Innovative ingredients in support of weight management

INTRODUCTION

Several innovative natural ingredients that support weight management have been discovered and developed by Sabinsa Corporation, a vertically integrated company. Based on their mechanisms of action, these ingredients may be divided into four groups:

- Group A: Citrin® and GarCitrin®;
- Group B: ForsLean®;
- Group C: LeanGard® – combination of GarCitrin® and ForsLean®, plus BioPerine®;
- Group D: Fabenol®;

BIOACTIVE INGREDIENTS

Group A: Citrin® and GarCitrin®

Citrin® and GarCitrin® are extracted from the fruit of the plant *Garcinia cambogia*, which has a long history of use in Indian foods (mostly as an acidulant). The bioactive ingredients of this fruit are Hydroxycitric acid (1) and Garcinol (2) (Figure 1).

Citrin®

Citrin® contains only one of the bioactive ingredients of the *Garcinia cambogia* fruit, namely, Hydroxycitric acid (HCA). HCA is a derivative of citric acid, the agent that gives citrus fruits (oranges, lemons) their characteristic tart flavor. Citrin is standardized for a minimum of 50% HCA (1-3).

Badmaev and Majeed (4) have conducted a clinical study on Citrin®. The design of the clinical study was as follows:

- Duration: 8 weeks, open field, physician-controlled;
- Subjects: 42 women and 13 men;
- Age of Subjects: 20-64 years;
- Daily Dose: 500 mg Citrin® (i.e., 250 mg HCA), 3 times a day (30-60 min. before meals).

Figure 2 shows the effect of daily administration of Citrin® on body weight in this study. As it can be seen, there is a modest decrease in body weight after 8 weeks – equally in females and males.

The most obvious question is about the mechanism of action behind the weight loss. There are two mechanisms involved here: Inhibition of fatty acid synthesis and stimulation of fatty acid oxidation (β oxidation).

As far as inhibition of fatty acid synthesis is concerned, Hydroxycitric Acid has 100 times greater affinity for the enzyme citrate lyase, and, therefore, it acts as a potent inhibitor of citrate lyase. Due to the inhibition of citrate lyase, very little Acetyl CoA and Malonyl CoA are formed; which results in inhibition of fatty acid synthesis. As far as promotion of fat loss via stimulation of fatty acid oxidation (or β oxidation) is concerned, fatty acids are transported into mitochondria by linking with L-carnitine. This linkage is facilitated by L-carnitine transferase. As stated above, in the presence of HCA, Malonyl CoA is not produced. The absence of Malonyl CoA facilitates the β oxidation of fatty acids.

Citrin® also affects appetite. Figure 3 shows the effect of daily administration of Citrin® on relative appetite (self assessment) in this study. The way this effect happens is as follows: The
activation of fat oxidation by HCA in the liver also tends to stimulate gluconeogenesis. This replenishes the stored glycogen storage in liver. The high level of glycogen, as a result of high glucose supply, is translated by the Central Nervous System as state of satiety.

The water-soluble potassium salt of Citrin, Citrin® K, is a self-affirmed GRAS (Generally Recognized As Safe) substance with the recommended use level of up to 2,500 ppm in selected non-alcoholic beverages (4.2 g/day for 70 kg person).

Recently, a meta-analysis of randomized clinical trials on the use of Garcinia extract (Hydroxycitric Acid) as a weight loss supplement was published in the Journal of Obesity (5). The authors of this paper concluded that “Garcinia extracts/HCA can cause short-term weight loss. The magnitude of the effect is small.” This conclusion is compatible with the small or modest weight loss shown in Figure 1. The reason for this observation could possibly be that HCA is poorly absorbed into the cytosol of the target cell, limiting its ability to inhibit citrate lyase. While searching for an effective molecule that facilitates the absorption of HCA into the cytosol, the ingredient Garcinol became the top candidate for consideration.

GarCitrin® contains both bioactive ingredients of the Garcinia cambogia fruit: HCA and Garcinol. Chemically-speaking, Garcinol is a poly-isoprenylated benzophenone. The recommended use level of GarCitrin is 500 mg which contains 250 mg HCA and 25 mg Garcinol – three times a day.

Badmaev, Majeed and Conte (6) compared Citrin® and GarCitrin® (initially called “New Citrin”) in a clinical trial. Design of the clinical study was as follows:
- Patients: 46 overweight healthy women;
- Dose: 500 mg Citrin® or GarCitrin®, three times a day;
- Duration: 12 weeks, double-blind;
- Conditions: no change in diet and exercise;
- Safety parameters: physical exam, pulse rate, blood pressure.

Figure 4 shows percentage of weight loss in groups C (Citrin) and NC (New Citrin, i.e., GarCitrin) in this study. The design of the clinical study was as follows:
- Patients: 46 overweight healthy women;
- Dose: 500 mg Citrin® or GarCitrin®, three times a day;
- Duration: 12 weeks, double-blind;
- Conditions: no change in diet and exercise;
- Safety parameters: physical exam, pulse rate, blood pressure.

Figure 4 shows percentage of weight loss in groups C (Citrin) and NC (New Citrin) (6).

GarCitrin® is more effective than Citrin®, it is postulated that Garcinol modulates regulatory cell signal pathways and, therefore, facilitates the uptake of HCA into the cells.

**Group B: ForsLean®**

ForsLean® is an extract obtained from the dried roots of the plant Coleus forskohlii. Interestingly, Coleus forskohlii roots also have a history of food use in India (as pickle or condiment). Coleus forskohlii has been studied extensively. The most recent review is a book chapter (soon to be published) titled “Coleus forskohlii Extract in the Management of Obesity” written by Dr. Majeed, the Founder and Chairman of Sabinsa Corporation.

The bioactive ingredient of ForsLean® is Forskolin, a Labdane di-terpenoid (Figure 5). ForsLean® is standardized for minimum 10% of the bioactive ingredient Forskolin (20% and 40% strengths are also available). Suggested use level of ForsLean® 10% is 250 mg (which corresponds to 25 mg Forskolin), twice a day, 30 minutes before meals.

As far as clinical trials are concerned, at least seven clinical studies have investigated the efficacy of ForsLean® for weight loss. Although efficacy was the primary purpose of these trials, parameters related to safety were also monitored.

Figure 6 shows results of one of the earliest clinical trials on ForsLean® (7). In this 8-week, pilot open field study, 6 overweight women received 500 mg ForsLean (or 50 mg Forskolin) per day. As it can be seen, after 8 weeks, there was a considerable weight loss and fat loss, and increase in lean body mass.

Figure 7 shows another clinical trial on ForsLean® (8). In this 12-week, double-blind...
and randomized study, 60 obese subjects received 500 mg ForsLean® (50 mg Forskolin) per day. As it can be seen, after 12 weeks, there was 1.73 kg of weight loss in the test group; compared to 0.25 kg of weight gain in the placebo group.

Figure 8 shows yet another clinical trial on ForsLean® (9). In this 12-week, randomized study, 50 male and female subjects received 250 mg of ForsLean or Placebo capsules - twice a day. As shown, after 12 weeks, there is 2.7% weight loss and 1.8% fat loss in the test group; compared to 0.9% and 0.2% for the placebo group. Also, there is 1.8% increase in lean body mass in the test group compared to 0.2% decrease in the lean body mass in the placebo group.

Considering the results of the clinical studies presented above, one may ask “what is the mechanism of action of ForsLean®?”.

Figure 9 graphically shows ForsLean’s mechanisms of action. Forskolin, the bioactive ingredient in ForsLean®, facilitates a cascade of biochemical events in the body. Specifically, Forskolin activates the enzyme adenylate cyclase, the main enzyme involved in the production of cyclic adenosine monophosphate, or cAMP, referred to in the literature as the “second messenger.”

Following the biochemical pathway shown on the right of Figure 9, cyclic AMP facilitates the action of “primary messengers” or various hormonal and bioactive substances in the body (such as insulin and thyrotropin). By facilitating hormonal action, cyclic AMP may contribute to the increase in the metabolic rate and thermogenesis. These events correspond to the buildup of lean body mass.

Following the biochemical path shown on the left of Figure 9, an increase in cyclic AMP leads to the subsequent activation of protein kinase. Protein kinase has been shown to activate the hormone sensitive lipase which is involved in the breakdown of triglycerides – known as building blocks of fatty tissue. These events correspond to the decrease in body fat.

As far as documented Safety is concerned, ForsLean® is well-tolerated, without adverse side effects. ForsLean® at 500 mg/day (50 mg forskolin/day) for up to 12 weeks, produced no significant detrimental effects on biochemistry, hematological parameters, blood pressure or thyroid functions (10).

Group C: LeanGard®

LeanGard® is a proprietary blend of GarCitrin®, ForsLean® and BioPerine® with the suggested use level of 500 mg two times per day. The composition of LeanGard® bioactive ingredients is as follows:

- GarCitrin® (25 to 30% HCA + 2 to 3% Garcinol);
- ForsLean® (4 to 5% Forskolin);
- BioPerine® (0.3 to 0.5% Piperine).

The key point about LeanGard® is that we are combining two different groups of bioactive ingredients with complementary mechanisms of action for weight management. The third ingredient, BioPerine® is a clinically proven, natural bioavailability-enhancer for nutrients. It may also have a role in preventing differentiation of adipocytes. BioPerine® is a standardized extract obtained from black pepper, containing 95-99% piperine and is a self-affirmed GRAS substance with the recommended use level of 5mg/dose.

Majeed et al (11) conducted a clinical trial to investigate the efficacy and safety of LeanGard®. The parameters of the study were as follows:

![Figure 6 – ForsLean Effect on Weight Loss, Body Fat and Lean Body Mass after 4 and 8 weeks (7).](image)

![Figure 7 – ForsLean® Effect on Weight Loss after 12 weeks (8).](image)

![Figure 8 – ForsLean Effect on Weight, Body Content and Lean Body Mass after 12 weeks (9).](image)

![Figure 9 – Mechanism of action of ForsLean®.](image)

![Figure 10 – LeanGard® – Reduction in Body Weight after 12 weeks.](image)
Lean Body Mass after 12 weeks. Fabenol® did not cause any significant changes in blood pressure or heart rate, hematological parameters, liver function, renal function, thyroid function, and plasma lipid levels. Based on the results of the above clinical study, it is concluded that LeanGard® is an effective and clinically safe dietary supplement in support of weight management.

Figure 12 – LeanGard® – % Increase in Lean Body Mass after 12 weeks.

Figure 13 – Seeds of Phaseolus vulgaris and alpha amylase inhibitory action of Fabenol®.

Group D: Fabenol®

Fabenol® is an alpha-amylase inhibitory natural extract obtained from Phaseolus vulgaris (common bean, kidney bean) that blocks the digestion of dietary starch. Alpha amylase catalyzes the hydrolysis of α-(1,4) glycosidic linkages of starch. The alpha amylase inhibitor is identified in the protein fraction of the bean. Fabenol® is not directly involved in the weight loss process. However, it indirectly supports weight loss as it supports the inhibition of sugar formation from starch break down.

Amylase inhibitors also alter the amount and pattern of food intake and reduce weight gain through inducing satiety and increasing carbohydrate delivery to the ileum and colon.

Excess starch in the diet is converted to glucose in the GI tract and upon absorption is converted to fats and stored in the body. An alpha-amylase inhibitor inhibits the digestion of starch thereby potentially improving postprandial carbohydrate tolerance in people with low glucose tolerance. As excess dietary carbohydrate is metabolized to fat, inhibition of carbohydrate digestion helps in weight management.

An amylase inhibitor obstructs the digestion of starch and absorption of glucose. Therefore amylase inhibitors are valued in conditions such as diabetes (to reduce blood sugar levels) and in weight management. Since the alpha-amylase inhibitor protein binds with the active sites of alpha-amylase and prevents its starch degradation activity, it is also called “Starch Blocker”.

Figure 13 shows seeds of Phaseolus vulgaris and Fabenol’s alpha amylase inhibitory action. Fabenol® is offered in two strengths: Standard Fabenol® (each gram prevents digestion of 120 grams starch) and Fabenol® Max (each gram prevents digestion of 300 grams starch). The recommended dose of Fabenol® is 2.5 to 3.75 g before meals and for Fabenol® Max is 1 to 1.5 g before meals.

CONCLUSION

Sabinsa Corporation, a science-driven, vertically integrated company, has discovered and developed several innovative natural ingredients (Citrin®, GarCitrin®, ForsLean®, LeanGard® and Fabenol®) in support of weight management. These patented ingredients which have shown safety and efficacy in clinical trials, may only be considered complementary to, not substitute for, sensible diet and exercise.

REFERENCES

1) Conte AA. The Bariatrician 1993; Summer: 17-19.
6) Badmaev V., Majeed M., Conte A. “Weight loss as a result of consumption of Citrin® can New Citrin® to be published.