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Abstract

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Keywords

botanical, obesity, approach, managing

Disciplines

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A BOTANICAL APPROACH TO MANAGING OBESITY

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Key words: Obesity, weight management, nutrition, *Garcinia cambogia*, *Magnolia officinalis*, hydroxycitric acid

ABSTRACT

Classed as an epidemic by the World Health Organisation, obesity is the result of an imbalance between energy input (food intake) and energy expenditure. Evidence is starting to emerge to support the view that an increase in the consumption of herbs is an effective strategy for obesity control and weight management. The use of plants has potential to keep the increasing prevalence of metabolic syndrome in check like obesity. There are few drugs in the market to ameliorate or prevent obesity but there are the costs, efficacy and side effects to consider. For centuries people across the countries have been using natural products and plant based dietary supplements for weight control. The current review will consist of one South Asian herb, *Garcinia cambogia* and one Chinese herb, *Magnolia officinalis*. Both herbs are very effective and acting through two different pathways. It is clearly evident from published information that the hydroxycitric acid from *Garcinia cambogia* is most acceptable considering its safety and efficacy properties.

INTRODUCTION

Obesity and the metabolic syndrome continue to plague the world at an alarming rate. In recent years it has been reported that obesity and its metabolic complications will cause both substantial socio-economic and physical burden on society (1,2). Furthermore, if untreated diabetes, hypertension, dyslipidemia and others more severe conditions will increase (3). Because weight perturbations are so prevalent and harmful, many different pro-pharmacological approaches have been developed to treat the overweight state and obesity. The use of pharmacological drugs has become a popular means to overcome excess weight (4). While these drugs generally are effective, severe adverse toxicities may limit their overall usefulness (5,6). A nutritional based intervention is being hailed as an inexpensive

alternative to the aid weight loss, and weight management (7). Accordingly, recent preliminary reports suggesting that herbs with a long history of use and other natural substances less likely to produce severe toxicity might be effective in reducing appetite and promoting significant weight loss are encouraging (Table 1).

New weight loss strategies have focussed on different mechanisms of products. This review will examine the role of two lead natural product interventions that can be used in conjunction with dietary manipulation, which in turn may aid an individual's ability to achieve weight loss, while maintaining key vitamins and mineral composition. In response to new understanding of obesity and weight management science, the current review will consist of one South Asian herb, Malabar tamarind tropical fruit (*Garcinia cambogia*) and one Chinese herb, magnolia (*Magnolia officinalis*). Both herbs are very promising and acting through two different pathways.

Table 1. Common dietary supplements used for weight loss¹

¹Adapted and modified from Saper et al. (37)

<p>Increased energy expenditure Ephedra Bitter orange Guarana Caffeine Country mallow Yerba mate Modulate carbohydrate metabolism Chromium Ginseng Increased satiety Guar gum Glucomannan Psyllium</p>	<p>Increased fat oxidation or reduced fat synthesis Hydroxycitric acid Green tea Licorice Conjugated linoleic acid Vitamin B₃ Block dietary fat absorption Chitosan Increased water absorption Dandelion Cascara Enhanced mood St. John's wort</p>	<p>Anxiolytic effect Magnolia Phellodendron Miscellaneous or unspecified Laminaria Spirulina Guggul Apple cider vinegar</p>
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Garcinia cambogia

The Indian fruit *Garcinia cambogia* (family Guttiferae), also known as Malabar tamarind, which has been used safely for centuries in south-eastern Asia as a food preservative, flavouring agent and carminative and also to render meals more filling. The active ingredient (10-30%) of the fruit rind is (-)-hydroxycitric acid (HCA), a component that reportedly promotes weight loss, in part, through number of mechanisms. Two of the major mechanisms

are metabolic and appetite suppressant effect (8, Fig.1). HCA is a competitive inhibitor of adenosine 5'-triphosphate-citrate lyase, leading to decreased acetyl coenzyme A production and decreased fatty acid synthesis (9,10). The putative weight reduction effect of HCA is due to suppression of fatty acid and fat synthesis. In addition, HCA is thought to suppress feed intake via loss of appetite by stimulation of liver gluconeogenesis (11). As mentioned, HCA has been shown to suppress food intake (12,13) and to decrease body weight gain (12,14), but the mechanism of the feeding suppressive effect of HCA is still unidentified. The findings that HCA decreased the energy conversion ratio (12,13) and weight gain compared with a pair-fed control group supports the idea that HCA increases energy expenditure. In this context, Leonhardt et al. (11) has demonstrated in animal model that HCA suppresses do novo lipogenesis and also improve glucose tolerance.

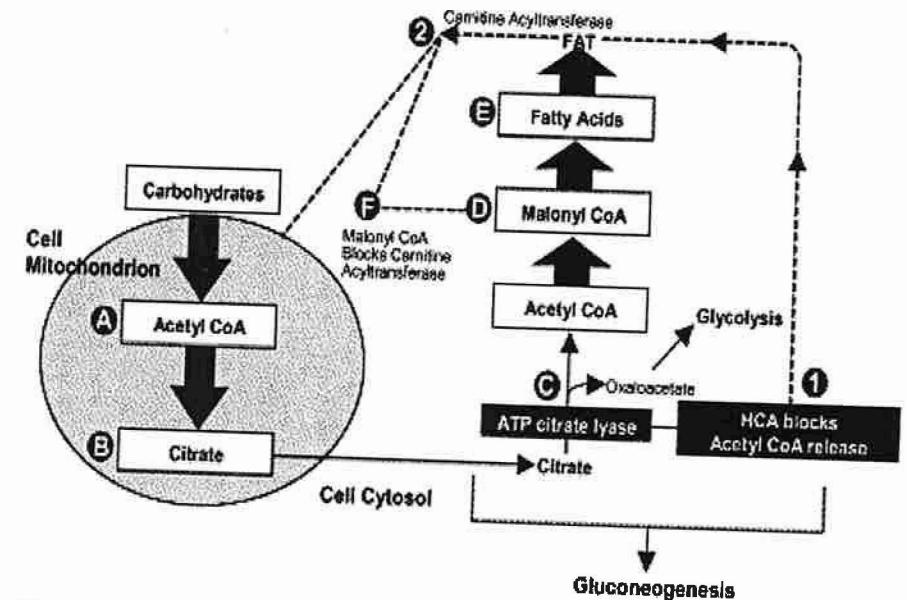


Figure 1. Proposed biochemical action of HCA. Adapted from Soni et al. (8). Copyright Permission from Elsevier.

Several *in vivo* studies have shown that HCA increases the release/availability of serotonin, neurotransmitter implicated in the regulation of eating behaviour and appetite control (15,16). It is also reported that extracts of *G.cambogia* decrease serum leptin, a hormone produced by fat tissue, is known to play a key role in regulating energy intake and

metabolism levels in mice (17) and in humans (18), and also reduce the expression of abdominal fat leptin in rats at doses that would be appropriate for human dietary consumption of HCA (19). A recent randomized, double-blind clinical trial of *G. cambogia* revealed, in comparison with a placebo group, significant changes in the body composition improvement index and decreases in the body fat of overweight subjects who had received the dietary supplement over a 12 week period (20).

Although HCA-SX (a calcium-potassium-HCA extract) seems to be conditionally effective in weight management in both experimental animals and humans, but its mechanism of action remains unclear. Several *in vitro* studies (19, 21) have shown that HCA-SX supplementation up-regulated the genes encoding serotonin receptors and neuropeptide signalling, which demonstrate its ability to suppress appetite (Table 2).

HCA-SX has also been shown to modulate a significant number of genes including prostaglandin D synthase (PGDS), aldolase B, lipocalin 2, fructose-1,6-biphosphatase 1 and low-density lipoprotein receptor related protein 2, which play a prominent role in lipid metabolism, carbohydrate metabolism, glycolysis, and cell communication (19, Table 3). In a recent *in vitro* microarray analysis, Roy et al. (19) has demonstrated down-regulation of 348 and up-regulation of 366 fat- and obesity-related genes. This study has directed guidance in generating a new hypothesis, i.e., transactivation of hypoxia inducible factor (HIF) in the management of obesity.

Table 2. Genes upregulated following HCA-SX supplementation¹

Genes/regulatory proteins	Function
PDZ domain containing 1	Serotonin receptor signalling
5-Hydroxytryptamine (serotonin) receptor 2A	Serotonin receptor
5-Hydroxytryptamine (serotonin) receptor 2B	Serotonin receptor
5-Hydroxytryptamine (serotonin) receptor 3a	Serotonin receptor
5-Hydroxytryptamine (serotonin) receptor 4	Serotonin receptor
5-Hydroxytryptamine (serotonin) receptor 7	Serotonin receptor
Preproenkephalin, related sequence	Neuropeptide signalling
Prostaglandin d synthase (PGDS)	Lipid metabolism
Aldolase B	Carbohydrate metabolism
Fructose-1,6-biphosphatase 1	Glycolysis
Lipocalin 2	Transporter
Low-density lipoprotein receptor-related protein 2	Lipid metabolism

¹Adapted from Downs et al. (21). Copyright Permission from Elsevier

This review will examine two proprietary products of HCA from *G.cambogia*, Super CitriMax®, a novel calcium/potassium-HCA extract

(HCA-SX) and Slim339®, fixed combination of *G.cambogia* with calcium pantothenate. The Super CitriMax® has been studied extensively in animal model and in randomised human clinical trials (8,18,19,21,22) and compare with relatively less studied product, Slim339® (23). Super CitriMax® (Fig. 2) is considerably more soluble and bioavailable than calcium-based HCA ingredients (21).

Table 3. Genes downregulated following HCA-SX supplementation¹

Genes/regulatory proteins	Function
Beta II spectrin-short isoform mRNA, partial cds	structural
C151_RAT platelet endothelial tetraspan antigen 3	cell contact
SPARC-like 1	structural
Inhibitor of DNA binding 3	cell cycle
Ficolin 2 precursor	sugar binding
Synaptic vesicle glycoprotein 2b	calcium binding
Nonerythrocyte beta-spectrin mRNA, partial cds	structural

¹Adapted and modified from Roy et al. (19)

In one rigorous safety assessment it was reported that there is sufficient qualitative and quantitative scientific evidence, including animal and human data suggesting the intake of HCA-SX at levels up to 4667 mg/day is safe for human consumption (8). HCA-SX has been shown to increase serotonin availability, reduce appetite, increase fat oxidation, improve blood lipid levels, reduce body weight, and modulate a number of obesity regulatory genes (Table 2,3) without affecting the mitochondrial and nuclear proteins required for normal biochemical and physiological functions (21). The combined results from two randomised, double-blind, placebo-controlled clinical studies indicated that HCA-SX and to a greater degree, the combination of HCA-SX plus niacin-bound chromium and *Gynema sylvestre* extract reduce body weight and BMI, suppress appetite, improve blood lipid profiles, increase serum leptin and serotonin levels and increase fat oxidation more than placebo (18,22).

A double-blind, randomized, parallel-group, placebo-controlled study has been carried out in order to evaluate the effect of orally self-administered Slim339®, a proprietary fixed combination of *Garcinia cambogia* extract with calcium pantothenate (standardized for the content of hydroxycitric acid and pantothenic acid) and extracts of *Matricaria chamomilla*, *Rosa damascena*, *Lavandula officinalis* and *Cananga odorata*, on body weight in overweight and obese volunteers (23). During a 60 day study...

average reduction in body weight for the group receiving Slim339 was 4.67% compared with 0.63% for the placebo group. Weight losses of ≥ 3 kg were recorded for 23 subjects in the treatment group and only one in the placebo group. No pharmacokinetics and toxicity studies have been done. Further studies will be needed to assess whether long term administration of this medication is warranted and to what degree it could improve the metabolic parameters in obese subject. From preliminary study, it is concluded that Slim339® represents a potential therapy for obesity.

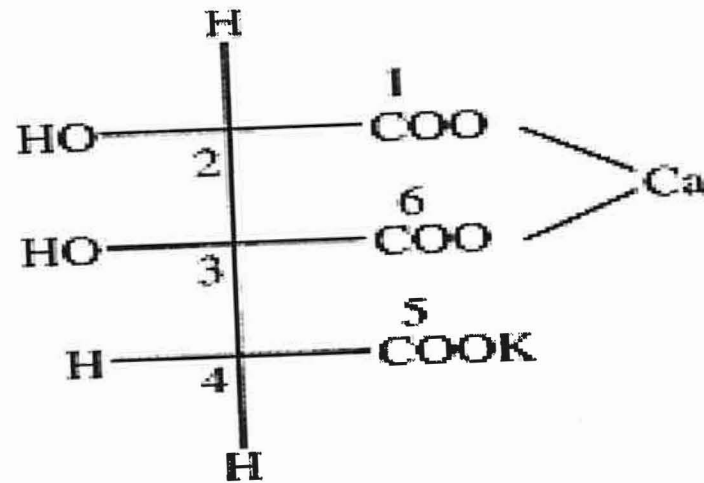


Figure 2. Structure of HCA-SX¹
¹Adapted from Downs et al. (21). Copyright Permission from Elsevier.

Magnolia officinalis

Obesity and work-related stress level is relatively high in American (24). A year of 2000 Labour Day Gallup Poll suggests that 80 percent of American workers feel stress on their jobs (25). They described the situation as "this is an overweight nation that is gripped by stress". Previous research has demonstrated a strong linkage between stress, lack of sleep and obesity (26,27).

A new approach to weight loss has been developed by managing stress level. Reduction of the effects of stress on the body, a feeling of reduced anxiety and stress, and reduced cravings for comfort foods can be possible by normalization of circulating cortisol levels. In response to this new understanding of obesity and weight management, a traditional Chinese

herb, *Magnolia (M. officinalis)* has been used specifically to control elevated stress-related cortisol level, sweet cravings, disrupted weight management, and poor quality of sleep (24). This particular herb has long history of traditional use in Chinese medicine.

Clinical studies have shown that the oriental herbal medicine *saiboku-to* (from *Magnolia spp.*) relieves anxiety-related disorders such as anxiety neurosis (28). Several mechanistic studies suggest that the anxiolytic effect of *Magnolia* compounds act as GABA-A receptor agonists (29), or more precisely via an indirect cholinergic activity such as inhibition of histaminergic neurons linked to cholinergic neurones (30,31). The *Magnolia* fraction also demonstrated very significant binding to the adenosine A₁, glutamate N-methyl-D-aspartate (NMDA) and serotonin transporter receptors. Several clinical data confirm the efficacy and safety of the *Magnolia* as a dietary supplement for supporting weight loss during stress period. In one ongoing placebo controlled, double-blinded clinical study the *Magnolia* supplement group show very encouraging result than a matching placebo control at the dosage of 1 capsule (250 mg) three times daily for 6 weekly in 26 healthy overweight, pre-menopausal female adults (24). The *Magnolia* supplemented group showed a statistically great reduction in anxiety and non-significant trend for lowered average cortisol. An earlier placebo controlled, double-blinded pilot study (32) demonstrated that the supplement was well tolerated with no side-effects at the recommended human dosage. Appetite for snacking was also significantly reduced in the supplement group at baseline and post-treatment.

DISCUSSION

The World Health Organization has recognized the epidemic of obesity as one of the top ten global health problems (2). Obesity is the result of an imbalance between energy input (food intake) and energy expenditure. Obesity appears in most individuals as a multi-genic, multi-factorial disease. Genetic determinants are account for at least 50 per cent of the obese phenotype, whereas the rest is due to the environment (33). Obesity is associated to several chronic and debilitating conditions including coronary artery disease, metabolic syndrome, hypertension, stroke, hyperlipidemia, diabetes, osteoarthritis, sleep apnoea, gout, gallbladder disease, several cancers and joint problems (34).

There are few drugs in the market to ameliorate or prevent obesity but there are the costs, efficacy and side effects to consider. For centuries people have used plants for healing and the use of plants has potential to keep the increasing prevalence of metabolic syndrome in check. Many people across

the countries are using natural products and plant based dietary supplements for weight loss (35).

During last decade, a spectacular advancement in the understanding of the molecular mechanisms that control food intake and body weight has been reported, but to date only two Food and Drug Administration (FDA)-approved medications for chronic weight loss and maintenance, sibutramine and orlistat (36) are available in the market. Continuous global efforts to treat the obesity pandemic have not been very successful and novel therapeutic agents are urgently required. In this respect, traditional medicine offers various herbal dietary supplements for reducing body weight that warrant further consideration in the light of risk-benefit balance scorecard.

Due to the financial and psychosocial stress of being overweight, the patients often turn to over-the-counter (OTC) proprietary weight-loss products containing single or multiple dietary supplements (e.g., herbs, vitamins, minerals, amino acids). The nutraceuticals mentioned in this article have been clinically evaluated and some have been marketed for obesity control and weight management. From the reported information, it is clearly evident that the hydroxycitric acid has been extensively studied for its safety and efficacy.

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