EFFECT OF GREEN TEA EXTRACT ON FOOD CONSUMPTION AND BODY WEIGHT IN EXPERIMENTALLY-INDUCED MYOCARDIAL INFARCTION IN ADULT MALE ALBINO RAT

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ABSTRACT

Background: There is an increasing realization that herbs can influence the course of heart disease and its treatment. Green tea is an important medicinal plant having strong anti-oxidant properties. Objective: Evaluation of the effect of green tea extract on food consumption and body weight of isoprenaline (ISO)-induced myocardial infarction in adult male albino rat. Material and Methods: Seventy adult male albino rats of local strain were chosen as an animal model for this study weighed 110 -130 g (average weight was 120 g). Myocardial infarction was induced in experimental rats by injecting isoprenaline. Food consumption was measured daily. Body weight was measured at the beginning and at the end of experiment. Heart weight/body weight ratio was calculated at the end of the experiment (30 days). Results: During the experiment, changes in body weight and food consumption in different groups were more or less concomitant together. Increase in body weight was associated with increase in food consumption and vice versa. ISO showed an increase of food consumption which was accompanied by an increase of body weight. GTE showed reduction of food consumption which was accompanied by loss of body weight, while metoprolol produced an increase of food consumption accompanied by an increase of body weight. GTE and metoprolol in combination produced the same effect that produced by green tea extract. Conclusion: Green tea extract is effective in decreasing food consumption and body weight.

Key words: Green tea, myocardial infarction, food consumption, body weight, isoprenaline

INTRODUCTION

Several varieties of green tea exist, which differ substantially due to growing conditions, horticulture, production processing, and time of harvest. Catechins are the main bioactive constituents of green tea leaves, and account for 25% to 35% of their dry weight. The main catechin group consists of eight polyphenolic flavonoid-type compounds, namely, catechin (C), Epicatechin (EC), Gallocatechin (GC), Epigallocatechin (EGC), Catechin gallate (CG), Epicatechin gallate (EG), Gallo-locatechin gallate (GCG) and Epigallocatechin gallate (EGCG). Epigallocatechin gallate is the most abundant of the tea catechins and thought to be responsible for the majority of the biological activity of green tea extracts (Sutherland et al., 2013). Other bioactive molecules are amino acids like theanine, proteins, caffeine, vitamin C, carbohydrates, polysaccharides and lipids. In the cells of a tea leaf, catchins reside in the cell sap, while oxidative enzymes are located in the cell wall.
Epigallocatechin-3-gallate (EGCG) purified from green tea decreases diet-induced obesity by decreasing energy absorption and increasing fat oxidation (Klaus et al., 2005). The increased and prolonged sympathetic stimulation of thermogenesis by the interaction between polyphenols and caffeine could be of value in assesting the management of obesity (Dulloo et al., 2000).

The consumption of green tea and green tea extracts may help reduce body weight, mainly body fat, by increasing postprandial thermogenesis and fat oxidation (Boschmann and Thielecke, 2007).

The present work aimed to study the changes of food consumption and body weight by green tea extract on isoprenaline-induced myocardial infarction in adult male albino rat.

**MATERIAL AND METHODS**

**Animals:** Seventy adult male albino rats of local strain were chosen as an animal model for this study, and were kept in suitable cages (20x32x20 cm for every four rats) at room temperature, with the natural light-dark cycle in the Physiology Department, Al-Azhar Faculty of Medicine. They weighed 110 -130 g (average weight was 120 g). They were fed on the standard food in addition to bread and green vegetables with free water supply. They were kept for 10 days for the adaptation to the new environments before the start of the experiment. The animals were divided into seven equal groups as follows:

(I)-Normal control group (II)-Intra-peritoneal saline-treated group received 0.5 ml normal saline / 100 g body weight intraperitoneally for two consecutive days (29th and 30th). (III)-Green tea extract-treated group received daily10 mg / 100 g body weight orally for 30 days. (IV)-Isoprenaline-treated (MI) group received 11 mg / 100 g body weight intraperitoneally for two consecutive days (29th and 30th). (V)-Green tea extract + Isoprenaline-treated group received green tea extract 10 mg / 100 g body weight /day orally for 30 days in addition to i.p. injection of isoprenaline in a dose of 11 mg / 100 g body weight intraperitoneally for two consecutive days (29th and 30th). (VI)- Metoprolol + Isoprenaline-treated group (standard group) received Metoprolol (1 mg / 100 gm body weight /day orally) for 30 days in addition to ISO 11 mg /100 gm i.p. on the 29th and 30th days. (VII)- Green tea extract + Metoprolol + Isoprenaline-treated group treated group received green tea extract (10 mg / 100g body weight /day orally for 30 days), Metoprolol (1 mg / 100 g body weight /day orally for 30 days), and i.p. injection of isoprenaline in a dose of 11mg / 100 gm body weight for two consecutive days (29th and 30th).

**Methods:** Myocardial infarction was induced in experimental rats by injecting isoprenaline (ISO) 11 mg (dissolved in physiological saline) / 100 g body weight i.p. for 2 days (29th and 30th).

Green tea extract (GTE) tablets (Arab Co. for Pharmaceuticals & Medicinal Plants, Mepaco-Pharma, Egypt): Each tablet contains 200 mg GTE. The stock solution was prepared by dissolving 6 tablets in 60 ml distilled water with a concentration of 20 mg GTE per 1 ml distilled water. From that stock solution,
appropriate volume of GTE was given to rat in a dose of 100 mg / kg body weight /day orally by orogastric tube for 30 days. Stock still stable at room temperature for seven days (Ojo et al., 2006).

Food consumption was measured daily. Body weight was measured at the beginning and at the end of experiment.

Heart weight/body weight ratio: The rat was weighed. Removal of the heart was performed by dissecting the aortic root immediately above the aortic valve and the superior vena cava above the atrium. Adjacent mediastinal fat pads were removed from the excised heart carefully. The dry heart was weighed and recorded, then heart weight/ body weight ratio was calculated (Neha and Lubna, 2014).

Statistical analysis: The computer program SPSS version "17" was used for one way ANOVA (Analysis Of Variance) test, calculation of the descriptive statistics in studied groups (means ± standard deviations), detection of any significant difference between different groups and between different samples, performing multiple comparisons between each group and another, and each sample and another by using the "Post Hoc LSD" multiple comparison test. P < 0.5 was considered significant.

RESULTS

Changes in food consumption during the whole experiment (Figure 1):

In group I, the mean ± SD was 15.6 ± 2.56 g /day/rat. In group II, the mean ± SD was 16.4 ± 2.7 g/day/rat during the whole experiment with no significant difference between group I and group II. In group III, the mean ± SD was 11.98 ± 3.4 g/day/rat with significant decrease as compared to group I. In group IV, the mean ± SD was 15.98 ± 4.5 g/day/rat during the whole experiment with insignificant difference between group IV and group II. In group V, the mean ± SD was 12.06 ± 2.3 g /day/rat with significant decrease when compared to group IV, but with no significant difference when compared to group III. In group VI, the mean ± SD was 15.3 ± 2.2 g/day/rat with significant increase when compared to group V. There was no significant difference between group IV and VI. In group VII, the mean ± SD was 11.6 ± 3.1 g/day/rat. In relation to group IV, group VII showed significant decrease in food consumption. In relation to group VI, group VII showed significant decrease in food consumption, but with no significant difference as compared to group V.

During the experiment, changes in body weight and food consumption in different groups were more or less concomitant together. Increase in body weight was associated with increase in food consumption and vice versa. ISO showed an increase of food consumption which was accompanied by an increase of body weight. GTE showed reduction of food consumption which was accompanied by loss of body weight, while metoprolol produced an increase of food consumption accompanied by an increase of body weight. GTE and metoprolol in combination produced the same effect that produced by green tea extract.

Changes in body weight during the whole experiment (Figure 1):

In group I (control-received oral distilled water), the means ± standard deviations of body weight (BW) were
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116.42 ± 9.4 g at the beginning of the experiment, 128.4 ± 7.37 g at the end of the 2nd week and 136 ± 8.6 g at the end of the 4th week. Within this group, BW showed significant increase at the 2nd measurement and the 3rd measurement in relation to the 1st one. No significant difference was shown between the 2nd and the 3rd measurements.

In group II (control-received saline 0.9% I.P.), the means ± standard deviations were 115.71 ± 8.01 g at the beginning of the experiment, 124.7 ± 8.2 g at the end of the 2nd week, and 135.1 ± 6.4 g at the end of the 4th week. Within this group, BW showed significant increase at the 2nd measurement in relation to the 1st measurement, significant increase at the 3rd measurement in relation to the 1st one and also significant increase at the 3rd measurement in relation to the 2nd one. The differences between control group I and control group II were insignificant at the three intervals.

In group III (control-received green tea extract orally), the means ± standard deviations were 122.14 ± 6.36 g at the beginning of the experiment, 114.7 ± 12.59 g at the end of the 2nd week, and 109.14 ± 13.5 g at the end of the 4th week. Within this group, there was no significant difference in BW between the 1st measurement and the 2nd one and between the 2nd measurement and the 3rd measurement, but there was significant decrease at 3rd measurement as compared to the 1st one. The difference between control group I and group III was insignificant at the beginning of the experiment, but it significantly decreased in group III as compared to group I at the latter two measurements.

In group IV (Myocardial infarction group received isoprenaline I.P.), the means ± standard deviations were 114.14 ± 9.65 g at the beginning of the experiment, 121.3 ± 12.63 g at the end of the 2nd week and 133.3 ± 13.2 g at the end of the 4th week. Within this group, the results also showed significant increase at the 3rd measurement in relation to the 1st one, but the difference between the 1st measurements and 2nd one, and between the 2nd measurements and 3rd one were insignificant. The difference between control group II and myocardial infarction group IV was insignificant at the three intervals.

In group V (received GTE. orally + ISO I.P.), the means ± standard deviations were 119.42 ± 8.30 g at the beginning of the experiment, 112.6 ± 12.99 g at the end of the 2nd week, and 106.9 ± 11.1g at the end of the 4th week. Within this group, the results showed significant decrease at the 3rd measurement in relation to the 1st one, but the difference between the 1st measurements and the 2nd one, and, between the 2nd measurements and the 3rd one were insignificant. The difference between group III and group V were insignificant at the three intervals. The difference in group V and group IV were insignificant at the beginning and at the end of the 2nd week, but significantly decreased at the end of the 4th week.

In group VI (received metoprolol orally+ ISO I.P.), the means ± standard deviations were 117.57 ± 10.6 g at the beginning of the experiment, 132.1 ± 9.26 g at the end of the 2nd week, and 136.9 ± 6.06 g at the end of the 4th week. Within this group, BW showed significant increase at the 2nd measurement (at the end of 2nd week) in relation to the 1st measurement (at the beginning of the
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experiment), and also significant increase at the 3rd measurement (at the end of the 4th week) in relation to the 1st one. No significant difference was shown between the 2nd and the 3rd measurements.

The difference between group IV and group VI were insignificant at any interval. The difference in group VI in relation to group V was insignificant at the beginning of experiment, but at the end of the 2nd and 4th week increased significantly.

In group VII (received Metoprolol + green tea extract orally + ISO I.P), the means ± standard deviations were 122.85 ± 6.36 g at the beginning of the experiment, 115.8 ± 10.90 g at the end of the 2nd week and 112 ± 12.8 g at the end of the 4th week. Within this group, the result showed significant decrease at the 3rd measurement (at the end of the 4th week) in relation to the 1st one, but the differences between the 1st measurements and 2nd one and between the 2nd measurements and 3rd one were insignificant. The differences in group VII in relation to group IV were insignificant at the beginning and at the end of the 2nd week, but at the end of the 4th week decreased significantly. The differences between group V and group VII were insignificant at the three intervals. The difference in group VII in relation to group VI was insignificant at the beginning of experiment, but at the end of the 2nd and 4th week decreased significantly.

So, ISO showed insignificant change in body weight. Green tea extract (GTE) decreased the body weight at the end of experiment, while metoprolol showed insignificant change in body weight. GTE and metoprolol in combination decreased body weight due to the effect of green tea.

Figure (1) Relation between food consumption and body weight in different groups (mean±SD).
Heart weight/body weight ratio (Figure 2):

In group I, the mean ± SD of heart weight and heart weight / body weight ratio were 0.55 ± 0.076 and 3.99 ± 0.36 g respectively. In group II, the mean ± SD of heart weight and heart weight / body weight ratio were 0.54 ± 0.057 and 4.02 ± 0.34 g respectively, with no significant difference between group I and group II. In group III, the mean ± SD of heart weight and heart weight / body weight ratio were 0.48 ± 0.077 and 4.4 ± 0.44 g respectively with insignificant change when compared to group I. In group IV, the mean ± SD of heart weight and heart weight / body weight ratio were 0.85 ± 0.14 and 6.4 ± 0.72 g respectively with significant increase when compared to group II. In group V, the mean ± SD of heart weight and heart weight / body weight ratio were 0.57 ± 0.10 and 5.3 ± 0.75 g respectively. In relation to group III, the results showed significant increase in the ratio and insignificant change in the heart weight. In relation to group IV, the result showed significant decrease in the heart weight and the ratio. In group VI, the mean ± SD of heart weight and heart weight / body weight ratio were 0.62 ± 0.07 and 4.7 ± 0.20 g respectively. As compared to group IV, the differences in the heart weight and the ratio significantly decreased. In relation to group V, the result showed significant decrease in the ratio and insignificant change in the heart weight. In group VII, the mean ± SD of heart weight and heart weight / body weight ratio were 0.49 ± 0.04 and 4.4 ± 0.22 g respectively. As compared to group IV, it was noticed that the difference in the heart weight and the ratio significantly decreased. In relation to group V, the results showed significant decrease in the ratio and insignificant change in the heart weight. As compared to group VI, it showed significant decrease in the heart weight without significant change in the ratio.

So, ISO showed elevation of heart weight/body weight ratio. GTE and/or metoprolol reduced the ratio. However, the effect of combination was better than the effect of GTE alone.
DISCUSSION

The present study showed valuable reduction in food consumption and body weight in the groups given green tea extract (GTE) as compared to other groups. The result showed reduction of body weight and food consumption in (GTE) group as compared to control group, (GTE + ISO) group as compared to ISO group or (ISO + metoprolol) group and (GTE + metoprolol + ISO) group as compared to ISO group or (ISO + metoprolol) group. The result was in agreement with Sayama et al. (2000) who observed that the mice given green tea in their diets had a significant suppression of food intake, body weight gain, and fat tissue accumulation.

Green tea demonstrated the ability to suppress appetite. The major appetite suppressant factor lies behind its effect on norepinephrine and dopamine. These catecholamines activate the sympathetic nervous system; one of the known effects includes a reduction in the desire for food. Epigallocatechin gallate (ECGC), one of the most active compounds in green tea, mediates this effect by inhibiting the breakdown of an enzyme that would normally break down the catecholamine (Kao et al., 2000).

Other mechanism by the body to manage appetite involves the production of cholecystokinin. This hormone, released in the intestines after the consumption of a meal, tells the brain that the body has received adequate amounts of food. The release of this hormone immediately reduces appetite. The consumption of green tea increases the release of CCK (Liao et al., 2001). Chantre and Lairon (2002) observed that administration of GTE to humans has been reported to decrease body weight and body fat. Also, Mandel et al. (2008) reported that the long term consumption of green tea and its extract have been associated with weight loss mainly through a thermogenic mechanism. The main active ingredients in GTE, i.e. catechins epigallocatechin gallate (EGCG, epigallocatechin (EGC), epicatechin gallate (EG), and epicatechin (EC) are responsible for many of the beneficial effects of green tea. Catechins influence metabolism in several ways, i.e. inhibiting intestinal lipases, decreasing fat absorption, increasing fat excretion, increasing uncoupling proteins, increasing thermogenesis, decreasing lipogenic enzymes and suppressing appetite (Klaus et al., 2005). Green tea prevents lipid absorption and stimulates energy consumption (Dulloo et al., 2000). Tea catechins can also provide modest shifts in metabolism that may improve weight loss and maintenance (Hursel et al., 2011).

Green tea extract has been shown to suppress the elevation of blood glucose during food intake and reduce the body weight. These mechanisms may be related to certain pathways such as modulations of energy balance, endocrine systems, food intake, lipid and carbohydrate metabolism, and redox status (Yang et al., 2001). Green tea extract have some
impact on increasing energy expenditure, perhaps through its catechin content. The mechanism for increasing energy expenditure is by inhibiting catecholamine-O-methyl transferase (COMT), an enzyme that degrades norepinephrine. The inhibition of COMT by catechins allows norepinephrine to exert a prolonged influence on thermogenesis and fat metabolism. Both of these metabolic processes are controlled by the sympathetic nervous system via norepinephrine. Most of the rise in metabolic rate is from increased fat oxidation, which would have the greatest impact upon decreasing body fat stores (Kao et al., 2000).

The present results showed valuable elevation in heart weight (HW) and heart weight / body weight ratio in ISO treated rats, as compared to control group. Our results were in harmony with those of Upaganlawar & Balaraman (2010) and Neha & Lubna (2014) who reported significant increase in heart weight and heart/ body weight ratio in ISO injected rat which indicate cardiac hypertrophy. Gayathri et al. (2002), Nirmala & Puvanakrishnan (2004) and Chauhan & Naik (2005) stated that rat injected with ISO S.C showed significant increase in heart weight accompanied by decrease in body weight. Li et al. (2012) observed a significant increase in the heart weight and the ratio of heart weight (HW) to body weight (BW) in ISO-induced rats. The increase in HW/BW ratio by ISO injection may be due to that ISO augmented the proliferation of non-contractile protein collagen in heart muscle (Kumar and Sharma, 2007). Relatively, short time period of administration of repeated low doses of isoproterenol induce cardiac hypertrophy (Kralova et al., 2008).

Busatto et al. (1999) stated that the cause of cardiac hypertrophy induced by isoproterenol by the increased local production of angiotensin II in the heart may make a significant contribution to the rapid development of cardiac hypertrophy in the presence of sympathetic hyperactivity. Nirmala & Puvanakrishnan (2004) and Patel et al. (2010) reported that the cardiac hypertrophy in rats after ISO injection may be due to ventricular stiffness, increased water content and extensive necrosis of cardiac muscle followed by invasion of the damaged tissues by inflammatory cells. Choudhary et al. (2006) revealed that increased generation of reactive oxygen species and oxidative stress is also implicated in the progression of cardiac hypertrophy and heart failure.

The present study showed that the prior administration of GTE to ISO- treated rats reduced the elevation of heart weight and heart weight/ body weight ratio which produced by ISO. Also, heart weight reduced, but the ratio was still higher when compared to GTE treated rats. GTE blocks the development of cardiac hypertrophy in an animal model of chronic renal failure. The administration of GTE results in attenuation of left ventricular hypertrophy, hypertension, and preserved cardiac Na-K-ATPase activity in rats subjected to remnant kidney surgery and prevents increases in reactive oxygen species (ROS) production (Li et al., 2013).

Prevention of cardiac remodeling due to increased pressure overload is important to reduce morbidity and
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mortality. Green tea extract prevents the development of left ventricular concentric hypertrophy by pressure overload. Cardiac hypertrophy can be induced by suprarenal transverse abdominal aortic constriction (AC) in rats. Experiment showed that after 3 weeks of AC surgery, heart to body weight ratio increased in the AC group by 34% compared to the sham group, while green tea extract administration suppressed the load-induced increase in heart weight by 69%. This suggests that increased left ventricular systolic dimensions and deteriorated systolic function were relieved by GTE (Hao et al., 2007). Green tea both prevents and reverses the cardiovascular remodeling and metabolic changes seen in high carbohydrate-fed rats. High carbohydrate diet-fed rats show glucose intolerance, hypertension and mild left ventricular hypertrophy. Administration of green tea to high carbohydrate diet-fed rats prevents and reverses glucose intolerance, increases systolic blood pressure, left ventricular wet weight, interstitial collagen and passive diastolic stiffness (Rickman et al., 2010).

The present study showed that the prior administration of metoprolol to ISO-treated rats reduced the elevation of HW and HW/BW ratio which were produced by ISO comparing to GTE group. The ratio decreased as a result of the effect of green tea on body weight without change in heart weight. The present study was in agreement with Hendawy et al. (2012) who observed that metoprolol significantly decreases the ventricular weight/body weight ratio. Mustonen et al. (2010) proved that metoprolol attenuates the elevated relative ventricular weight in a rat model of hypertensive cardiac hypertrophy. Mączewski and Mączewski (2008) reported that metoprolol and ivabradine similarly improve LV function, although metoprol prevents left ventricular dilation and hypertrophy in the post-infarction rat heart.

The attenuation of HW/BW after administration of metoprolol might be attributed to the reduction of collagen content in muscles due to the inhibitory effect of metoprolol on the concentration of hydroxyproline which plays an important role in collagen synthesis (Wei et al., 2000). Metoprolol directly inhibits the hypertrophic mediators including the adrenergic (Bristow, 1997), renin-angiotensin-aldosterone (Blumenfeld et al., 1999), and endothelin systems (Krum et al., 1996) as well as various inflammatory cytokines (Prabhu et al., 2000). In addition, Chan et al. (2011) found that chronic metoprolol treatment decreases the increased thoracic aortic wall thickness without affecting endothelium-dependent relaxation in the spontaneously hypertensive rats.

Prior administration of both GTE and metoprolol in combination to ISO rats reduced the elevated HW and HW/BW ratio produced by ISO. This indicated that they reduce the stimulus for hypertrophy. Comparing with group which pretreated with GTE alone, the ratio only decreased. Also, on comparing to group which pretreated with metoprolol alone, the heart weight only reduced. Thus, GTE or metoprolol has nearly the same ability to decrease the hypertrophy.

REFERENCES
1. Blumenfeld, J.D., Sealey, J. E., Mann, S. J., Bragat, A., Marion, R., Pecker, M. S. and...


عادل شلبى – محمد عكاشة – سعيد شرف – البيومي فودة
قسم الفسيولوجيا الطبية – كلية طب الأزهر

خلفية البحث: هناك زيادة في إدراك دور الأعشاب وتاثيرها على أمراض القلب. والشاي الأخضر كنبات طبي هام له تأثير قوي كمضاد للأكسدة.

الهدف من البحث: تقييم تأثير خلاصة الشاي الأخضر على إستهلاك الطعام ووزن الجسم في حالات الإحتشاء القلبي في ذكور الفئران البيضاء البالغة.

مواد وطرق البحث: استخدم في هذا البحث سبعون فأرا أبيضا بالغا من فصيلة محلية تتراوح أوزانها بين 110 – 130 جم (متوسط الوزن 120 جم). وقد تم إحداث الإحتشاء القلبي بالحقن بالأيزوبريناليل. وتم قياس الإستهلاك اليومي للطعام، ووزن الفئران في نهاية فترة التجربة (ثلاثين يوما). كما تم حساب نسبة وزن القلب إلى وزن الجسم في تلك الفئران.

النتائج: أحدث الأيزوبرينالين والمتوبروالول زيادة في إستهلاك الطعام بنسبة متوازية مع زيادة وزن الجسم، بينما أحدثت خلاصة الشاي الأخضر نقصا في إستهلاك الطعام وكذلك وزن الجسم.

الاستنتاج: خلاصة الشاي الأخضر ذات فعالية في نقص إستهلاك الطعام وفي وزن الجسم بنسبة متساوية.