

Healthy weight management: **Natural botanicals** may offer significant boost to the quest

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Overweight and obesity have become major public health problems worldwide as recent data suggest that prevalence of corpulence and obesity has increased by three times in the last decade. As per the World Health Organization (WHO), corpulence and obesity are the fifth leading cause of mortality across the world (1).

Overweight and obesity are defined as the abnormal or excessive accumulation of body fat resulting in weight gain, above the ideal, that poses multiple health risks. A person with a body mass index (BMI), a crude population measure of obesity, of 30 or more is generally termed as 'obese,' whereas a person with a BMI equal to or more than 25 is classified as 'overweight' (2).

In the United States, almost 70% of adults are overweight, and of these, one-third of the population is found to be clinically obese. Both overweight and obesity are considered as major risk factors associated with mortality and morbidity from a host of chronic conditions, ranging from cardiovascular diseases and diabetes to osteoarthritis to cancer. However, obesity, once considered a problem only confined to high-income countries, has now become one of the most public health problems even in low- and middle-income countries, particularly in urban areas (3,4).

PHARMACOTHERAPY HAS POTENTIAL DRAWBACKS

Although a number of strategies have been adapted to manage overweight and obesity, according to the National Heart, Lung, and Blood Institute guidelines, lifestyle modifications such as diet and exercise intervention are the ideal modalities for the

healthy weight management. A few studies have also suggested that pharmacotherapy may be considered if the interventions are ineffective for individuals with a BMI ≥ 30 or for those with a BMI ≥ 27 when co-morbidities, such as hypertension or type 2 diabetes are diagnosed. However, therapeutic intervention using anti-obesity drugs has not been very satisfactory because of various reasons like limited long-term success, regaining of weight upon treatment discontinuation, and of course undesirable side effects (4,5).

According to a recently published systematic review, over the past 60 years – i.e. between 1964 and 2009 – 25 anti-obesity drugs have been withdrawn from the market worldwide due to adverse drug reactions. In more than 80% cases, the reason for withdrawal was psychiatric disturbances, cardiotoxicity, or drug abuse and dependence. Deaths were observed in 28% of cases (1).

NATURAL BIOACTIVES COULD BE YOUR 'SAFER' ALTERNATIVES

Because of not so promising benefits as well as undesirable adverse effects, traditional herbal medicines are being considered as an excellent alternative to synthetic counterparts for developing future efficacious, sustainable, well-tolerated, and above all safe drugs to better manage a healthy weight.

Unlike chemical-based anti-obesity drugs that mainly act on the appetite, several natural products manage healthy weight through synergistic action in addition to their ability to target multiple molecular pathways, viz. absorption, metabolism, and thermogenesis, increasing lipolysis and decreasing lipogenesis, and differentiation and proliferation of preadipocytes (4,6). Following are some of

the natural ingredients that have been clinically validated for their weight management support.

GARCINIA CAMBOGIA

Garcinia cambogia, also known as 'Malabar



Garcinia cambogia fruits.

Tamarind,' is a tropical fruit belonging to the family Clusiaceae. This plant, native to Southeast Asia, has been extensively used as a culinary spice, flavoring agent, and preservative due to its characteristic sweet and sour taste.

Hydroxycitric acid (HCA), an alpha-hydroxytricarboxylic acid, is the principal active which exists in four isomers, of which, biologically active (-)HCA isomer is found naturally in the fruit rind (7).

Mechanism of Action

(-)Hydroxycitric acid helps manage healthy weight by two following mechanisms:

- **Inhibition of Fatty Acid Synthesis and Lipogenesis:** (-)HCA reversibly inhibits the enzyme adenosine triphosphate (ATP)-citrate lyase, a key enzyme responsible for fatty acid and cholesterol biosynthesis, leading to the reduction of fatty acid synthesis and lipogenesis, thus supporting healthy weight management. Additionally, it also facilitates the oxidation process of fatty acid, which meets the energy requirements of the body – thus, promoting the fat loss.
- **Supports Curb Hunger:** It has been reported that (-)HCA provides a sense of satiety to the user as (-)HCA-mediated fat metabolism stimulates gluconeogenesis-glycogen storage in the liver. This high level of glycogen is signaled by CNS as a state of satiety, in turn, decreased food intake (8).

Garcinol is a benzophenone derivative present in the fruits of *G. cambogia*, which is believed to enhance the biological activity of (-)HCA and contributes to its antioxidant properties (7).

The amphibio action of the (-)HCA/garcinol combination has been found to work by the antioxidant property – neutralizing negative charges surrounding the cell and by affecting fluidity of cell membranes to facilitate transport and uptake of (-)HCA into the cell, and

inverse relationship between appetite and energy levels was observed, which may be the result of increased levels of glycogen stores in the body (9).

Clinical Study 2

In a 12-week, double-blind study, supplementation of a combination of (-)HCA (500 mg) + garcinol (25 mg) (the product was Sabinsa's GarCitrin®) three times a day in 46 overweight women produced a better efficacy in terms of weight loss (Figure 2), body composition, and self-assessed appetite and energy levels compared to (-)HCA alone (8).

COLEUS FORSKOHLII

Coleus forskohlii is an aromatic herb, native to India, and is a member of the mint family. It is the only known plant source of forskolin, a bioactive compound having a range of pharmacological benefits, including healthy weight management and building lean body mass. Traditionally, the roots have been used in the form of pickle or condiments in the Indian subcontinent.



Coleus forskohlii roots

Mechanism of Action

Forskolin is believed to activate adenylate cyclase enzyme, a 'second messenger,' which further enhances cellular concentrations of the cyclic AMP (cAMP) and cAMP-mediated functions. Furthermore, cAMP facilitates the action of "primary messengers" or various hormonal and bioactive substances in the body, e.g. insulin, hormone-sensitive lipase. Hence, cAMP may contribute to increased metabolic rate and thermogenesis, thus corresponding to the build-up of lean body mass as well as reduced body fat (Figure 3).

Several clinical studies have demonstrated that forskolin significantly improves lean body mass, as well as helps reduce body fat without any side effects.

Clinical Study 1

In an 8-week, open-field, pilot study, overweight women were supplemented with 250 mg of forskolin

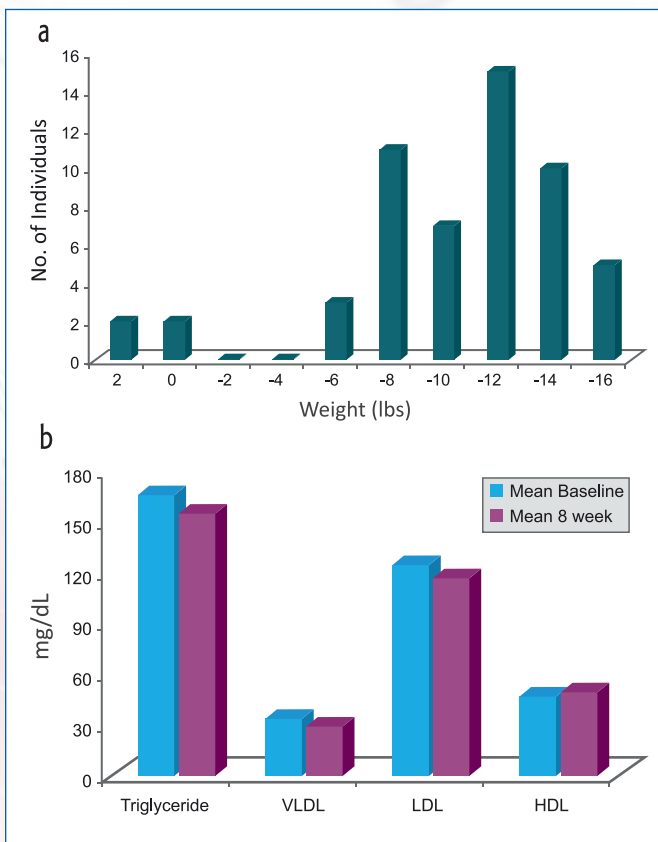


Figure 1 – Effect of (-)HCA on body weight (a); and on lipid profile (b).

synergistically inhibiting citrate lyase, thus lowering the threshold for such inhibition with the (-)HCA.

Clinical Study 1

In an 8-week, open-field clinical trial, supplementation of calcium salt of (-)HCA (750 mg of pure (-)HCA; Sabinsa's Citrin®) and 300 µg of elemental chromium per day in 55 overweight human subjects resulted in a significant reduction in body weight, blood levels of triglycerides (TG), very low-density lipoprotein (VLDL), and improved LDL:HDL cholesterol ratio (Figure 1). In addition, an

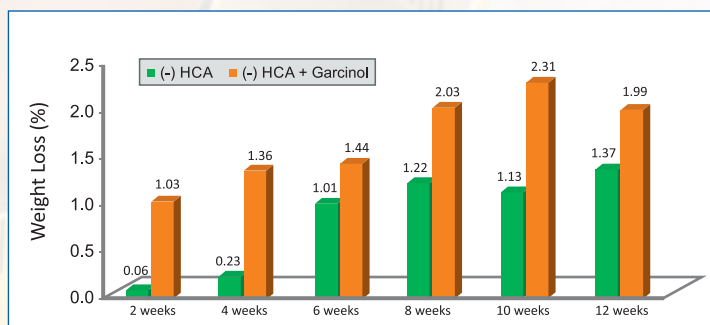


Figure 2 – Effect of (-)HCA and (-)HCA + garcinol on weight loss.

(the sample was Sabinsa's ForsLean®) twice a day. At the end of the study, a significant reduction in the body weight and fat content was observed. Mean lean body mass was found to be increased as compared to the baseline (Figure 4).

Clinical Study 2

In another randomized, double-blind study, 60 overweight male and female volunteers received 250 mg forskolin (the product was ForsLean by Sabinsa) twice daily for 12 weeks. In the active group, a statistically significant reduction in the body weight and body fat was observed, while lean body mass was increased (10).

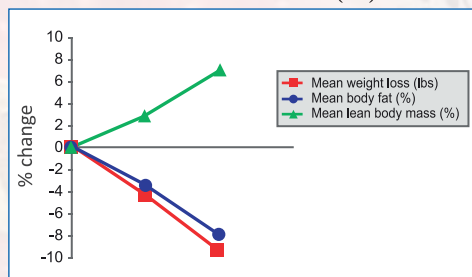


Figure 4 – Effect of forskolin on weight loss, body fat, and lean body mass.

(-)-HCA, GARCINOL, FORSKOLIN, AND PIPERINE: A SYNERGISTIC COMPOSITION

The unique composition of (-)-HCA, garcinol, forskolin, and piperine acts synergistically to manage the level of satiety, improve lean body mass, and support healthy body weight in a natural way.

Each of these natural ingredients acts via different mechanisms, thus complementing each other in the weight management process:

- **(-)-HCA and Garcinol:** Both work via amphibio action to inhibit fatty acid synthesis and lipogenesis, and also to regulate satiety.

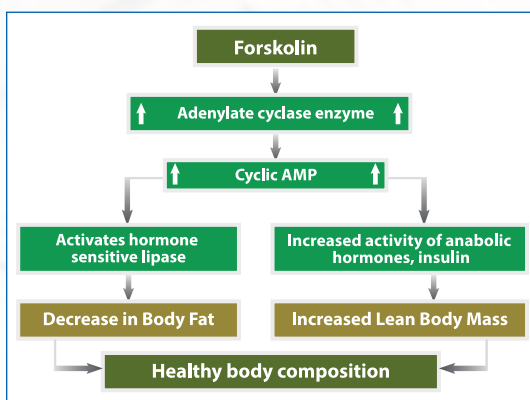


Figure 3 – Mechanism of action of forskolin.

Forskolin: It helps build lean body mass as well as maintain healthy body composition.

- **Piperine:** A natural bioavailability enhancer sourced out of black pepper (*Piper nigrum*) which helps improve absorption of the nutrients (the product is Sabinsa's BioPerine®).

Clinical Study 1

In a double-blind, randomized, placebo-controlled clinical trial, 50 overweight male and female volunteers were advised to take 500 mg of botanical weight management formula (BWMF) (the composition was Sabinsa's LeanGard®) or placebo twice a day for 12 weeks. By the end of the study, a significant change in mean body fat and body weight, and lean body mass (LBM) was observed in the active group in comparison to placebo (Figure 5) (11).



CONCLUSION

In view of growing prevalence of obesity and related health conditions worldwide, a drastic change in the approach to the weight management is highly warranted. Though healthy diet and lifestyle modifications are the cornerstones to attain a healthy weight, natural bioactives that are scientifically validated for body weight management may also significantly contribute to achieving meaningful weight loss.

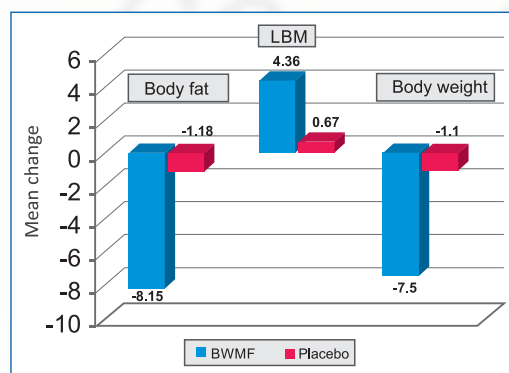


Figure 5 – Effect of BWMF on body weight, body fat, and lean body mass.

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YOUR NEXT CHALLENGE WILL BE MUCH SIMPLER

Sabinsa's wide array of award-winning, patented, natural ingredients will help you focus on making your not-so-secret-dream of shedding that extra flab a reality. Our multifaceted ingredients are clinically proven to support and maintain healthy weight, promote lean body mass, regulate satiety, burn that extra fat and build a healthy body composition, in the most natural way.* Starting with the right ingredients, with proven safety and efficacy, the challenge to re-shape your weight, will be much simpler.

PATENTS: US 5,804,596; CA2281562; EP0977564; US 7,063,861; JP4205943; EP1254209; NZ518116; AU773081

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