LEAN + GREEN TEA

white paper provided by Archmore Botanical Research Group, LLC

A Javita International product



Lean + Green Tea

a Javita International product

• A technical overview outlining the safety and efficacy of Lean + Green Tea, a dietary supplement

designed to support healthy weight management *

- This technical white paper will include:
 - o Formulation breakdown
 - Synopsis of health benefits associated with the proprietary ingredients
 - o Efficacy
 - Cellular, animal, and human trials demonstrating weight management
 - A review of any known negative outcomes found in clinical trials involving the proprietary ingredients
 - Potential secondary health benefits outside the scope of weight management
 - Safety
 - In vitro and in vivo trials demonstrating safety of ingredients in Lean + Green

Tea at recommended levels

- A review of any adverse events associated with the ingestion of the proprietary ingredients
- Recommended guidelines for use
 - Dosing recommendations for supporting weight management
 - Potential adverse events and warnings

*These statements have not been evaluated by the Food and Drug Administration and are meant for research purposes only.



Overview

The epidemic of obesity is a staggering one that continues to rise throughout much of the civilized world. This condition, although debilitating itself, leads to several far more serious conditions, such as cardiovascular issues, high blood pressure, diabetes, stroke, and even some cancers. However, by addressing the weight issue first, many of these deadly conditions may be prevented. Scientists and medical professionals have made it their mission to reverse this condition, discovering new remedies that assist in weight loss. Lean + Green Tea is the product of much of this research.

Designed to not only stimulate weight loss itself, Lean + Green Tea has additional powerful properties that help in weight management. It was designed to reduce appetite as well as those pesky food cravings that seem to increase when one is trying to lose weight. By reducing the cravings and the appetite, calorie reduction can more easily be achieved. Along with this, Lean + Green Tea also works inside the body to help prevent the conversion of excess carbohydrates into fat. By reducing the excess fat storage, Lean + Green Tea allows for more energy to burn and less fat to try to work off later. Finally, it targets blood sugar homeostasis as well, helping better regulate sugar processing for added fat storage reduction and reduced weight gain.

This white paper will review the available scientific evidence to support the formulation and use of Lean + Green Tea as a weight management product. It will provide an overview of how the ingredients work both in vitro as well as in the body. For those wishing to pursue information further, a highly detailed review of the studies is also provided in this paper along with available citations for further reading. This paper is meant to assist in the education of consumers to determine the best weight management product for their needs. It is not meant to diagnose or treat, or be used in place of medical advice.



Formulation

Lean + Green Tea was designed with the non-coffee drinker in mind. It is based on green tea, a delicious alternative to coffee, that still provides the kick dieters are looking for to improve their energy levels while they are reducing caloric intake. In addition to a green tea base, Lean + Green Tea also includes two powerful herbal ingredients at efficacious doses to help reduce appetite and minimize food cravings many dieters experience while trying to reduce weight. These ingredients are *Garcinia cambogia* and *Gymnema sylvestre*. In addition to the reduction in appetite and cravings, these herbs also help stimulate weight loss itself through definable mechanisms that work well in beverage form.

- Formulation includes two key herbal ingredients for enhanced efficacy of green tea
- Garcinia cambogia provides naturally occurring hydroxycitric acid (HCA)
 - HCA plays a role in inhibiting the conversion of carbohydrates to fat in the body
 - o HCA contributes to an increase in available energy for calorie burning
 - HCA increases serotonin levels, assisting in the reduction of emotional overeating and craving reduction
- Gymnema sylvestre
 - Assists in suppressing appetite and sweet cravings
 - o Assists in blood sugar regulation by reducing glucose absorption



Garcinia cambogia- overview

Garcinia cambogia, also known as Malabar tamarind, has been consumed by indigenous people throughout Southeast Asia for centuries. It is used as a food and flavor enhancer but has widespread anecdotal evidence of providing satiation to the consumer, a feeling of fullness after consumption. Because of this effect, researchers began studying the fruit to determine its usefulness in weight management. It was during this research that scientists determined that the naturally occurring chemical hydroxycitric acid (HCA) is the main active constituent providing weight loss potential.

HCA is a non-essential nutrient that is known for its ability to inhibit the enzyme ATP-dependent citrate lyase, which plays a role in the transformation of carbohydrates into fat in the body. It does this by competitively blocking the enzyme as it works to convert leftover glucose into adipocytes (fat cells), a storage mechanism utilized to supply energy at a later date. By blocking this conversion, excess glucose is no longer stored in fat cells and remains available for the body to use as energy. This is how *G. cambogia* provides an increase in energy levels without containing a "stimulant", like natural caffeine. An increase in available energy may also assist in increased exercise potential and output, further assisting in weight management benefits.

In addition, HCA has been shown to increase serotonin levels. Serotonin is a hormone naturally produced in the body which assists in regulating mood. Researches have determined that, in many cases, overeating is directly related to emotions and mood. In cases of depression and anxiety, serotonin levels are dramatically reduced. Thus, by increasing serotonin production, negative emotions are diminished, and emotional overeating is markedly reduced.





Gymnema sylvestre- overview

Gymnema sylvestre is an herb found throughout the tropical rain forests of southern and central India as well as parts of Sri Lanka. It is commonly referred to as *cowplant* or *gurmar*, which is translated from Hindi to be "sugar destroyer". This is because for over two millennia, *Gymnema sylvestre* has been used in Ayurvedic medicine for balancing blood sugar levels and treating diabetes. Although this effect is mainly carried out inside the digestive system of the body, gymnema has an interesting side effect on sugary foods when they are eaten. Researchers noted that natives would chew this plant to help eliminate cravings for sweet foods, an effect that lasts for several hours. Scientists believe it is the herb's ability to block sugar receptors that provides the benefit. They further discovered these same receptors in the gut; therefore, by taking gymnema in supplement form, this same craving suppression can be achieved.

Several compounds known as triterpenoid saponins found in this herb play a role in body systems dealing with blood sugar. Gymnema extracts have been shown to help balance blood sugar after food consumption by reducing the absorption of glucose in the intestine as well as reducing the production of glucose by the liver. This is beneficial not only for those individuals suffering from compromised blood sugar regularity, such as in type-2 diabetes mellitus, but also in those individuals looking to lose weight. By maintaining healthy blood sugar levels, excess blood sugar will be reduced and thus not converted and stored as fat.

<u>Safety</u>

- Lean + Green Tea was designed such that a single cup daily could produce results, but that multiples cups would maintain safety parameters.
- All safety studies outlined below are relevant to the dosages recommended for Lean + Green
 Tea
- Adverse safety and toxicity trials are also reviewed

Garcinia Cambogia- safety

Garcinia cambogia, also known as the Malabar tamarind from which HCA is extracted and supplied in Burn + Control Coffee, has no known serious side effects, particularly at dosages commonly associated with supplements and beverages. *G. cambogia* has been consumed in high quantities as a food product for several decades in Southeast Asia, and thus is usually considered safe. However, when formulating with an extract of an herbal product, additional safety studies must be conducted before that ingredient can be considered safe for human consumption.

In early research on *Garcinia cambogia*, and specifically the extract of HCA found in Burn + Control Coffee, Preuss et al. determined that in a standard 90-day toxicity study, no remarkable toxicity results were detected. They then moved on to clinical trial using 60 human volunteers. They demonstrated that no adverse effects were reported, nor were any negative physical changes in the parameters measured. Researchers concluded that HCA is safe and effective in this highly bioavailable form [1]. Marquez, et al. conducted a thorough examination in 2012 of the available published research to date for *Garcinia cambogia*, and more specifically extracts standardized to hydroxycitric acid (HCA), with regards to safety and efficacy in humans. They concluded that except in extremely rare cases, the research proved that *G. cambogia* does not increase mortality nor toxicity, and that no significant differences have been reported in terms of side effects or adverse events in humans treated with *G. cambogia* versus control [2]. Although still considered a food additive or herbal supplement and thus not granted GRAS status (Generally Recognized As Safe- a designation awarded by the FDA), it is assumed that *G. cambogia* is considered a relatively safe herbal product even at higher dosages than those found in Burn + Control Coffee.

Further confirmation of these findings was reported in a separate review of available literature conducted by Li Oon Chuah and colleagues. Chuah concluded that even at levels up to 2800mg/day, *G. cambogia* did not show adverse effects, suggesting its safety for use as a food ingredient or supplement [3].

More recently, HCA from Garcinia was tested for adverse effects in the liver. It was determined that HCA does not promote inflammation or hepatotoxicity but that it actually reduces markers of inflammation in the brain, intestines, kidney and serum [4].



Adverse Events in Clinical Trials: A Review

A controversial dose dependent animal trial was conducted in 2005 to determine the "no observed adverse effect level" (NOAEL) of *Garcinia cambogia* extract standardized to HCA content. Although the highest dosages of 154 mmol/kg showed a suppression of epididymal fat accumulation in developing obese male rats, a potent testicular atrophy and toxicity was observed. This same toxicity was not observed in diets containing a third of this dose HCA. There, a lower NOAEL was reported and is recommended when formulating with this ingredient [5].

However, K. Hayamizu, et al. conducted a more recent study to evaluate the specific effect of *Garcinia extract* on serum sex hormones in overweight human subjects. In Hayamizu's double blind placebo controlled trial, researchers conclusively determined that dosages of 1000mg of HCA per day over 12 weeks had no significant effect on serum testosterone, estrone, or estradiol levels. In addition, hematology, serum triacylglycerol and serum clinical pathology parameters did not reveal any significant adverse effects. Hayamizu concluded that as dosages commonly recommended for human consumption, *Garcinia cambogia* extract (HCA) does not affect serum sex hormone levels and blood parameters [6].

It must be noted that studies have not been conducted on pregnant or nursing women nor on children; thus care should be exercised when taking any herbal supplements if in these categories of individuals [7].



Gymnema sylvestre- safety

Gymnema has been used for centuries in Ayurvedic medicine, mainly for its ability to assist in blood sugar regulation and weight management. However, as modern medicine has adopted its use due to the positive outcomes in trials, toxicology research had to be completed to determine this herb's safety. In a detailed, prolonged toxicology study, *Gymnema sylvestre* was dosed daily over 52 weeks in both genders of Wistar rats, the standard for measuring toxicity in humans. Graded doses of extract ranging from 0.01, 0.10 and 1.00% of diet were used. General conditions were recorded daily. Body weights and food consumptions were recorded weekly. At 26 weeks an intermediate examination took place, and then again at 52 weeks, a final examination was conducted. During the trial period, no animals died. There were also no exposure-related changes in body-weight, in food consumption, in hematological examinations, or in serum biochemical examinations. Therefore researchers concluded that there are no toxic effects up to 1.00% of diet for 52 weeks. The no-observable-effect level from this study was 1.00%, which translates to 504mg/kg/day for male rats and 563mg/kg/day for female rats [8]. Translated into human figures, the no-observable effect doses would be between 5 and 5.5 grams per day of gymnema extract, a dose that far exceeds several cups of Lean + Green Tea.

In addition, in animal trials measuring the anti-obesity effect of gymnema, researchers noted histopathological studies of tissues showed no pathological changes [9].

Adverse Events in Clinical Trials: A Review

In one animal study that evaluated different types of gymnema extract for hypoglycemic and antihyperglycemic potential, researchers administered extracts alone or in combination with a popular prescription drug, glimepiride, used to treat type 2 diabetes. The extracts alone showed safe and potent hypoglycemic and antihyperglycemic activities without creating severe hypoglycemia in normal rats. However, when the extract was administered at the highest dose of 200mg/kg body weight along with 10-20 mg/kg of glimepiride, lethal hypoglycemia was induced in normal rats. Translated to human dosages, this would be equivalent to almost 2 grams of gymnema in combination with 100-200mg of glimepiride [10]. Although it would be impossible to consume this much gymnema following the recommended doses of Lean + Green Tea, care should be exercised if an individual is taking glimepiride for type-2 diabetes. Individuals being treated with this prescription should consult their primary physician prior to consuming Lean + Green Tea.

Formulation Efficacy

Lean + Green Tea contains two powerful herbal ingredients that work in multiple ways to reduce weight. Outlined below are the mechanisms of action conclusively defined in the available published literature. In some cases, mechanisms of action outside the scope of weight management were discovered. For the purposes of this paper, these mechanisms will not be addressed. Should any potentially negative outcomes in clinical trials be discovered, they are presented here as well, and potential rationale for these outcomes are discussed.

- Garcinia cambogia
 - Competitively inhibits citrate lyase to prevent the formation of fat cells
 - Increases energy
 - o Increases serotonin levels to reduce emotional overeating
- Gymnema sylvestre
 - Maintains blood sugar homeostasis through glucose suppression
 - Suppresses sweet receptors to perceive sensation of sweet

Garcinia cambogia- efficacy

Mechanism of Action: competitively inhibits citrate lyase to prevent excess fat cell formation

Garcinia cambogia extract standardized for HCA content has been extensively studied for its use in weight management. This is primarily due to the mechanism of action of the HCA itself, namely competitively inhibiting the enzyme that converts excess carbohydrates into fat in the body [11]. In the metabolic processes of the body, a particular enzyme called ATP-dependent citrate lyase is necessary to catalyze the cleavage of citrate to oxaloacetate and acetyl-CoA. This cleavage, or separation, is necessary for lipogenesis, or the formation of fat cells. If the enzyme is inhibited, lipogenesis is also inhibited. Therefore, it has been hypothesized and later shown in cellular and animal trials that *G. cambogia*/HCA can in fact competitively inhibit extra-mitochondrial citrate lyase and reduce the formation of fat cells [12].

Another study by Roy et al., utilized female human subcutaneous preadipocytes collected from obese women which were then differentiated to adipocytes (fat cells) for 2 weeks in culture. This allowed researchers to test the effect of HCA on lipid metabolism as well as study the genetics involved in this process. It was determined that HCA significantly down regulated (or reduced) the expression of fat- and obesity-related genes, supporting the antilipolytic and antiadipogenic effects of HCA from *G. cambogia*. In other words, HCA was shown to prevent the expression of obesity-related genes as well as the formation of fat cells, reducing weight and improving long term health [13].

Mechanism of Action: Increases energy

The second known mechanism of action for *Garcinia cambogia* (HCA) may be directly related to its ability to inhibit citrate lyase, as outlined above. The outcome of this action is the reduced formation of fat storage cells from glucose. Therefore, excess glucose remains available in the body to be used as an energy source. Having excess glucose readily available in the body should produce a rise in energy, allowing for the opportunity to burn excess calories. Researchers were able to scientifically demonstrate this property by showing that HCA is capable of activating hypoxia inducible factor (HIF). This is a transcription factor involved in energy metabolism and, when activated, increases the burning of energy [14].

Energy is also available for use due to *G. cambogia's* ability to assist in fat oxidation. In human clinical trials, urinary fat metabolites significantly increased in subjects taking HCA over an 8 week trial period. Urinary fat metabolites are a biomarker of fat oxidation. If fat is being oxidized, it is being released from its dormant state to be used as energy in the body. Thus weight reduction is achieved through increased energy expenditure as fat is oxidized [15].

A pleasant side effect of HCA is the decrease in oxidative stress, inflammation, and insulin resistance associated with obesity [16]. This is a synergistic effect with the other proprietary ingredient and will be discussed in further depth with regards to Yerba mate.

Mechanism of Action: Increases serotonin to diminish emotional overeating

With obesity being a global health epidemic, billions of dollars and countless hours of research have been spent to determine the cause. One of the main causes of obesity and overweight is overeating due to emotional stressors, such as depression and anxiety. Although a highly complex relationship, researchers have shown that various moods can enhance or diminish eating primarily due to a subject's unique response to pleasure and gratification. For example, eating a particular food may stimulate the production of dopamine, a special excitatory neurotransmitter that helps with depression and focus. Dopamine activates the pleasure center of the brain and enlists the subject to continue to consume this food to experience the positive feeling of gratification that dopamine provides. This repetitive behavior is extremely strong and can override other signals, such as satiety and hunger. Thus a gratification habit may be formed leading to overeating and obesity. The effect of the individual's mood can also play a role in the gratification. If the individual is stressed, anxious, or depressed, they may seek gratification by eating foods known to previously stimulate their pleasure centers, thus providing relief from the stressor, albeit for a short period of time. This is known as "stress- or emotional- overeating" [17].

Serotonin is an inhibitory neurotransmitter, which means that it does not directly stimulate the brain. Adequate amounts are necessary for stabilizing mood and balancing the excitatory neurotransmitters, such as dopamine, that are firing in the brain. As emotional-overeating has been linked to a desire for dopamine release, it was hypothesized that an increase in serotonin production should help assuage this desire for pleasure and gratification from eating. This was tested in animals by measuring body weight and abdominal fat gene expression profile after consuming *G. cambogia* extract (HCA). By conducting genetic assays on fat leptin expression as well as physical measurements on body weight, researchers were able to show that HCA is effective in restricting body weight gain, and that it does so through the upregulation of genes encoding serotonin receptors [18].

Furthermore, these same researchers went on to publish data postulating that this mechanism also contributed to a feeling of satiety (fullness) as a direct result of HCA supplementation [19]. This two prong approach shows the neurological benefits of HCA for managing weight through the reduction of emotion overeating and increasing satiety [20].

Garcinia cambogia: a review of negative outcomes from clinical trials

Although the majority of the published cellular, animal, and human studies show *Garcinia cambogia* (HCA) to be highly effective for weight management, there has been a human trial published in the highly reputable Journal of the American Medical Association that attempts to show the opposite. In this randomized controlled trial, 135 subjects received HCA or placebo for twelve-weeks. Following the trial, there were no significant differences estimated between the two groups in terms of body fat mass loss [21].

There have been over sixteen years' worth of additional clinical testing on *Garcinia cambogia* since this study was published, the majority of which have found significant improvements in body weight and fat loss, as outlined earlier in this white paper. However one particular study cited the JAMA article, noting that there was a flaw in the study design that eliminated the positive results other have seen. They claim that because researchers administered a high-fiber, low-energy diet, HCA absorption was impaired and thus did not have a significant effect in the body [22]. Although the precise reason remains unknown, researchers have shown that administering HCA on an empty stomach or prior to feeding, achieved optimal reduction in hepatic lipid synthesis [23].



Gymnema sylvestre-efficacy

Mechanism of Action: Maintains blood sugar homeostasis through glucose suppression

Homeostatis is a condition of balance, and *Gymnema sylvestre* has the ability to balance blood sugar in the body [24]. It does this through two means- decreasing glucose absorption in the intestine and reducing glucose production in the liver. Through various trials, researchers have determined that gymnema is able to suppress glucose uptake in the intestine. In one such trial, researchers examined several different plant fractions containing triterpenoid saponins, known as gymnemic acids, and how they affected glucose transport through the muscles of the intestine. By observing lower levels of blood glucose after administration of these fractions, researchers determined gymnemic acid inhibits glucose uptake by the intestine [25]. This mechanism was duplicated in another study showing the inhibitory affect gymnemic acid also has on oleic acids in the intestine as well, another beneficial therapy for diabetes and obesity [26].

The other side to this equation is the reduction of glucose production. In multiple studies involving diabetic rats, gymnema extract was administered for a prolonged period of time. Not only were several parameters reduced that normally lead to obesity, glucose itself was significantly reduced. This is one of the leading causes of overweight and obesity . Researchers concluded in all studies that gymnema extract could be a very useful intervention for the treatment of obesity as well as type-2 diabetes mellitus through the suppression of glucose production. The other improvements were seen in visceral fat pad, mean arterial pressure, heart rate, serum leptin, and apolipoprotein B, to name a few. [27, 28, 29].

Another study took these results a step further to determine a precise mechanism for this glucose reduction. By administering various levels of gymnema extract against glucose load, they were able to measure Dipeptidyl peptidase-4 (DPP-4) inhibitors; these inhibitors are the emerging class of antidiabetic agents currently used in modern medicine. They found that at all gymnema doses administered, DPP-4 was inhibited through an increase in plasma active glucagon-like peptide-1 (GPL-1), a potent antihyperglycemic hormone that induces glucose-dependent stimulation of insulin secretion while suppressing glucagon secretion. Following a complex biochemical pathway, GLP-1 also contributes to a satiating effect [30].



Researchers then determined that gymnema also has a protective effect prior to the glucose load. By administering gymnema extract 30 minutes before an intraperitoneal glucose load, they were able to significantly improve their glucose tolerance. These promising results demonstrate the use of gymnema as a potential therapy for hyperglycemia associated with obesity-related type-2 diabetes mellitus [31]. Therefore, gymnema may be used as both a weight gain preventative to keep the weight off in addition to enhancing the weight loss itself.

Although mechanism of action is demonstrated internally in these studies, other studies investigated the more visible external results with regards to weight management. One study showed a significant reduction in food and water intake along with a reduction in body weight by animals supplemented with gymnema extract. The researchers felts it was gymenma's ability to reduce hyperlipidemia that lead to this significant weight loss. They also saw no withdrawal rebound effect once gymnema was removed from the diet, meaning these were maintainable results that were acheived [32]. Similar results were seen in a separate independent study, where animals were supplemented with gymnema for a period of eight weeks. Body weight was significantly decreased as was food consumption itself. Also reduced were levels of triglycerides, total cholesterol, low-density lipoproteins, while levels of high-density lipoproteins were increased [33].

Mechanism of Action: Suppresses sweet receptors to perceive sensation of sweet

Sweet cravings generally drive consumers to over-indulge in foods that are not going to contribute positively to weight loss. In fact, many sweet foods will convert rapidly into fat in the body, thus causing over-weight and obesity. Gymnema contains many compounds that actually help to suppress the sensation of sweet. These compounds include gymnemic acids, gymenmasaponins, and the polypeptide gurmarin [34]. Many native peoples will chew gymnema leaves to help alleviate cravings during the day, an effect that lasts up to about 2 hours [35].

However it is not simply the taste buds that drive sweet cravings. These same taste receptors are also expressed in the gut where they are involved in intestinal absorption, metabolic regulation, and glucose homeostasis. Therefore, by suppressing the sweet taste receptors on the tongue and in the gut, gymnema has the ability to reduce those cravings for sweet foods, helping with weight management [36].

Phone: 281-360-7282 Fax: 713-583-8615 archmorebotanical@gmail.com www.archmorebotanical.com In animal studies, nerve responses to various taste substances before and after treatment with gymnema extracts have shown the selective suppression of responses to sucrose without affecting responses to NaCl (salt), HCO, and quinine; thus, only sweet response was suppressed, and this response was found to be reversible; therefore, no permanent taste changes were seen [37].



Gymnema sylvestre: a review of negative outcomes from clinical trials

An interesting meta-analysis was conducted on all publications through the end of 2012 that used acceptable human clinical trials to analyze natural supplements used to suppress appetite for obesity control and management. Of the thousands of available studies, only 14 were found to meet the strict inclusion criteria these particular researchers set for their analysis- among these were randomized, double blind, placebo controlled design, sample size >20, and measurable outcomes on appetite or food intake. The research revealed that while most contained inconclusive evidence that plant extracts are effective in reducing body weight through appetite suppression, only the unique combination of Garcinia cambogia and Gymnema sylvestre showed weight loss directly linked to appetite suppression [38]. This limited, although positive result, could be due to the strict inclusion criteria the researchers randomly assigned for their analysis or from the subjective measurement of appetite suppression. While food intake itself is often indicative of appetite suppression, in human subjects this may not always be the case. Availability of food, time management, and forgetfulness are also factors that may lead to a reduction in calories consumed during the day, not just appetite suppression. Therefore, lifestyle and daily events need to also be considered when determining appetite suppression. In regards to Lean + Green Tea, however, this study is actually a positive one, as it conclusively demonstrates that the unique combination of Garcinia cambogia and gymnema do indeed suppress appetite for weight management.

Usage Guidelines

As there are varying degrees of weight loss desired by consumers, a personalized weight management program should be designed on a case by case basis. However, for the purposes of Lean + Green Tea, it is advised to consume 1-3 cups per day to achieve results. This is based on the available research and proven efficacy of the active ingredients at these recommended dosages. This should be combined with a healthy diet and exercise routine to achieve optimal results.

By taking this product in combination with diet and exercise, a reduction is weight should be experienced by most individuals, along with a reduction in cravings and appetite. Once optimal weight is achieved, Lean + Green Tea may continue to be consumed for these added benefits to help manage the weight and minimize cravings.

As noted in this white paper, safety studies were conducted using doses of the herbal ingredients much higher than those provided in Lean + Green Tea, even when multiple cups are consumed per day. Therefore, consuming even 1-3 cups of this tea should yield health benefits without negative safety concerns. However, should you be under the care of a physician for any ailment, but specifically for type-2 diabetes, consult your physician before consuming Lean + Green Tea to insure there will not be an interaction with any medications.

As this tea contains caffeine, it is best to consume it earlier in the day so as not to disturb sleep patterns. In addition, by consuming the tea on an empty stomach, the benefits of HCA are markedly increased, although they are still present even when consumed after a meal.

As always, pregnant and nursing women as well as children should consult their health care professional before beginning any supplement program, particularly caffeine-containing products.

Should adverse effects be felt when consuming any new supplement, discontinue use and contact your healthcare professional immediately.



Citations

- 1. Preuss HG, Rao CV, Garis, R, et al. An overview of the safety and efficacy of a novel, natural(-)hydroxycitric acid extract (HCA-SX) for weight management. J Med. 2004;35(1-6):33-48.
- Marquez F, Babio N, Bullo M, Salas-Salvado J. Evaluation of the safety and efficacy of hydroxycitric acid or Garcinia cambogia extracts in humans. Crit Rev Food Sci Nutr. 2012;52(7):585-94
- 3. Chuah LO, Yeap SK, Ho WY, Beh BK, Alitheen NB. In vitro and in vivo toxicity of Garcinia or hydroxycitric Acid: a review. Evid Based Complement Alternat Med. 2012; 2012: 197920
- 4. Clouatre DL, Preuss HG. Hydroxycitric acid does not promote inflammation or liver toxicity. World J Gastroenterol. 2013 Nov 28;19(44):8160-2
- 5. Saito M, Ueno M, Ogino S, Kubo K, Nagata J, Takeuchi M. High dose of Garcinia cambogia is effective in suppressing fat accumulation in developing male Zucker obese rats, but highly toxic to the testis. Food Chem Toxicol. 2005 Mar; 43(3):411-9
- 6. Hayamizu K, Tomi H, Kaneko I, Shen M, Soni MG, Toshino G. Effects of Garcinia cambogia extract on serum sex hormones in overweight subjects. Fitoterapia. 2008 Jun;79(4):255-61
- 7. Preuss HG, Rao CV, Garis, R, et al. An overview of the safety and efficacy of a novel, natural(-)hydroxycitric acid extract (HCA-SX) for weight management. J Med. 2004;35(1-6):33-48.
- 8. Ogawa Y. Gymnema sylvestre leaf extract: a 52-week dietary toxicity study in Wistar rats. Shokuhin Eiseigaku Zasshi. 2004 Feb;45(1):8-18.
- 9. Kumar V. Anti-obesity effect of Gymnema sylvestre extract on high fat diet-induced obesity in Wistar rats. Drug Res (Stuttg). 2013 Dec;63(12):625-32.
- Yadav M. Complementary and comparative study on hypoglycemic and antihyperglycemic activity of various extracts of Eugenia jambolana seed, Momordica charantia fruits, Gymnema sylvestre, and Trigonella foenum graecum seeds in rats. Appl Biochem Biotechnol. 2010 Apr;160(8):2388-400
- Seifert SM, Seifert SA, Schaechter JL, Bronstein AC, Benson BE, Hershorin ER, Arheart KL, Franco VI, Lipshultz SE. An analysis of energy-drink toxicity in the National Poison Data System. Clin Toxicol. 2013 Aug;51(7):566-74
- Heymsfield SB, Allison DB, Vasselli JR, Pietrobelli A, Greenfield D, Nunex C. Garcinia cambogia (hydroxycitric acid) as a potential antiobesity agent: a randomized controlled trial. JAMA 1998 Nov 11;280(18):1596-600
- Marquez F, Babio N, Bullo M, Salas-Salvado J. Evaluation of the safety and efficacy of hydroxycitric acid or Garcinia cambogia extracts in humans. Crit Rev Food Sci Nutr. 2012;52(7):585-94
- 14. Roy S, Shah H, Rink C, Khanna S, Bagchi D, Bagchi M, Sen CK. Transcriptome of primary adipocytes from obese women in response to a novel hydroxycitric acid-based dietary supplement. DNA Cell Biol. 2007 Sep;26(9):627-39
- 15. Roy S, Shah H, Rink C, Khanna S, Bagchi D, Bagchi M, Sen CK. Transcriptome of primary adipocytes from obese women in response to a novel hydroxycitric acid-based dietary supplement. DNA Cell Biol. 2007 Sep;26(9):627-39
- 16. Preuss HG, Rao CV, Garis, R, et al. An overview of the safety and efficacy of a novel, natural(-)hydroxycitric acid extract (HCA-SX) for weight management. J Med. 2004;35(1-6):33-48.



Providing research solutions to the wellness industry

- Asghar M, Monjok E, Kouamou G, Ohia SE, Bagchi D, Lokhandwala MF. Super CitriMax (HCA-SX) attenuates increases in oxidative stress, inflammation, insulin resistance, and body weight in developing obese Zucker rats. Mol Cell Biochem. 2007 Oct; 304(1-2):93-9
- 18. Singh M. Mood, food, and obesity. Front Psychol. 2014; 5: 925
- Roy S, Rink C, Khanna S, Phillips C, Bagchi D, Bagchi M, Sen CK. Body weight an abdominal fat gene expression profile in response to a novel hydroxycitric acid-based dietary supplement. Gene Expr. 2004;11(5-6):251-62
- 20. Bagchi M, Zafra-Stone S, Sen CK, Roy S, Bagchi D. DNA microarray technology in the evaluation of weight management potential of a novel calcium-potassium salt of (-)-hydroxycitric Acid. Toxicol Mech Methods. 2006;16(2-3):129-35
- 21. Downs BW, Bagchi M, Subbaraju GV, Shara MA, Preuss HG, Bagchi D. Bioefficacy of a novel calcium-potassium salt of (-)-hydroxycitric acid. Mutation Research. 2005;579(1-2):149-162
- Heymsfield SB, Allison DB, Vasselli JR, Pietrobelli A, Greenfield D, Nunex C. Carcinia cambogia (hydroxycitric acid) as a potential antiobesity agent: a randomized controlled trial. JAMA. 1998 Nov 11;280(18):1596-600
- 23. Chuah LO. Ho WY. Beh BK. Yeap SK. Updates on antiobesity effect of Garcinia origin (-)-HCA. Evid Based Complement Alternat Med. 2013;2013:751658
- 24. Bhansali S. Effect of a deacyl gymnemic acid on glucose homeostasis & metabolic parameters in a rat model of metabolic syndrome. Indian J Med Res. 2013 Jun;137(6):1174-9.
- 25. Shimizu K. Suppression of glucose absorption by some fractions extracted from Gymnema sylvestre leaves. J Vet Med Sci. 1997 Apr;59(4):245-51.
- 26. Wang LF. Inhibitory effect of gymnemic acid on intestinal absorption of oleic acid in rats. Can J Physiol Pharmacol. 1998 Oct-Nov;76(10-11):1017-23.
- 27. Kumar V. Protective Effect of Gymnema sylvestre Ethanol Extract on High Fat Diet-induced Obese Diabetic Wistar Rats. Indian J Pharm Sci. 2014 Jul;76(4):315-22.
- 28. Kumar V. Evaluation of antiobesity and cardioprotective effect of Gymnema sylvestre extract in murine model. Indian J Pharmacol. 2012 Sep-Oct;44(5):607-13.
- 29. Al-Romaiyan A. A novel extract of Gymnema sylvestre improves glucose tolerance in vivo and stimulates insulin secretion and synthesis in vitro. Phytother Res. 2013 Jul;27(7):1006-11.
- 30. Kosaraju J. A molecular connection of Pterocarpus marsupium, Eugenia jambolana and Gymnema sylvestre with dipeptidyl peptidase-4 in the treatment of diabetes. Pharm Biol. 2014 Feb;52(2):268-71.
- 31. Al-Romaiyan A. A novel extract of Gymnema sylvestre improves glucose tolerance in vivo and stimulates insulin secretion and synthesis in vitro. Phytother Res. 2013 Jul;27(7):1006-11.
- 32. Luo H. Decreased bodyweight without rebound and regulated lipoprotein metabolism by gymnemate in genetic multifactor syndrome animal. Mol Cell Biochem. 2007 May;299(1-2):93-8.
- 33. Reddy RM. The saponin-rich fraction of a Gymnema sylvestre R. Br. aqueous leaf extract reduces cafeteria and high-fat diet-induced obesity. Z Naturforsch C. 2012 Jan-Feb;67(1-2):39-46.
- 34. Tiwari P. Phytochemical and pharmacological properties of Gymnema sylvestre: an important medicinal plant. Biomed Res Int. 2014;2014:830285.
- 35. Lemon, CH; Imoto, T; Smith, DV (2003). "Differential gurmarin suppression of sweet taste responses in rat solitary nucleus neurons". Journal of neurophysiology 90 (2): 911–23.
- Sigoillot M. Sweet-taste-suppressing compounds: current knowledge and perspectives of application. Appl Microbiol Biotechnol. 2012 Nov;96(3):619-30.



- 37. Ninomiya Y. Gurmarin inhibition of sweet taste responses in mice. Am J Physiol. 1995 Apr;268(4 Pt 2):R1019-25.
- Astell KJ. Plant extracts with appetite suppressing properties for body weight control: a systematic review of double blind randomized controlled clinical trials. Complement Ther Med. 2013 Aug;21(4):407-16.

