:12 h light/dark cycle with free access to food and water. The animals were divided into 3 groups of 10 animals each. Group-1: the sham group (sham operated, no obesity). Group-2: the vehicle group (obesity induced rats treated with normal saline). Group-3: the ghrelin group (obesity induced rats treated with EGCG).

Results: Body weight, fat deposits, adiposity index and serum cholesterol increased significantly in a time-dependent manner in obese and control animals but were higher in the obese group (HFD > SD). High fat diet caused significant increases in the serum cholesterol level indicating high body lipid and obesity but when EGCG was administered after the beginning of high fat diet, these elevations were significantly depressed. In the vehicle group (obesity induced + saline), areas of hepatocyte necrosis in the liver parenchyma, lymphocytic infiltration, expansion of sinusoids and scattered congestion were detected. Hepatocyte damage was not observed in the liver parenchyma of the EGCG group (obesity induced + EGCG) except for scattered necrotic hepatocytes. Expansion of blood sinusoids was less compared to the vehicle group (obesity induced + saline).

Conclusion: In conclusion, since the administration of EGCG increase lipolysis and the accumulation of neutrophils in the damaged hepatic tissue, this agent appears to play a cytoprotective role in the liver insulted by fatty infiltration with obesity. It seems likely that Green tea (EGCG) is put in consideration as a potential therapeutic agent against obesity and hyperlipidemia.

Keywords: Green Tea; EGCG; Obesity; Hyperlipidemia.

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INTRODUCTION:
Tea is one of the most common famous drink used daily in many countries in the world. It can be categorized into unfermented tea as green tea and white tea, semi-fermented tea as oolong tea and fully fermented tea as black tea. The main chemical constituents in unfermented tea are catechins and caffeine, while in semi-fermented and fully fermented tea are theaflavins, thearubigins and caffeine. Catechins, caffeine and theaflavins have been reported that they have a great biological effect [1].

Tea has been used as a drug in ancient times. Many studies have shown that tea polyphenols are the major effective components in teas, e.g., used for its anti-oxidation [2], anti-carcinoma [3], and arteriosclerosis prevention [4], and in the prevention of Alzheimer’s and Parkinson diseases [5].

In green tea manufacturing, the leaves are heated in order to inactivate the enzymes, after that they are rolled and dried. This process prevents the autolysis of the leaves and the oxidation of the constituents. The drying of the tea leaves also helps to stabilize the tea constituents during storage [6].

Green tea contains polyphenolic compounds as catechins, which include: (−)-epigallocatechin gallate (EGCG), (−)-epicatechin gallate (ECG), (−)-epigallocatechin, and (−)-epicatechin. Catechins account for about 30–42% of the dry weight of brewed green tea, and EGCG is the major form of tea catechin. Tea leaves have low amounts of other polyphenols, as quercetin, kaempferol, myricetin and alkaloids, as caffeine and theobromine. A typical brewed green tea beverage (e.g., 2.5 g tea leaves in 250 ml of hot water) contains 240–320 mg of catechins, of which 60–65% is EGCG, and 20–50 mg of caffeine [7].

The health effects of tea depend on the biochemical properties and bioavailability of the constituents in tea. Tea catechins, especially EGCG, have received most of the attention. It is commonly recognized that tea catechins are strong antioxidants, efficiently scavenging free radicals and also preventing the formation of reactive oxygen species (ROS) by chelating metal ions [8].

The lowering of plasma cholesterol levels and blood pressure as well as improvement of insulin sensitivity and endothelial function by green tea have been reported by many investigators [9].

Green tea has been used in alternative medicine for aid in treating clogged arteries, endometrial and ovarian cancer, low blood pressure, bone health (osteoporosis), changes in cervical cells due to human papiloma virus (HPV), white patches in the gums, the prevention of Parkinson's disease. It decreasing cholesterol and blood pressure and diabetes. Oral health, weight loss, antiaging, Asthma, immunity, liver diseases, flu and cold [10].

Other uses included various cancers (bladder, esophagus, pancreas, breast, colon, stomach, leukemia, mouth, prostate, and lung); acne, heart disease, diabetes, infertility, heart health (high blood pressure, respiratory infections, improvement of athletic performance, wrinkles and others [11].

Due to high consumption of green tea in Libya, we study the effect of green tea on obesity, blood lipid level and its effect on fatty liver.

MATERIALS AND METHODS:
Experimental Animals:
All animal procedures were approved by the ethical committee of Faculty of Medicine, Tanta University. Thirty male Albino rats in the range of 230–280 g body weight were used in this study. All subjects were kept in an animal room of Physiology Department of Faculty of Medicine, Tanta University, in a controlled temperature and 12:12 h light/dark cycle with free access to food and water.

The animals were divided into 3 groups of 10 animals each. 

Group-1: the sham group (sham operated, no obesity).

Group-2: the vehicle group (obesity induced rats treated with normal saline).

Group-3: the ghrelin group (obesity induced rats treated with EGCG).

The first group received a standard diet (SD) with 4% fat content, the second group was fed a high-fat diet (HFD), with a content of 20% fat to induce obesity and treated with normal saline and the third group was fed a high-fat diet (HFD), with a content of 20% fat to induce obesity and treated with intraperitoneal injection of EGCG.

At the end of the experimental procedure, the animals were decapitated and trunk blood samples were collected to determine serum cholesterol. Liver samples were fixed with 10% formaldehyde for histopathological evaluation.

Administration of EGCG:
EGCG administration (20 mg/kg, i.p., 3 times weekly) was administered intraperitoneally. This dose of EGCG was determined from a previous model of study [12]. An equal volume of the saline was injected into the vehicle rats. The sham group of animals only underwent liver biopsy and serum cholesterol level.

**Estimation of serum Cholesterol level:**
Serum cholesterol was determined to assess serum blood lipid and obesity (Roche Diagnostic, Mannheim, Germany) commercial kits in a Roche- Hitachi Modular Auto analyzer (Roche Diagnostic).

**Adiposity index:**
In order to estimate the adiposity index in rats, we sum epididymal, visceral and retroperitoneal fat weights and divided by body weight × 100. It is expressed as adiposity percentage [13].

**Histopathological Evaluation**
For light microscopic examinations, liver samples were fixed in 10% neutral buffered formalin solution. The tissues were embedded in paraffin. The paraffin blocks were cut in 5 µm thick. The sections were stained with Hematoxylin-Eosin (H&E). All tissue sections were examined microscopically to detect the histopathological changes.

**Statistical Analysis:**
- The collected data were coded then entered and analyzed using the SPSS version 22 (Statistical package for social science).
- Descriptive statistics was done for categorical variables by frequency and percentage, and for numerical variables in the form of mean and standard deviation (mean ± SD).
- Suitable statistical tests of significance were used:
  - Chi-Square (χ²) test for categorical data
  - P-values equal to or less than 0.05 were considered statistically significant.

**RESULTS:**
Body weight, fat deposits, adiposity index and serum cholesterol increased significantly in a time-dependent manner in obese and control animals but were higher in the obese group (HFD > SD).

**Effect of EGCG on Cholesterol level:**
High fat diet caused significant increases in the serum cholesterol level indicating high body lipid and obesity but when EGCG was administered after the beginning of high fat diet, these elevations were significantly depressed (P < 0.05) (Table 1).

| Groups                             | Cholesterol level |
|-----------------------------------|------------------|
| Sham group                        | 62 ± 4.3         |
| Vehicle group (obesity induced + saline) | 267 ± 8.6*     |
| EGCG group (obesity induced + EGCG)  | 143 ± 6.7*      |

Table (1): Changes in serum cholesterol level in the Sham, Vehicle (obesity induced + saline), and EGCG (obesity induced + EGCG) Groups. Each group consists of ten rats. *P < 0.05 compared with sham group.

**Histopathological Study**
In the vehicle group (obesity induced + saline), areas of hepatocyte necrosis in the liver parenchyma, lymphocytic infiltration, expansion of sinusoids and scattered congestion were detected. Hepatocyte damage was not observed in the liver parenchyma of the EGCG group (obesity induced + EGCG) except for scattered necrotic hepatocytes. Expansion of blood sinusoids was less compared to the vehicle group (obesity induced + saline). These observations are illustrated in Figure 1.
DISCUSSION:
The anti-obesity effect of tea extract and individual tea polyphenols has been extensively studied in animal models. We found that many studies measure obesity-related parameters over periods of 12 weeks in mice that were divided into groups of high-fat diet, normal diet, and high-fat with tea added.

Many studies decided that consumption of green tea extracts (GTE) or EGCG reduced body weight and adipose tissue weight, decreased blood glucose or insulin levels, and increased insulin sensitivity in body. These studies used rodents on high-fat diets or genetically obese/diabetic animal models. For example, in mice fed with a high-fat (60% of the calories) diet, we found that dietary EGCG treatment (0.32 % in diet) for 16 weeks significantly reduced body weight gain, body fat and visceral fat weight compared to mice without EGCG treatment [14].

Henning et al., 2017 revealed that green and black tea polyphenols decrease weight gain in mice with diet-induced obesity by a mechanism that increase hepatic AMPK phosphorylation and changing gut microbiota [15]. In this study, subcutaneous body fat percentage of both black and green tea groups were significantly lower than the high-fat diet group and even slightly lower than the low-fat diet group. Jobu et al., 2013 measure the anti-obesity effects of green tea in comparing with Japanese dark tea (goishi tea) [16].

A recent metabolomic study with healthy male subjects demonstrated that green tea extract supplementation (1200 mg catechins and 240 mg caffeine daily) for 7 days increased lipolysis, fat oxidation and citric acid cycle activity under resting conditions without enhancing adrenergic stimulation [17].

EGCG treatment also attenuated insulin resistance, plasma cholesterol and monocyte chemomtractant protein concentrations in mice on the high-fat diet [14, 18].

Similar results were also observed in several recent studies [19–20]. For example, treatment of male Swiss mice with green tea extract (GTE, 50 mg/kg, i.g., daily) for 8 weeks decreased body weight and white adipose tissue weight [19]. In another study, EGCG administration (20 mg/kg, i.p., 3 times weekly) to C57BL/6b mice that were fed a high-fat diet significantly reduced body weight and liver fat accumulation at 42 and 66 weeks [12].

CONCLUSION:
In conclusion, since the administration of EGCG increase lipolysis and the accumulation of neutrophils in the damaged hepatic tissue, this agent appear to play a cytoprotective role in the liver insulted by fatty infiltration with obesity. It seems likely that Green tea (EGCG) is put in consideration as a potential therapeutic agent against obesity and hyperlipidemia.

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