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Revisión

The effect of *Garcinia Cambogia* as coadjuvant in the weight loss process

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Abstract

Introduction: **due to the significant increase in the obesity rate in recent years, public health has been facing in many countries of the world, one of the major problems caused by this disease. Because of this, natural products arise, herbal, to assist in the treatment of obesity due to their safer effects. Among these, stands out the extract obtained from dried fruits of *Garcinia Cambogia* (GC), which has been studied and used as a natural supplement for weight loss.**

Objective: **to investigate the GC administration as a coadjuvant factor in the treatment of obesity regarding to its effectiveness, way of action, recommended daily amount, side effects and contraindications, as a way of food and nutritional security for the population.**

Methodology: **literature review. There were consulted the database of LILACS-BIREME data, SciELO and MEDLINE and there were selected scientific articles published in English, Portuguese and Spanish, between the period of 2007 and 2014 that conducted studies involving the administration of the GC as a way of treatment for obesity. The descriptors used for research articles in the databases were the following: *Garcinia Cambogia* in Portuguese, and in English the terms used were "*Garcinia Cambogia*", "weight loss and obesity", and "Hydroxycitric Acid (HCA)"; this last one is not a descriptor indexed in Decs, but given the importance of this term for the search, it was adopted as a keyword. Thirty-four articles were identified, but only 21 were related to the objectives of this study. The first analysis of the articles was conducted by the title and then by the summary. In addition, 17 references were included because of their relevance to the study.**

Results: **in some analyzed works, there was observed that the GC showed positive effects on weight loss process, appetite reduction, body fat percentage, triglycerides, cholesterol and glucose levels, lipogenesis process, while others had no effect.**

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EL EFECTO DE LA *GARCINIA CAMBOGIA* COMO COADYUVANTE EN EL PROCESO DE PERDIDA DE PESO

Resumen

Introducción: **debido al aumento significativo de la tasa de obesidad en los últimos años, la salud pública se ha enfrentado en muchos países del mundo a los principales problemas causados por esta enfermedad. Debido a ello, surgen productos naturales, a base de hierbas, para ayudar en el tratamiento de la obesidad debido a sus efectos más seguros. Entre estos productos destaca el extracto obtenido a partir de frutas secas de *Garcinia Cambogia* (GC), que se ha estudiado y utilizado como un suplemento natural para la pérdida de peso.**

Objetivo: **investigar la administración de GC como un factor coadyuvante en el tratamiento de la obesidad en cuanto a su eficacia, la forma de acción, la cantidad diaria recomendada, los efectos secundarios y las contraindicaciones, para su uso como un suplemento alimentario natural en la pérdida de peso.**

Metodología: **revisión de la literatura. Se consultaron las bases de datos LILACS-BIREME, SciELO y MEDLINE, y se seleccionaron los artículos científicos publicados en inglés, portugués y español, entre el período de 2007 y 2014, llevando a cabo estudios sobre la administración de la GC como una forma de tratamiento de la obesidad. Los descriptores utilizados para los artículos de investigación fueron: en portugués *Cambogia Garcinia,* y en inglés *"Garcinia Cambogia",* "pérdida de peso y obesidad", y "ácido hidroxicítrico (HCA)"; este último no es un descriptor indexado en Decs, pero dada la importancia de este término para la búsqueda, se adoptó como una palabra clave. Se identificaron treinta y cuatro artículos, pero solo 21 estaban relacionados con los objetivos de este estudio. El primer análisis de los artículos fue realizada por el título y luego por el resumen. Además, se incluyeron 17 referencias por su relevancia para el estudio.**

Resultados: **en algunos trabajos analizados se observó que GC mostró efectos positivos en el proceso de pérdida de peso, reducción de apetito, porcentaje de grasa corporal, triglicéridos, niveles de colesterol y glucosa y proceso de lipogénesis; mientras que en otros no produjo ningún efecto.**

Conclusion: **studies suggest positive results about the effectiveness of the GC on the weight loss process. However, the ideal dosage has not been well established yet. There is little evidence of adverse effects and signs of protective effect against hepatotoxicity induced by ethanol. Therefore, it becomes necessary to carry out further studies to confirm the efficacy of this phytotherapy in the weight loss process.**

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Key words: *Obesity. Public health. Garcinia Cambogia. Weight loss.*

Conclusión: **los estudios sugieren resultados positivos con respecto a la eficacia de la GC en el proceso de pérdida de peso. Sin embargo, la dosis ideal no ha sido aún bien establecido. Hay poca evidencia de efectos adversos y signos de efecto protector contra la hepatotoxicidad inducida por el etanol. Por lo tanto, se hace necesario llevar a cabo más estudios para confirmar la eficacia de esta fitoterapia en el proceso de pérdida de peso.**

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Palabras clave: *Obesidad. Salud pública. Garcinia Cambogia. Pérdida de peso.*

Abbreviations

ABESO: Brazilian Association for the Study of Obesity and Metabolic Syndrome.
ANVISA: National Health Surveillance Agency.
FCN: Federal Council of Nutritionists.
TC: Total Cholesterol.
DNL: De novo lipogenesis.
EGML: Glycine max leaves extract.
GC: Garcinia Cambogia.
GCE: Garcinia Cambogia extract.
M: Men.
CHO: Carbohydrates.
HCA: Hydroxycitric acid.
HDL-c: High Density Lipoprotein.
HFD: High-Fat Diet.
HSD: High Sucrose Diet.
BMI: Body Mass Index.
LDL: Low Density Lipoprotein.
LIP: Lipids.
W: Women.
MDA: Malondialdehyde.
MoH: Ministry of Health.
WHO: World Health Organization.
BW: Body Weight.
PROT: Proteins.
TG: Triglycerides.
VIGITEL: Telephone-based Surveillance of Risk and Protective Factors for Chronic Diseases.

Introduction

The World Health Organization (WHO) classifies obesity as an epidemic resulting from the imbalance between intake and energy expenditure, as a consequence of a sedentary lifestyle and poor eating habits[1,2,3], as well as the socio demographic conditions[4]. This disease constitutes a significant global health problem that attacks adults and children and affects a worldwide, growing number of people[5]. It is characterized as a chronic disease caused by excessive accumulation of body fat resulting in significant loss of quality of life and longevity. It occurs in developed and developing countries[3,6], and it has the involvement of a complex interaction of environmental and genetic factors, besides being associated to morbidity and mortality related to heart attack, high blood pressure, diabetes and even cancer[7,8]. Consequently, obesity is a public health problem that requires attention and multisectoral actions to promote a healthy lifestyle and improve the prevention and its control among population[4,9].

The Ministry of Health (MoH), through Vigitel (Telephone-based Surveillance of Risk and Protective Factors for Chronic Diseases)[10], in 2013, revealed overweight in 51% of the Brazilian population; men are the majority. In 2006, this percentage was 43%, a fact that shows that the obesity rate has been growing in the country. In 2012, ABESO (Brazilian Association for the Study of Obesity and Metabolic Syndrome)[11] released the report "World Health Statistics 2012" of WHO revealing that obesity is the death cause of 2.8 million of people per year and that 12% of the world population is considered obese, and the American continent has the highest incidence of the disease.

Since obesity is reaching epidemic proportions, its effective management is an important clinical problem. Despite scientific efforts to understand the mechanisms that lead to overconsumption of food and overweight, at the moment, few weight management approaches are effective in a long-term[12].

Therapeutic strategies to treat obesity include synthetic drugs and surgery, which can result in high costs and serious complications. Medicinal agents, herbal products, offer an alternative approach to manage weight, in combating obesity and co-morbidities associated resulting in a safer and more efficient treatment without risks to health[2,13], due to their fewer side effects compared to synthetic drugs[3]. Thus, the phytotherapic represent a new potential coadjuvant or alternative therapy for the treatment of obesity[14] and have frequently been used to promote weight loss[15].

These agents act through five basic mechanisms, including the stimulation of thermogenesis, reduction of lipogenesis, increase of lipolysis, appetite suppression and decrease of lipids absorption[13]. Currently, the term "thermogenic - fat burner" has been used to describe nutritional supplements that promote, somehow, the

fat metabolism by increasing energy expenditure, fat burning, weight loss, lipid oxidation during the exercise[16].

The probable reasons for obese people prefer herbal products for weight control include healthy weight loss without any side effects; lower demanding in lifestyle changes such as diet and exercise; ease of acquisition, available without a prescription; more easily accepted than a professional consultation with a doctor or a nutritionist; 100% natural with the perception that natural means safe[7].

For these reasons, people in all countries have been using herbal medicines for weight control and treatment of obesity[1,6,8]. But despite these substances promise to improve or prevent the obesity, costs, effectiveness and side effects have to be considered and, for these reasons, they must be studied intensively[1,2].

Among the natural supplements, herbals for the treatment of obesity, stands out the natural extract obtained from dried fruit of the tree *Garcinia cambogia* (GC), which is found in the forests of South India and South Asia, has been studied extensively and used as a supplement for weight loss[1,2,6,8,17].

The hydroxyl citric acid or hydroxycitric acid (HCA) is extracted from the rind of the fruit. It is an organic acid considered the main active ingredient, which acts as a potential supplement to the weight control[3,17,18,19] by causing the appetite suppression and reducing the body's ability to form adipose tissue[3]. Besides acting as a phytotherapic coadjuvant for the treatment of obesity, the GC extract and its active component HCA have also been used to reduce cholesterol and triglycerides. It is also available with addition of calcium, magnesium, potassium and mixtures thereof due to other effects, such as improvement of glucose tolerance and of blood pressure[20,21].

Unlike chemical stimulants used for weight loss, it does not act on the central nervous system and does not cause insomnia, nervousness, changes in blood pressure or heart rate and its efficiency does not decrease along the time[17,21]. This way, the GC extract is quickly becoming a popular ingredient among many supplements for weight loss and has been used routinely for many centuries for not showing toxic effects[3].

The evaluation of its toxicity to the weight control is extremely important, as it requires a continuous consumption in the long term in order to maintain its effects[8]. Currently, the GC is being released by the National Health Surveillance Agency (ANVISA) and has been indicated as a coadjunct of overweight for participating in the regulation of appetite[22], but the sale can only be made under a medical prescription.

The Resolution of the Federal Council of Nutritionists (FCN) of Brazil nr.390/2006[23] regulates the dietary prescription of nutritional supplements by the nutritionist and determines that it can be done based on the nutritional diagnosis in the following cases: I. specific physiological states; II. pathological conditions; III. metabolic changes, and the prescription of nutritional supplements should still be based on the following premises: I. food consumption adequacy; II. definition of the period of supplementation use; III. systematic re-evaluation of the nutritional status and of the dietary plan.

Due to the large supply in the market, marketing and popular use of herbal medicines, such as GC to act as a coadjuvant in treatments for obesity, this study aimed to deepen the scientific evidence on the effects of GC administration as a coadjuvant factor in the treatment of obesity regarding to its effectiveness, form of action, recommended daily dosage, side effects and contraindications, as a way of food and nutritional security for the population.

Methodology

Literature review study for which there were consulted the LILACS-BIREME, MEDLINE and SciELO databases and selected scientific articles published in English, Portuguese and Spanish, between the period of 2007 and 2014 that conducted studies involving the administration of GC as a way of treatment for obesity. The descriptors used for research articles in the databases were the following: Garcínia Cambogia in Portuguese, and in English the terms used were "*Garcinia cambogia*", "weight loss and obesity" and "Hydroxycitric Acid (HCA)"; this latter is not an indexed descriptor in the Health Science Descriptors (DeCS), but given the importance of this term for the search, it was adopted as a keyword. Thirty-four articles were identified, but only 21 were related to the objectives of this study. The first analysis of the articles was conducted by the title and then by the summary. In addition, 20 references were included because of their relevance to the study.

Results

Table I shows the main results of non-randomized studies with supplementation of GC/HCA and table II presents the main results of randomized studies with supplementation of GC/HCA.

Discussion

Due to the dramatic increase of the number of obesity cases in recent years, this disease has become one of the most important problems that public health has faced in several countries around the world, nowadays. In view of this, several methods to assist weight loss have arisen, like miracle diets and dietary supplements, but, often, little is known about the regular use and long-term of certain substances.

According to Kimet *et al*.[24], GC is a popular supplement for weight loss. Studies suggest that the use of

Table I
Main results of non-randomized studies with supplementation of ***Garcinia cambogia****/HCA*

Duration of the study	*Participants*	*Treatment*	*Result*	*References*
16 weeks	20 rats divided in two groups of 10	Group 1: HFD (45% LIP, 20% PROT e 35% HC) without supplementation; Group 2: HFD + supplementation of GC (1%, kg/weight)	GC protected against obesity induced by HFD through the modulation of the synthesis of fatty acids and β-oxidation, but induced hepatic fibrosis, inflammation and oxidative stress.	[24]
12 weeks: 1st to 8th week (period of induction); 8th to 12th (period of treatment)	32 rats divided in three groups: group 1 (8 rats), group 2 (8 rats) and group 3 (16 rats)	Group 1: control (normal diet during the whole study); Group 2: HFD (35% LIP) until the 8th week, subdivided in two groups from the 8th to the 12nd week: one group with GC 50mg/day + HFD and other with HFD; Group 3: HSD (65% of sucrose) until the 8th week, subdivided in two groups from the 8th to the 12nd week: one group with GC 50 mg/day + HSD and other with HSD.	The HFD and HSD groups showed a significant increase in feed intake, BW, BMI, TG, LDL, oxidative stress and renal disorder, while the groups supplemented with GC showed improvement of the harmful effects of HFD and HSD diets, with consequent reduction of feed intake, increase of the MDA level and decreased oxidative stress in renal tissue.	[25]
10 weeks	30 rats divided in three groups of equal numbers	Group 1: control (basal diet 2% of liquid vegetable oil and 0% of cholesterol); Groups 2 and 3: diets 2% of liquid vegetable oil, 5% of hydrogenated vegetable oil and 3% of cholesterol. Group 3 received 2390 mg/day of GC from day 45 on.	The supplementation of the GC HFD failed to reduce the rising levels of serum lipids.	[26]
16 weeks	C57BL/6J mice prone to obesity	Mice were fed with HFD (45% LIP) with and without CG (1% kg/weight).	High intakes of HCA alone did not lead to signs of inflammation or hepatotoxicity.	[20]

*HFD = High Fat Diet; LIP = Lipids, PROT = Proteins, CHO = Carbohydrates, GC = Garcinia *Cambogia*, HSD = High Sucrose Diet; BW = Body Weight; BMI = Body Mass Index, TG = Triglycerides, LDL = Low-Density Lipoprotein, MDA = Malondialdehyde (a marker for oxidative stress); HCA = Hydroxycitric Acid.

GC stimulates the burning of body fat, helps to inhibit appetite by reducing the desire to eat with a consequent reduction in food intake, and promotes satiety, and also acts in weight maintenance.

Being a study that aims the GC administration as a coadjuvant in the treatment of weight reduction, it can provide important information for both scientific uses as for the general population about the effects of its administration as a way to help in the treatment of obesity.

Effectiveness and way of acting

In the analysis of the effectiveness of GC, the study of Kovacs and Westertep-Plantenga[28] concluded, in an experimental condition in humans, that the treatment with HCA during overfeeding with CHO can reduce the DNL. In rats, Kim *et al*.[24] verified that the supplementation of this herbal medicine helped to reduce the body fat, but not to decrease weight or appetite. Although, in humans, Kim *et al*.[15] observed that the GC supplementation did not reduce the percentage of body fat, as it did not act on the decrease of appetite, BW, BMI and waist-hip ratio (WHR). Murer[2] concluded that individuals with and without GC supplementation showed reduction of body fat and emphasized that the combination of diet and physical activity still remains the most suitable for positive changes of body composition.

The experiment of Anton *et al*.[14] in humans also did not observe significant effects with the administration of GC dosages on food intake, satiety, weight loss, and oxidative stress levels. They highlighted that further research is needed to explore the promising effects of herbal medicines on food intake and satiety levels. However, they chose the compound derived from GC for their study because they noted in the literature its potential in acting in the reduction of food intake, in BW and in the levels of oxidative stress with safety, affecting the neuroendocrine pathways related to satiety.

Lira-García *et al*.[29], in their review study with among sixteen assessed studies, found only one study that demonstrated significant weight loss between the control group and the experimental group with dosage of 1200 mg/day of GC and concluded that it was not possible to prove the effectiveness of the alternative products for weight loss because there is not enough

Table I
*Main results of randomized studies with **Garcinia Cambogia** supplementation/HCA*

Duration of the study	*Participants*	*Treatment*	*Result*	*References*
10 weeks	86 subjects (46 M and 40 W) ranging from 20 to 50 years old, overweight (BMI> 23 and <29) randomly divided into three groups.	Group 1: use of pills with Glycinemax extract (EGML 2 g/day); Group 2: Intake of GC extract (GCE 2 g/day) Group 3: placebo (starch 2 g/day).	EGML and GCE did not promote BW loss neither decreased the TC in overweight individuals consuming usual diet. EGML increased levels of HDL-C. There were no serious adverse effects reported by the intake of EGML, GCE or placebo (starch).	[15]
18 weeks	48 W postmenopausal, healthy, normal biochemical exams, between 50 and 70 years, BMI between 25 and 39.9 divided into three groups.	Group 1: 2800 mg/day GC; Group 2: 5600 mg/day of GC; Group 3: Control (placebo = 12 capsules totaling 4080 mg/day palm oil).	No significant effects were observed with the administration of the GC dosages or adverse effect level (NOAEL) in humans at doses of 4000mg/day.	[14]
1 week	8 healthy men aged 22+ 0.3 years.	After 60 min of cycling exercise at 70-75% VO_{2max} received 500mg of HCA with a meal high in (CHO 80%, 8% LIP, 12% PROT).	The supplementation of HCA enhances the rate of glycogen synthesis in human skeletal muscle and improves the postprandial insulin sensitivity.	[27]
8 weeks	20 practitioners of regular physical activity separated into two groups of 10 members.	Group 1: normocaloric diet; Group 2: normocaloric diet + 2 capsules of 500 mg/day GC.	The combination of diet and physical activity remains the most suitable for positive changes in body composition.	[2]
10 days	10 men, sedentary, lean (BMI: 21.8 + 2.1 kg/m^2) and aged 24+ 5 years.	3 days of diet rich in fat (60% LIP, 25% HC, 15% PROT) and 7 days diet rich in HC (5% LIP, 85% HC, 10% PROT) supplemented with 3 capsules of 500 mg/day HCA.	The treatment with HCA during overfeeding with carbohydrates can reduce DNL.	[28]

*H = men; W = Women; BM = Body Mass Index; EGML = Glycine max leaves extract; GC = *Garcinia Cambogia*; GCE = *Garcinia Cambogia* Extract; BW = Body Weight; TC = Total Cholesterol; HDL-c = High Density Lipoprotein; HCA = Hydroxycitric Acid; CHO = Carbohydrates, LIP = Lipids; PROT = Proteins, DNL = De novo Lipogenesis.

evidence to justify their usage for weight loss. The study of Onakpoya *et al*.[30], also of review, using data from randomized clinical trials (RCTs) in order to examine the effectiveness of GC/HCA extract as weight reducing agent, observed a small significant difference in loss weight, favoring the HCA over the placebo and they concluded that the ECR suggest that the GC/HCA extracts can cause short term weight loss, confirming the review study of Astell *et al*.[31], who concluded that the results of the RCT showed that the GC extract is effective in reducing body weight by suppressing appetite. The study of Amin, Kamel and Eltawab[25], with rats, also concluded that the GC supplementation decreased the feed intake.

The theory behind the GC/HCA is that it works as anti-obesity agent by acting in the neuroendocrine pathways, related to the satiety, producing an anorectic effect, by promoting the inhibition of citrate lyase enzyme that suppresses the appetite and increases the burning of body fat. Thus, it assists in regulating appetite, with consequent reduction of food intake, caloric restriction and weight loss. By inhibiting this enzyme, the body increases the oxidation of carbohydrates and inhibits the lipogenesis[3,14,17,18,32,33]. According to the ANVISA[34], the register situation of GC in Brazil is classified in the category of appetite modulators and products for special diets, and it is indicated as a coadjuvant of overweight to participate in the regulation of appetite[22].

Recently, there was found that the GC supplementation can be used as a metabolic regulator of obesity and lipid abnormalities in the system of mammals.[19] Pandya *et al*.[21], Sethi[3], and Krishnamoorthy[17] claim that GC/HCA reduces the lipid levels in blood, such as triglycerides and cholesterol, besides of increasing the thermogenesis. The HCA inhibits competitively the

extramitochondrial citrate lyase enzyme that catalyzes the cleavage of citrate to acetyl-CoA and oxaloacetate, a key step in lipogenesis, necessary for the synthesis of fatty acids and cholesterol[35,36].

However, in some studies, such as by Kim *et al*.[24], in rats, there was found that the GC supplementation did not cause significant differences in the levels of TG, TC, HDL-c, phospholipids and free fatty acids. Similarly, the study of Ates *et al*.[26] observed that the GC supplementation coupled with the high fat diet failed to reduce the increased serum levels of lipids in rats. In humans, Kim *et al*.[15] also observed that after the supplementation of GC there were no significant differences in lipid levels (triglycerides and low-density lipoprotein - LDL-c), or of adipocytokines (hormones of high adipocytes in obesity). A laboratory study performed by Simon *et al*.[6] also concluded that there were not observed significant effects for the treatment of obesity and of other dyslipidemia with GC.

In contrast, the study of Amin *et al*.[25] in rats, concluded that the GC supplementation improved the harmful effects caused by HFD or HSD, such as hypertriglyceridemia, increase of production of LDL, and of oxidative stress. Santos *et al*.[36] reported in their review study that the administration GC showed inhibition of lipogenesis in the liver of rodents, adipose tissue, and small intestine but without confirmation in humans and claim that the only applicability of the HCA as anti-obesity agent seems to be the reduction of appetite, due to its anorectic effect.

Pandya *et al*.[21] and Krishnamoorthy[17] claim that the GC/HCA acts in the suppression of appetite by making glycogen synthesis in the liver and in other body tissues, increasing the energy levels.

The study done by Cheng *et al*.[27] found that the HCA supplementation reinforced the glycogen synthesis rate in human skeletal muscle, improved the post-meal insulin sensitivity, and demanded higher energy expenditure in fat oxidation. Kim *et al*.[2] observed that in rats the GC supplementation caused lower glucose levels, assuming that this could improve glucose tolerance by contributing to the reduction of visceral fat, since it is responsible for insulin resistance even in hyperlipidic diets.

Several *in vivo* studies have contributed to the understanding of the anti-obesity effects of GC/HCA via the release of serotonin in the brain, which has been considered as the main mechanism to decrease appetite and absorption of glucose and also in the increase of oxidation of fat, reducing DNL[29,33]. In recent studies in female mouse, there has been observed the effect of HCA on the regulator genes of obesity[29]. However, studies related to the presence of enzymatic inhibitors in extracts of these plants that participate or are responsible for its anti-obesity properties are scarce in the literature. Since the research conducted to evaluate the effective and safe use of herbal medicines is incipient, the notifications of events help in the generation of new information, promoting its rational use[32].

Santos *et al*.[36] still claim that in order to qualify the HCA as an anti-obesity effective metabolic agent it should produce a stimulating effect on the skeletal muscle, on the total fat oxidation or on the calorie consumption, but this has not been proved yet. Studies with this herbal demonstrated its effectiveness in combating obesity; however, there miss further studies on its mechanism of action to generate more security in its therapeutic use.

Tucci[12] also states that the GC can contribute to the appetite suppression, but it still should be better demonstrated. In his review study, he noted that some phytochemicals show promising effects on weight control, however, more data is needed to define the real magnitude of effects and ideal doses. For Chandrasekaran[7], an ideal anti-obesity herbal has to reduce the weight by 10% in relation to the placebo during the period of treatment, showing evidence of improvement of biochemical tests, like in the levels of lipids and glucose, without any side effects.

Daily Recommended Amount

The study of Amin *et al*.[25] observed positive effects, such as decreased appetite and improve of the harmful effects caused by high fat and sucrose diets in rats that received supplementation of 50 mg/day of GC. The study of Cheng *et al*. [27] highlighted that the HCA supplementation enhanced the rate of glycogen synthesis in human skeletal muscle and improved the post-meal insulin sensitivity in the amount of 500 mg/day combined with a meal high in CHO (80% CHO, 8% LIP, 12% PROT) after 60 minutes of bicycle. Kovacs and Westertep-plantenga[28] observed that the treatment with three capsules of 500 mg/day (1500mg/day) of HCA during the overfeeding with carbohydrate can reduce the DNL.

Ates *et al*.[26] observed in rats that the GC supplementation combined with the hyperlipidic diet was not able to reduce the increase of the serum lipid levels in a dose of 2.390 mg/day of GC and suggest that higher dosages of GC extract should be investigated. Kim *et al*.[15], noticed that for humans the intake of 2000 mg/day of GC did not promote weight loss neither decreased the total cholesterol in overweight individuals consuming their usual diet. Anton *et al*.[14] also did not observe significant effects in individuals with the administration of higher dosages of GC, 2800 mg/day and 5600 mg/day.

Murer[2] concluded in his study that the combination of diet and physical activity remain the most suitable for positive changes in body composition by observing the combination of normocaloric diet associated with the intake of two capsules of 500 mg/day of GC (1000 mg/day), since the supplemented group and the unsupplemented group, fed only with normocaloric diet reduced body fat.

Although Onakpoya *et al*.[30], in their review article with ECR have concluded that the dosage of HCA

used among the studies ranged from 1000 mg/day to 2800 mg/day, which resulted in a small weight loss, and they said that the magnitude of the effect is small and the clinical relevance is uncertain; so, future clinical trials should be stricter and better reported and that the ideal dose of HCA is currently unknown.

GC supplements are available in various forms, including pills, capsules and powders. The herbal medicine is usually standardized to contain fixed percentage of HCA, and the usual dosage from 300 mg to 500 mg should be administered three times a day and ingested half an hour before meals with water[3].

Side effects and contraindications

About the side effects and contraindications of the GC usage, there was observed in the study of Kim *et al*.[24] that the prolonged use of GC in the administered dose in rats can cause hepatotoxic effects and even develop non-alcoholic hepatic steatosis because of the accumulation of collagen in the liver, independently of being caused by hyperlipidic diet.

Lobb[37] claims that there are a growing number of reports of hepatotoxicity caused by supplements containing HCA. In his study, he approached six case reports: two women, of 33 and 40 years old, and four men of 19, 27, 28, and 30 years old; underestimating the incidence of hepatotoxicity associated with weight loss with the HCA. Each report showed similarities; in the screening of hepatic abnormalities and in the symptoms presented by patients, who were healthy and with normal hepatic functions. Among the laboratory findings and symptoms there were reported fatigue, nausea, vomiting, colic, fever, chills, anorexia, abdominal pain, jaundice in a period ranging from three days to three weeks; deregulated levels of aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase and bilirubin. Onakpoya *et al*.[30], in their review study, observed, gastrointestinal adverse events twice more common in the HCA group in comparison to the placebo group.

In contrast, Clouatre and Preuss[20] claim that the results obtained about the HCA safety and efficacy are different from a variety of studies performed with animals and humans, since they observed in rats that the HCA produced protective effect against the hepatic toxicity associated with ethanol and administration of dexamethasone, and kept levels of SGOT, SGPT, and alkaline phosphatase at almost normal levels. The compound was found to reduce the inflammatory response in the brain, intestine, kidney and serum, and they highlight that high intakes of HCA, by itself, did not lead to signs of inflammation or hepatotoxicity. Sethi[3] also affirms the protection capacity of the GC against external hepatotoxins such as alcohol, and a recent study showed its effect preventing liver cells becoming fibrocytes. Shivashankara *et al*.[38], observed in their review study that pre-clinical studies conducted recently have shown that some herbal medicines, such as GC, protect against ethanol-induced hepatotoxicity, through the mechanism mediated by antioxidant action, elimination of free radicals, anti-inflammatory and antifibrotic, but they emphasized that future studies would be required to establish its applicability in humans.

In humans, Kim *et al*. [15] did not observe reports of serious adverse effects by the individuals who consumed GC supplements, corroborating the study of Anton *et al*.[14] who also did not observe adverse effect (NOAEL) in humans with doses higher than 4000 mg/dia. Lira-García *et al*.[29], concluded in their review study that among the eight studies that were evaluated, in none of them were observed adverse effects on the use of GC.

The review studies conducted by Chuah *et al*.[8], and Chuah *et al*.[33], concluded that there was not observed adverse effect (NOAEL) in dosages of GC/HCA of up to 2800 mg/day, suggesting its safety for use. Most of the reports demonstrated the efficacy of GC/HCA, and there wasn't found any toxicity.

Sethi[3] concluded in his review study that the herbal medicines are more beneficial in the treatment of obesity due to its fewer side effects and also act on the prevention of diseases such as type 2 diabetes, heart disease, high blood pressure. Until now, there is no case study or report showing the direct adverse effect of HCA[8], as well as there is no evidence that demonstrates hepatotoxicity associated with the HCA, and the true agents need to be firmly identified, along with the dose to which the negative effects are induced[39].

Pandya *et al*.[21] also claim that there aren't any known side effects for the usage of this herb. However, it is not recommended for people diagnosed with diabetes or people suffering from any kind of dementia or syndrome, including Alzheimer disease as well as pregnant and lactating women and has contraindications regarding the concomitant use of certain drugs.

Egras *et al*.[40] concluded in their review study that many obese people use food supplements for weight loss and that, so far, there is little clinical evidence to support their findings, but it is necessary to determine their efficacy and safety. Health professionals should be aware of the products available for weight loss to help their patients and to determine the risks and benefits of the supplement used to loss of weight. Yuliana *et al*.[41] still claim that despite insufficient data regarding to its safety and efficacy, many herbal medicines are available for sale without a prescription, such as the GC, which reduces the appetite, and that the quality control of these herbal medicines also becomes important.

This review study has several limitations. Although the research has involved studies in electronic media, there may not have identified all those available involving the use of GC/HCA as a supplement for weight loss. Furthermore, the methodological quality of most studies identified from this study is short. These

factors hinder conclusive findings about the effects of GC/HCA on body weight.

Final considerations

Studies suggest positive results concerning the effectiveness of the GC in weight loss process, by reducing the appetite, the percentage of fat, the lipogenesis process, as well as the improvement of biochemical levels, such as triglycerides, cholesterol and glucose, muscle glycogen synthesis, and postmeal insulin sensitivity. However, the ideal dose has not been well established yet; however the GC supplements are available in 300 mg and 500 mg dosages, with the intake direction of three times a day, with water, half an hour before the meals.

There is little evidence of adverse effects and signs of protective effect against the hepatotoxicity induced by ethanol. Therefore, it is necessary to carry out more randomized, controlled studies, clinical trials to evidence the efficacy of this herbal in the weight loss process, as well as the set of the posology, dosages, indications and contraindications.

Declaration

The authors listed below declare, for the proper purposes, that this work, entitled "The effect of ***Garcinia Cambogia*** as coadjuvant in the weight loss process" is an original not redundant article and that is not in the evaluation process by another journal. Also, the authors declare that there aren't any conflicts of interests or economic relation.

The authors declare thereto that they participated and contributed to this study, as well as they read and approved the final version of this manuscript.

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