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Effect of Dietary *Garcinia cambogia* Extract on Serum Essential Minerals (Calcium, Phosphorus, Magnesium) and Trace Elements (Iron, Copper, Zinc) in Rats Fed with High-Lipid Diet

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Abstract The aim of the study was to investigate the effect of *Garcinia cambogia* extract on serum calcium (Ca), phosphorus (P), magnesium (Mg), iron (Fe), zinc (Zn) and copper (Cu) concentrations in rats fed with the normal or the high-lipid and -cholesterol diet. Thirty 1-year-old female Sprague–Dawley rats (pathogen-free), weighing an average of 229 g, were randomly assigned to three experimental groups of ten animals each. Diets and tap water were given ad libitum for 75 days. Group 1 (control group) was fed with basal diet (2 % liquid vegetable oil, 0 % cholesterol), while the diets of groups 2 and 3 contained vegetable oil (2 % liquid vegetable oil and 5 % hydrogenated vegetable oil) and cholesterol (3 %) in high levels. 4,5 % *G. cambogia* extract containing 65 % HCA was added to the diet of group 3 as from day 45. Blood samples were withdrawn on days 0, 45 and 75. Serum mineral levels were analyzed using standard enzymatic colorimetric methods with a spectrophotometer. All significant differences were $p < 0.05$. Serum Ca levels were not significantly different between all groups on days 45 and 75. Serum P level was significantly higher in the group fed with high-lipid diet and *G. cambogia* extract than in the control group on day 45. Serum Mg level was significantly higher in group 2 than in the control group on day 45. Serum Fe levels were significantly lower in the control group than in the other groups on days 45 and 75. Serum Zn level of the group fed with high-lipid diet and *G. cambogia* extract was significantly higher than in the control group on day 75. Serum Cu levels were significantly higher in group 2 than in the control group, and in group 3 than in group 2 on day 75. In conclusion, a diet containing the high fat amounts may lead to the increase in circular levels of some minerals due to the short-chain fatty acid production lowering the luminal pH which increases mineral solubility, or serving as a fuel for mucosal cells and stimulating cell proliferation in the large intestine. *G. cambogia* extract may be used in the P and Cu deficiencies due to increases resulting in the present P and Cu amounts in *G. cambogia* extract, or the use of phytate P in diet. It was hoped that with further evidence-based study this product will enter to mainstream medicines.

Keywords *Garcinia cambogia* · High-lipid diet · Serum mineral

Introduction

The body requires a number of minerals in order to maintain good health [1]. A number of minerals essential to nutrition are accumulated in different parts of plants [2]. Plants are known to supply the needed vitamins, iron (Fe), calcium (Ca), magnesium (Mg), and others important for health, and they are the most affordable source of minerals and vitamins [3]. Mg works with Ca to maintain healthy bones. Ca is needed for bone growth and muscle contraction and in blood clotting. Ca is also very important in the maintenance of a healthy heart [1]. Zinc (Zn) is an essential trace element playing a vital role in several physiological processes, including cell division and

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growth, and fetal and brain development. It is also essential in the composition or function of over 70 enzymes involved in digestion and other major metabolic functions. It is a cofactor for alkaline phosphatase that has been implicated in bone formation and mineralization [4]. Deficiency of this element, although not completely assessed, is believed to be as widespread as that of Fe and is a cause for concern especially in the developing countries [5]. Fe is an essential trace element whose biological importance arises from its involvement in vital metabolic functions by being an intrinsic component of hemoglobin, myoglobin, and cytochromes. Despite large-scale intervention programs, Fe-deficiency anemia remains the most widely prevalent nutritional problem in the world [6].

The knowledge of minerals and trace elements in natural products is highly important. Fruits and vegetables are the main external source of these nutrients for animals and humans alike [6]. Tropical fruit trees are rich in xanthones which have potent antioxidative, anti-inflammatory, antibacterial and various other bioactivities enriched with multivitamins, essential minerals, catechins and polysaccharides [7]. *Garcinia cambogia*, a tropical plant native to Southeast Asia, is one such plant [8]. Lewis and Neelakantan [9] isolated the principal acid in the fruit rinds of *G. cambogia* and identified it as (−)-hydroxycitric acid (HCA). Commercial samples of *G. cambogia* extracts contain Ca salt of HCA to preserve stability [9]. *Garcinia mangostana* contains fibers, important phenolic acids (caffeic, *p*-coumaric, cinnamic, and vanillic), flavonoids (quercetin, morin, myricitin, apigenin, and campherol), minerals, trace elements, and vitamins. Nwokocha et al. [10] reported that the active components of *Garcinia kola* inhibited the cellular redox mechanisms and membrane protein activities which are caused by heavy metals in the liver while also enhancing drug-detoxifying enzymes, and that *G. kola* offers more protection in acute exposure to heavy metals and aids greater elimination of heavy metals than if it is administered together with heavy metal.

Many plants have been used as raw materials in drug development [11]. Although several supplements hold promise, more high-quality clinical research is needed to confirm current findings and provide additional information on efficacy and safety [12]. The use of fruits in disease-preventing diets and the results of the studied exotic fruits are interesting and important [13]. For these fruits to be included in disease-preventing diets, the contents of their bioactive compounds and their antioxidant activities have to be relatively high. Until now, some of these fruits were not investigated enough, *G. cambogia* was among them. The nutritional values of exotic fruits, especially *G. cambogia*, and their influence on serum essential minerals and trace elements are almost not known. Therefore, the aim of this study was to investigate the effect of *G. cambogia* extract on serum Ca, phosphorus (P), Mg, Fe, zinc (Zn), and copper (Cu) concentrations in rats fed with the high-lipid and -cholesterol diets.

Materials and Methods

This study was approved by the Ethical Committee of Istanbul University Faculty of Veterinary Medicine (no. 2006-181). Thirty 1-year-old female Sprague–Dawley rats (pathogen-free), weighing an average of 229 g, were housed individually in standard cages (33×23×12 cm) under controlled conditions of temperature, lighting, and humidity. Rats were randomly assigned to three experimental groups of ten animals each. Diets and tap water were given ad libitum for 75 days.

G. cambogia rind fruit extract was provided by General Nutrition Products, Inc., SC, USA. After 1 week of adaptation to housing conditions, group 1 (control group) was fed with basal diet (2 % liquid vegetable oil, 0 % cholesterol), while the diets of groups 2 and 3 contained vegetable oil (2 % liquid vegetable oil and 5 % hydrogenated vegetable oil) and cholesterol (3 %) in high levels. 4,5 % (*w*/*w*) *G. cambogia* extract containing 65 % HCA was added to the diet of group 3 as from day 45. The level of *G. cambogia* extract added to the diet of Group 3 was determined according to Leonhardt et al. [14, 15]. The trial period was 75 days. Composition and calculation of nutrients in diets are indicated in Table 1.

Blood samples were withdrawn on days 0, 45, and 75. They were taken by coccygeal venipuncture after animals were fasted overnight and anesthetized with diethyl ether. Sera were separated by centrifugation at 2,700×*g* for 15 min and stored at −80 °C until analysis.

Table 1 Composition and calculation of nutrients in diets

	Group 1	Group 2	Group 3
Composition of nutrients (%)			
Cracked barley	23	11	5.5
Cracked wheat	42.5	42.5	52.5
Rasmol	15	15	5
Soybean meal	14.5	17.5	17.5
Fish meal	2	3	4
Liquid vegetable oil	2	2	2
Vitamin–mineral mixture	1	1	1
Cholesterol	–	3	3
Hydrogenated vegetable oil	–	5	5
Garcinia cambogia extract	–	–	4.5
Calculation of nutrients			
Metabolizable energy (MJ/kg)	12.5	13.7	13.7
Crude protein (%)	19.5	19.5	19.5

Vitamin–mineral mixture, in kilograms: Vitamin A 12.000 IU, Vitamin D_3 1.500 IU, Vitamin E 104 IU, Vitamin K 15 mg, Vitamin B_1 14 mg, Vitamin B_2 11 mg, Vitamin B_6 14 mg, Vitamin B_{12} 20 mg, Folic acid 2.5 mg, Nicotinic acid 78 mg, Pantothenic acid 26 mg, Biotin 334 mcg, Choline chloride 1,635 mg, Selenium 0.36 mg, Cobalt 0.46 mg, Iodine 1.41 mg, Zinc 95 mg, Manganese 68 mg, Copper 20 mg, Iron 104 mg

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Serum Ca, P, Mg, and Fe levels were determined using commercially available spectrophotometric kits (BSM (Bioscience Medical) c/Velazquez, 28006 Madrid, Spain) and also serum Zn and Cu levels were determined using commercially available spectrophotometric kits (LTA s.r.l., Via Milano-20060 Bussero, Milano, Italy) by standard colorimetric enzymatic methods.

Data were compared using analysis of variance (Duncan's multiple range test) between groups within each blood sampling week for all blood minerals. Results are presented as mean±standard deviation. All statistical analyses were performed using software package program (SPSS for Windows, Standard version 10.0, 1999, SPSS Inc., Headquarters, Chicago, IL, USA). A significance level of $p<0.05$ was employed in the analysis of data from groups.

Results

The values for blood constituents are shown in Table 2. All examined serum mineral and element levels were not significantly different between groups on day 0.

Serum Ca levels were not significantly different between all groups on days 45 and 75. Serum P level was significantly higher in the group fed with high-lipid diet and *G. cambogia* extract (group 3) than in the control group on day 45 ($p<0.05$). The levels were not significantly different between groups 1 and 2, and groups 2 and 3 on the same day. Serum P levels were significantly higher in the group fed with high-lipid diet and *G. cambogia* extract (group 3) than in groups 1 and 2 on day 75. There was no significant difference between groups 1 and 2 on the same day.

Serum Mg level was significantly higher in group 2 than in the control group on day 45 ($p<0.05$). The levels were not significantly different between groups 1 and 3, and groups 2 and 3 on the same day. Serum Mg levels were not significantly different between all groups on day 75. Serum Fe levels were significantly lower in the control group than in the other groups on days 45 and 75. The levels were not significantly different between groups 2 and 3 on the same days.

Serum Zn levels were not significantly different between all groups on day 45. The level of the group fed with high-lipid diet and *G. cambogia* extract (group 3) was significantly higher than in the control group (group 1) on day 75. However, there was no significant difference between groups 2 and 3 on the same day for serum Zn level. Serum Cu level was significantly higher in the group fed with high-lipid diet and *G. cambogia* extract (group 3) than in the control group on day 45 ($p<0.05$). The levels were not significantly different between groups 1 and 2, and groups 2 and 3 on the same day. Serum Cu levels were significantly higher in group 2 than in the control group, and in group 3 than in group 2 on day 75 ($p<0.05$).

Table 2 Serum calcium, phosphorus, magnesium, iron, zinc, and copper levels in female rats fed atherogenic diet and *Garcinia cambogia* extract

	Day 0	Day 45	Day 75
Calcium (mg/dl)			
Group 1	8.92±1.72	9.99±1.96	9.30±0.84
Group 2	9.41±2.08	10.6±1.60	10.6±2.66
Group 3	9.64±0.95 ^{A}	11.0±1.45 ^{B}	10.8±1.39 ^{B}
Phosphorus (mg/dl)			
Group 1	4.06±0.68	5.35±1.38 ^{a}	5.48±0.88 ^{a}
Group 2	3.51±1.19 ^{A}	7.47±3.60 $^{ab, B}$	7.23±2.68 $^{a, B}$
Group 3	4.37±1.17 ^{A}	9.20±4.92 $^{b, B}$	13.5±4.76 $^{b, C}$
Magnesium (mg/dl)			
Group 1	1.94±0.57	2.31±0.84 ^{a}	2.59±0.58
Group 2	2.21±0.45 ^{A}	3.20±1.22 $^{b, B}$	2.65±1.00 ^{AB}
Group 3	2.11±0.30 ^{A}	2.58±0.53 $^{ab, B}$	2.50±0.21 ^{B}
Iron (μg/dl)			
Group 1	464±203	421±143 ^{a}	326±154 ^{a}
Group 2	413±158 ^{A}	713±309 $^{b, B}$	631±355 $^{b, B}$
Group 3	442±126 ^{A}	831±278 $^{b, B}$	841±355 $^{b, B}$
Zinc (μg/dl)			
Group 1	214±105	244±129	213±107 ^{a}
Group 2	149±86.0	227±134	250±101 ^{ab}
Group 3	237±112	272±129	342±92.9 ^{b}
Copper (μg/dl)			
Group 1	207±39.3	284±202 ^{a}	207±81.0 ^{a}
Group 2	245±93.9 ^{A}	448±167 $^{ab, B}$	546±262 $^{b, B}$
Group 3	189±42.7 ^{A}	621±225 $^{b, B}$	1,032±272 $^{c, C}$

Mean±standard deviation, $n=10$. Different lowercase letters indicate significant differences within columns (the comparisons between groups) ($p<0.05$). Different uppercase letters indicate significant differences within lines (the comparisons between days) ($p<0.05$)

Group 1 control group, *Group 2* group fed with high-lipid diet, *Group 3* group fed with high-lipid diet and *Garcinia cambogia* extract

Discussion

Garcinia is a natural weight loss product containing the active ingredient HCA. This substance inhibits the enzyme adenosine triphosphate–citrate–lyase and theoretically plays a role in inhibition of the synthesis of lipids and a reduction in body fat leading to weight loss [16]. HCA has been reported to increase serotonin availability [17], reduce appetite and body weight, increase fat oxidation, and improve blood lipid concentrations [18].

The use of Mg supplementation has been suggested to improve glucose metabolism by increasing the release of insulin [19]. American Diabetes Association [19] reported

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that the deficiency of Mg seems to be associated with an increase in insulin resistance. Corsonello et al. [20] noted that serum Mg levels were reduced in diabetic patients compared with controls and showed a negative correlation with plasma HbA_{1c} and triglycerides. A low ratio of intracellular Mg to intracellular Ca has been implicated as a precipitating factor in metabolic syndrome and Mg supplementation at a dose of 1 to 2 g in divided doses daily has been recommended [21]. Chausmer [22] noted that insulin-dependent patients were deficient in Zn and that Zn supplementation may be helpful in controlling blood sugar levels in patients with insulin-dependent diabetes mellitus in doses of 15 to 25 mg/day.

Dietary lipids have strong effects on mineral absorption and bioavailability, and dietary lipid composition plays an important role in skeletal biology and bone health [23]. The changes in mineral bioavailability may be influenced by dietary lipid composition, and the changes in the level of unsaturation and acyl chain length in intestinal cell membranes may result in increased intestinal mineral absorption by altering membrane fluidity and function [24]. Dietary supplementation with polyunsaturated fatty acids improves Ca balance and bone Ca content in animal and human studies [23]. Consumption of fish oil rich in ω-3 polyunsaturated fatty acids can affect Fe homeostasis by enhancing membrane lipid peroxidation. This indirectly influences intestinal Fe absorption and liver Fe stores [25].

Lobo et al. [26] reported that the apparent mineral absorption was improved by dietary combination with fish oil, and Cu absorption was positively affected when in combination with fish oil. Mineo et al. [27] reported that the luminal presence of short-chain fatty acids increased the transepithelial Ca transport in rat cecum and colon. Mollard and Weiler [28] noted that dietary arachidonic acid and docosahexanoic acid elevated femur Ca and reduced Zn content in piglets. However, Xiao et al. [29] indicated that high-fat diet caused significant decreases in apparent Ca absorption and retention, and suggested that administration of high-fat diet produces excessive reactive oxygen species and changes redox balance into an oxidation state of the duodenum affecting the expression of the genes involved in Ca absorption, thus resulting in inhibitory effects on intestinal Ca absorption. In the present study, female rats were preferred because females are more tended to obesity than males due to estrogen hormone. In the present study, the fatty feeding significantly increased serum Fe and Mg levels, and no significantly increased serum P and Cu levels. These findings are similar to the findings of Miret et al. [25] and Lobo et al. [26].

Some ideas have been suggested in relation to the increasing the absorption and serum levels of minerals of fatty feeding. Stubbs and Smith [24] suggested that the effect of fatty acids on mineral absorption might be exerted directly on mineral uptake or indirectly by altering the fatty acid composition of the intestinal brush border membrane, which in turn modifies membrane properties and function. Moreover, Lopez et al. [30] had reported that short-chain fatty acid production (mainly acetate, propionate, and butyrate) in the large intestine lowers the luminal pH which increases mineral solubility and which raises the mineral gradient between the luminal and serosal side allowing passive mineral transport to increase, and that short-chain fatty acids, especially butyrate, serve as a fuel for mucosal cells and stimulate cell proliferation which in turn could increase the absorptive surface area of the large intestine.

Monago and Akhidue [31] noted that *G. kola* contains oxalates and tannins which have also been reported to form chelates with divalent metals at certain concentrations. Burdock et al. [32] reported that, typically, dietary supplements containing HCA consist of various salts, including HCA-sodium, -Ca, -potassium, -Mg, or combinations thereof. A diet containing *G. mangostana* seeds will help to prevent deficiency of Mg and Ca since the seeds are rich in these minerals [1].

Ajayi et al. [1] determined that *G. mangostana* seeds had Mg 8,650 mg/kg and Ca 454 mg/kg, other minerals present in the seeds were manganese, Fe and Zn. Also, the Fe content of *G. mangostana* seed, 90.0 mg/kg, was found higher than those of *Cicer arietinum*, 60.0 mg/kg; *Phaseobus mango*, 41.0 mg/kg; and *Phaseobus aureus* 30.0 mg/kg. Haruenkit et al. [6] determined that *G. mangostana* fruit had Mg 13.2 mg/100 g fresh weight (FW), Ca 12.3 mg/100 g FW, Fe 512.6 mg/100 g FW, Zn 31.6 mg/100 g FW and Cu 8.7 mg/100 g FW. Authors [6] also reported that the mineral and trace element contents of fruits may change because of the geographical regions, climatic conditions, cultivars, and levels of maturity. Unfortunately, we could not find the mineral and trace element data of *G. cambogia* which is one of the *Garcinia* species.

Citric acid is an analog of HCA. Supplementation of P-deficient corn–soybean meal diets with compounds such as citric acid have been shown to increase phytate P use in chicks [33]. Snow et al. [34] reported that citric acid increases phytate P use by chicks. Similarly, Angel et al. [35] stated that 3 % citric acid released 0.035 % P in broilers and 0.031 % P in turkeys fed corn–soybean meal diets. In the present study, the feeding with high-lipid diet and *G. cambogia* extract significantly increased serum P and Cu levels. These increases are in agreement with Boling-Frankenbach et al. [33], Snow et al. [34], and Angel et al. [35], and could be arose from the present P and Cu amounts in *G. cambogia* extract [1] or from HCA increasing the use of phytate P in diet. It was impossible to find the serum mineral and trace element data for comparison of *G. cambogia* that was investigated in this study.

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Conclusions

A diet containing the high fat amounts may lead to the increase in circular levels of some minerals due to the short-chain fatty acid production lowering the luminal pH which increases mineral solubility, or serving as a fuel for mucosal cells and stimulating cell proliferation in the large intestine. *G. cambogia* extract may be used in the P and Cu deficiencies due to increases resulting in the present P and Cu amounts in *G. cambogia* extract, or the use of phytate P in diet. It was hoped that with further evidence-based study, this product will enter to mainstream medicines.

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