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Evidence of *Garcinia cambogia* as a fat burning and appetite suppressing agents

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Key words: Appetite, "*Garcinia cambogia*", "hydroxycitric acid", hypolipidemic effect, obesity

ABSTRACT

Aim: The aim of this study is to assess the uses of products containing *Garcinia cambogia* to burn fat and suppressed the appetite.

Introduction: The availability and popularity of natural dietary supplements for the treatment of obesity have risen dramatically in recent years. Investigation and analysis on the efficacy and effectiveness of the *G. cambogia* are challenging. Furthermore, consuming the products that claimed the anti-obesity effect without a strong judgment is not an appropriate way to losing weight. The overweight prevalence of 29.71% for the Malaysian adults aged 18–59 years indicates that the overweight problem in Malaysia is almost as serious as that for the developed countries.

Methodology: An electronic search of PubMed, CINAHL, ScienceDirect, Clinical Key for studies, case report, trials and reviews using the following search criteria. Examining the product registration in Pharmaceutical Division Services, Ministry of Health. The Malaysian Advertisement Board was referred.


Results: Consumers in Malaysia most likely tend to have a fast method in losing the weight. When the product is advertised inappropriately without any strong evidence based, the Malaysian society is solely at risk in buying the product that does not have a confirmed effectiveness and efficacy. The doubts in using *G. cambogia* are because the marketed product is there is no single formulation that contains only *G. Cambogia*.

INTRODUCTION

Garcinia cambogia is cultivated in Southeast Asia, India, and West and Central Africa and is used extensively for culinary purposes in Asian countries. *G. cambogia* is also included in the US Department of Agriculture inventory of perennial edible fruits of the tropics. The extract of *G. cambogia* has been widely marketed as a weight

loss supplement worldwide. Its weight loss effect has mainly been attributed to its high (–)-hydroxycitric acid (HCA) content. Several mechanisms of action have been linked to the weight loss effect of HCA through prior animal studies, including:

- Inhibition of lipogenesis through adenosine triphosphate (ATP) citrate lyase inhibition, which

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- prevents the conversion of carbohydrate to fat
- Suppression of appetite through increasing glycogen storage thus stimulating the glucoreceptors in the liver and inducing satiety via vagus nerve
- Reduction of the hunger feeling by increasing the level of serotonin and
- Improved glucose metabolism through regulation of leptin and insulin plasma level.^[1]

Several products of *G. cambogia* or its derivatives had been patented and commercialized.

As of August 2012, a total of 66 patents that apply to *G. cambogia* or HCA derived from *Garcinia* were filed with the US Patent and Trademark Office (USPTO) since 1976 (search of USPTO in the year 2012 using Google patent search). These patents are on various aspects, including HCA enrichment from *Garcinia* rind, HCA and food products/dietary supplements prepared therefrom, methods of production, and their use.^[2]

EFFICACY AND SAFETY OF GARCINIA PLUS

There are a few drugs in the market to ameliorate or prevent obesity, but there are costs, efficacy, and side effects to be considered. For example, the currently available pharmacological agents, sibutramine, rimonabant, orlistat, and phentermine which are licensed for weight reduction therapy, appear to possess some adverse effects.^[3-5] Phentermine, for instance, has been reported to cause dry mouth, insomnia, headache, dizziness, fatigue, and palpitation.^[4,5] In the year 2010, Food and Drug Administration had announced the market withdrawal of Meridia (sibutramine) due to its risk of serious cardiovascular events.^[4,5] Natural products and plant-based dietary supplements have been used by people for centuries. The evidence is starting to emerge to shed light on the consumption of herbs as an effective strategy for disease treatment and health maintenance. Several ethnobotanical studies have reported the bioprospecting surveys on the positive application of herbs.^[6]

Plant extracts have been used for many centuries in the Eastern world. However, the use of these extracts have recently become increasingly prevalent around the world. Several chemical constituents isolated from plants and crude extracts have been found to prevent diet-induced obesity and significantly reduce body weight in the treatment of obesity. Due to the prevalent use of plant extracts, evidence is required

to support claims of efficacy.^[7] However, these studies failed to show any effect of HCA on appetite variables in the active treatment group compared with placebo. It is also worth noting, that safety parameters were not measured in the majority of these trials and the percentage biochemical characterization of *G. cambogia* extract was not described in any of the studies. Overall, the evidence for *G. cambogia* in isolation is not compelling. Several factors might contribute to the controversial results of the efficacy of HCA in human studies.^[2]

HCA and *G. cambogia* exerted potential effects in weight management, but clinical studies have yet to prove optimum conditions for HCA to be effective. For instance,^[2] reported that hepatic lipid synthesis was reduced only if HCA was administered before the beginning of feeding, reaching optimum 30–60 min before feeding. The reason for this remains unknown.^[2] We have previously reviewed and concluded that *Garcinia* extract and HCA were generally safe to be consumed. Collective results from 17 clinical studies which involved 873 subjects demonstrated the safety of HCA. These studies provided scientific evidence that intake of alone did not produce adverse effects and a dietary dosage of up to 2800 mg/day was regarded as the “no observed adverse effect level” of HCA in human based on these animal and human safety data, HCA-also received self-affirmed generally recognized as safe status in the USA by the Burdock group in whereas taken together, the number of patients reporting adverse events in the supplemented groups was not significantly different from the placebo group.^[2,3]

However, recent review of animal and human studies established the safety profile of HCA (Chuah *et al.*, 2012). However, the weight loss efficacy of HCA in the human study has shown equivocal findings with studies reporting both negative (Heymsfield *et al.*, 1998) and positive results^[2,4,8] and its uncertainty required more trials with adequate sample size and duration are still needed to confirm HCA's weight loss efficiency.^[1]

In spite of the vastly reported prominent role of HCA in inducing satiety, reduced energy intake and weight gain, and improved blood parameters and substrate oxidation, controversial results regarding its efficacy and safety as an antiobesity dietary supplement had also been reported. Evidence from the *in vitro*, *in vivo*, and clinical trials on the safety of *Garcinia*/HCA as a dietary supplement for treating obesity had

been extensively reviewed. However, the efficacy of *Garcinia*/HCA remains the subject of debate. Despite the previously stated issues, on conclusive evidence for HCA's efficacy in promoting weight loss and suppressing food intake, the marketing of a plethora of over-the-counter slimming aids containing HCA has taken place.^[2,3,9]

According to Chuah *et al.* and Mattes and Bormann reported a lack of efficacy of HCA in suppressing food intake in human subjects might be due to the low doses of a relatively low-effective HCA preparation. Nevertheless, significant suppression of food intake was observed in the studies. There is another hypothesis where Sprague-Dawley rats were supplemented with HCA for 10 days after substantial, fasting-induced weight loss. It seemed that HCA might be more effective in regulating weight gain^[10] than promoting weight loss; thus, it was more useful for weight maintenance after an initial loss. Hence, differences in the experimental setups such as the difference in rat strains could contribute to such discrepancy.^[2]

However, there is a case report by Li and Bordelon regarding acute kidney injury caused by an herbal product containing HCA. HCA drug interactions are unknown because HCA has not been studied in combination with other drugs or adulterants used in supplements. However, the effect of long-term use is unclear because all studies were <12 weeks with relatively small sample sizes (1000 subjects combined.) A major concern is an herbal toxicity from numerous factors: Excessive or prolonged ingestion, addition of harmful adulterants or heavy metals, consumption of toxic chemicals, and effects of combining herbs with pharmacologic. A number of reports about the toxicity of *G. cambogia* itself or *G. cambogia* - containing supplements are available.^[8,11] In agreement with previous studies on soy and *Garcinia cambogia* extract (GCE) supplements we used doses of 2 g/day, it was beyond the scope of this study to determine whether higher doses were more effective for promoting weight loss and improving plasma lipid profiles.

PHARMACOKINETICS HYDROXYCITRIC ACID IN *GARCINIA CAMBOGIA*

HCA, up to 30% by weight is present in the pericarp or the fruit rind^[2] of the fruit of *G. cambogia*.^[1,2,4] HCA can exist as a free acid or in the lactone form. The former form is considered to be biologically active. However, the free acid is unstable and is usually converted to its less active lactone form to attain higher stability.

To prevent the cyclization of HCA into its less potent lactone, the acid has been combined with various counter ions to form stable salts. Commercial HCA is available in free acid form and as single, double, or triple salts. Preparations with different counter ions contribute to the different degree of solubility as well as bioavailability. For example, Na⁺ salt of HCA had been shown to be more effective than its lactone in inhibiting lipogenesis. However, Na⁺ salt is highly hygroscopic when bound to (-)-HCA, which would deem unfavorable for the production of pharmaceuticals for dry delivery.^[2]

According to Chuah *et al.*, observed that of the four isomers of HCA ([−]-HCA, [+]-HCA, [−]-allo-HCA, and [+]-allo-HCA), (-)-HCA, which is also known as (2S, 3S)-HCA, was the only potent inhibitor of ATP citrate lyase. (-)-HCA can be chemically synthesized using citric acid as starting material. Synthetic (-)-HCA offers several advantages including higher purity and lactone stable as compared to natural (-)-HCA. On the other hand, (-)-HCA is a good starting material to synthesize other important chiral synthons and compounds. On account of the discovery of (-)-HCA as an effective compound in weight management, market demand for the acid has increased tremendously.

(-)-HCA is one of the important supplements for antiobesity and weight management. Its effect on weight management is mainly contributed by giving the feeling of full and satisfaction. While the antiobesity effect is by reduction of *de novo* lipogenesis and acceleration of fat oxidation.^[2]

ABSORPTION

No findings in *G. cambogia* alone. The figure found is varies, depending on which formulation is being tested during the research. According to Kovacs *et al.*, a compound complexed with calcium and potassium like the one used in this study is 100% soluble and creates pH level that is favorable for maximal gastrointestinal absorption. Whereas, study done by Preuss *et al.*, found that many HCA products are <50% soluble in water and poorly absorbed. Thus, more further study should be carried out to confirm the actual absorption percentage for HCA.

DISTRIBUTION

Ingestion of a single dose of HCA (4.4 g) resulted in maximal plasma HCA concentration after 60–90 min (0.12 mmol/L - 1.4% of the administered HCA, assuming 4.5 L

blood and an hematocrit of 45%. HCA remained present at least for 3 h. It believed the low concentration of HCA continuously present in plasma. Furthermore, HCA can act directly on adipocytes, causing lipid droplet dispersion, and altering transcription. Other bioactive components of *G. cambogia* including benzophenone are reported to reduce oxidative stress levels based on *in vitro* experiments in human plasma, hence *G. cambogia* may protect against diseases associated with oxidative stress.^[5]

METABOLISM

Increased blood ketones and hepatic or muscle glycogen levels have been posited as potential mechanisms for the satiety effect of HCA. The fat-degradation or fat-oxidation ability of HCA was evaluated based on the excretion of urinary fat metabolites. Enhanced beta-oxidation of fat may be the prime sources of these four fat metabolites. Enhanced excretion of malondialdehyde (MDA) was observed during increased oxidative stress. In the same study, radiolabelled MDA administered to rats was found to be extensively metabolized to acetate and carbon dioxide.^[10]

EXCRETION

Metabolism of glycerol to fatty acid has been reported in rat liver microsomes and is a result of the metabolism of triglycerides by adipose tissue and other tissues that possess the enzyme that activates glycerol, namely glycerol kinase. High glycerol kinase levels are found in liver and brown tissues.^[3] Although, a previous report suggest higher doses may be futile, as oral administration of higher doses of *G. cambogia* extract to normal subjects leads to increased urinary excretion of (-)-HCA, attributed to limitations in (-)-HCA absorption efficiency.^[12]

METHODOLOGY

An electronic search of PubMed, CINAHL, ScienceDirect, Clinical Key for studies, case report, trials and reviews using the following search criteria.

Search strategies

Keywords used	" <i>Garcinia cambogia</i> ," "hydroxycitric acid," appetite, obesity, hypolipidemic effect
Years searched	All
Total no. of articles reviewed	46
Relevant full text articles reviewed	16
Relevant abstracts reviewed	16

RESULTS

The prevalence of overweight among the Malaysian adults has increased almost 2-fold from 16.6% to 29.7%. Overweight was highest among the Indians (31.01%), and affects the minority ethnic groups too, for example, 15.06% among the Orang Asli of Peninsular Malaysia, 28.07% in the Bumiputera Sarawak and 23.73% for the Bumiputera Sabah. In fact, the prevalence of overweight among the Bumiputera Sarawak women was high at 31.68%.

The overweight prevalence of 29.71% for the Malaysian adults aged 18–59 years indicates that the overweight problem in Malaysia is almost as serious as that for the developed countries reported in the 1999–2002 National Health and Nutrition Examination Survey and WHO (2006). Overall, overweight increased with age and household income. This pattern of increase was also observed among the men.^[6,13] This finding is not consistent with other population-based studies, which reported that females had a higher rate of obesity than males.^[2,13,14] Sociodemographic, psychosocial factors, and working hours were found to contribute to obesity in this sample of adults.^[14] The analyses showed a significant relationship between education status and body mass index (BMI) and waist circumference (WC) in this sample of subjects. There were significant differences in mean BMI and mean WC between the subjects who had secondary or less education and those with preuniversity and matriculation and diploma education. Hence, this finding suggests that lower education status is associated with a higher BMI and WC.

As obesity has reached epidemic proportions, the management of this global disease is of clinical importance. The availability and popularity of natural dietary supplements for the treatment of obesity has risen dramatically in recent years.^[7] Due to the difficulty in maintaining sustained lifestyle changes, potential complications of surgery and accompaniment of serious adverse effects associated with pharmacotherapy, it is not surprising that the general public frequently turn to easily obtainable over the counter proprietary weight loss products such as herbal products, nutritional supplements, and meal replacements.^[7]

The findings of a multi-state survey conducted in the US revealed that 7% of adults used nonprescription/over the counter weight loss supplements, with a greater proportion of use among young obese women.^[1] In

addition, retail sales of weight loss supplements were estimated to be >\$1.3 billion in 2001.^[3] Plant extracts possessing appetite suppressing properties for obesity treatment.

According to the findings from this systematic review, the evidence is not considerable in demonstrating that most dietary supplements used as appetite suppressants for weight loss in the treatment of obesity are effective and safe. A balance between conclusive findings by double blind randomized controlled trials (RCTs) and advertisement is required to avoid safety concerns and dissatisfaction from consumers.^[5,7,10,11]

Although the use of internet continues to grow rapidly, its impact on health care is unclear. The advantages of the internet as a source of health information include convenient access to a massive volume of information, ease of updating information, and the potential for interactive format that promotes better understanding. However, health information on the internet may be misleading or misinterpreted.

Malaysia is a developing country with growing internet usage. Current data showed that there were 15.355 million internet users in 2009 compared with 5.700 million in 2002. Addictive use of the internet can lead to physical or familial problems, as well as academic and occupational deficiency. Thus, there is a need to validate a scale to measure internet addiction in the Malaysian population for clinical practice and research purposes.^[15]

In information technology literature, attitudes influence a person's adoption of computer technologies and adaptation of purchasing behavior. The attitude toward intention to use information technology is multidimensional, involving perceived usefulness, accessibility, and quality.

Consumers in Malaysia most likely tend to have a fast method in losing the weight. When the product is advertised inappropriately without any strong evidence based, the Malaysian society is solely at risk in buying the product that does not have a confirmed effectiveness and efficacy.

RECOMMENDATION AND CONCLUSION

Studies show that Indians have the highest prevalence of abdominal obesity and diabetes while Malays are at greater risk of developing hypertension. These findings also identified women as the group with

the highest risk to such diseases.^[16] It is reasonable because individuals with a higher education status tend to adopt healthier lifestyle behaviors. Such as a higher consumption of fruit and vegetables, less dietary fat intake, and engagement in exercise as most of them have a higher awareness of weight control.^[14] Overweight employees are assumed to lack self-discipline, be lazy, less conscientious, less competent, sloppy, disagreeable, and emotionally unstable. Obese employees are also believed to think slower, have poorer attendance records, and be poor role models.^[17,19]

Chronic energy imbalance due to excess energy intake that exceeds energy expenditure is the reason behind weight gain in humans. The multiple health complications of obesity, poor response to medical treatment and its economic costs justifies the need for effective prevention strategies.^[18]

The pressure to eat subscale evaluates parental child feeding practices by assessing the extent to which a parent encourages the child to eat by insisting that the child finishes all the food on the plate. The scores range from 1 to 5 indicating low to high levels of pressure on the child. In this study, the mean score was significantly higher in the normal body weight group (4.0 ± 0.6) compared to the overweight/obese group (3.5 ± 0.9) ($P < 0.001$). This meant that parents of overweight/obese children seemed to exert less pressure on their children.^[18] Wan Abdul Manan *et al.* 2012 showed that parental feeding attitudes and practices were correlated with childhood obesity. Parents should be more responsible toward their children by practicing appropriate child feeding strategies without exerting force during feeding so as to avoid unwanted circumstances such as weight problems and eating disorders.^[18]

There are a variety of effective options for weight loss in the treatment of overweight and obesity which include dietary therapies, altering physical activity, behavioral techniques, pharmacotherapy, surgery and a combination of these strategies. The first-line of therapy for the management of obesity has the least risk which consists of lifestyle changes including diet, exercise and behavioral modification. The second line of therapy for obesity treatment is pharmacotherapy,^[19] which is often recommended when lifestyle modification is ineffective in producing sufficient weight loss. The last approach in extreme cases of morbid obesity is through surgical therapy. Surgical treatment is an option for a limited

number of patients with clinically severe or morbid obesity (BMI >40 or >35 with comorbid conditions) and is reserved for those who are suffering from the complications associated with extreme obesity or are unresponsive to nonsurgical treatment.^[7]

Studies have found that the availability and accessibility of exercise equipment and facilities in the workplace environment, such as sports centers, jogging track, swimming pool, and tennis court correlated with higher physical activity in the workers, resulting in better control of weight. The large amount of sitting time spent in sedentary activities such as working at a desk and using computers has played a role in the development of the current overweight and obesity.^[3,14]

As a conclusion, consuming the products that claimed the antiobesity effect without a strong judgment is not an appropriate way in losing weight. Treatment obesity requires a two-divided reducing energy intake as well as increasing energy expenditure.^[1]

Weight control programs are required in order to increase physical activity and promote healthier eating in the workplace. Several approaches are suggested for weight control intervention, such as counseling, skills training, writing materials, partnerships, and local projects.^[14] Other than that, pharmacotherapy using antiobesity Current available drug treatments for obesity, for example, appetite suppressant (e.g., phentermine and topiramate) or lipase inhibitor (orlistat), focus primarily on reducing caloric intake, while IQP-GC-101, investigated in this study, offers the possibility of increasing thermogenesis and metabolism in supporting weight loss.^[1] Under the physician consultation is highly suggested.

According to Chong *et al.*, 55% reduction in the risk of diabetes and other cardiovascular disease can be achieved if the obese manage to lose about 5 kg over time).^[1] The doubts in using *G. cambogia* is because the marketed product is there is no single formulation that contains only *G. cambogia* as the active ingredient. Most of the preparation is a combination of more than one active ingredient. It is found quite difficult to carry an investigation and analysis on the efficacy and effectiveness of the *G. Cambogia*. For example, the study indicated that the use of herbal extracts combination in IQP-GC-101 results in better weight loss effect in comparison to products containing only *G. cambogia* extract used in the other studies.^[1]

Thus, scientific surveys on the probable health stimulating effects of herbal preparations as diet

supplement are requirements for new discoveries of alternative therapies.^[2] In addition, the difference in mean weight loss observed in the current study is higher than the net mean effect of 0.88 kg reported in a meta-analysis of RCTs of *G. cambogia* extracts with daily dose of HCA ranging from 1.0 to 2.8 g. Most of the undesirable reports have been related to cases where multi-ingredient preparations were consumed and the effect could not be accredited to a specific ingredient. However, as *G. cambogia* may increase the levels of serotonin, it is especially crucial to investigate a possible interaction between medicines that increase serotonin levels such as selective serotonin reuptake inhibitors and *G. cambogia*.^[8]

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Conflicts of interest

There are no conflicts of interest.

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