BURN

A Dollar Coffee Club Product

white paper provided by Archmore Botanical Research Group, LLC
2018

Burn

a Dollar Coffee Club product

A technical overview outlining the safety and efficacy of Burn, an encapsulated dietary supplement designed to support healthy weight management*.

This technical white paper will include:

- Formulation breakdown
  - Synopsis of health benefits associated with the proprietary ingredients
- Efficacy
  - Cellular, animal, and human trials demonstrating weight management benefits
  - A review of any negative outcomes found in clinical trials using 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 Burn capsules at recommended levels
  - A review of any adverse events associated with the ingestion of the proprietary ingredients
- Recommended guidelines for use
  - Dosing recommendations for 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.*

Phone: 281-360-7282
Fax: 713-583-8615
archmorebotanical@gmail.com
www.archmorebotanical.com

TABLE OF CONTENTS

Phone: 281-360-7282
Fax: 713-583-8615
archmorebotanical@gmail.com
www.archmorebotanical.com

Product Overview

Obesity and overweight are growing epidemics for much of the civilized world, leading to chronic diseases commonly associated with this health condition, such as cardiovascular issues, high blood pressure, diabetes, stroke, and potentially cancer. Preventing or reversing this debilitating condition has been the focus among complementary and alternative medicines, particularly within the nutraceutical and functional food industries. Many herbal products make claims toward weight loss and weight management, yet scientific research is scanty for these products at best. Researching and reviewing available scientific evidence prior to formulating novel products is ideal to insure the safety and efficacy of natural products.

When formulating Burn, DCC made extensive use of available research to confirm their own findings- that this product is not only safe at the recommended dosages, but that it is highly effective for supporting healthy weight management. It targets multiple metabolic functions including increasing energy metabolism, controlling appetite, and burning fat while reducing the formation of new fat stores. In addition to the scientific evidence supporting the functionality of this product for weight management, it was formulated to be an adjunct product to the DCC's existing beverage formulations. This means that although it can be taken as a stand-alone product for weight management, it can be combined easily with one or many of Javita's weight management products to further enhance the benefits. This white paper will focus on the scientific evidence used to support the formulation and use of Burn as a weight management product. It will also touch on the synergistic benefits that can be found through its use with Javita's full line of products.

This paper will include descriptions and conclusions from various in vitro and in vivo trials showing efficacy and safety of the proprietary ingredients. As the 103rd US Congress dictated when passing the historical Dietary Supplement Health and Education Act (DSHEA) in 1994, "…consumers should be empowered to make choices about preventive health care programs based on data from scientific studies of health benefits related to particular dietary supplements." This paper is meant to assist in the empowerment of the educated consumer, to determine the best weight management product for their needs.

Phone: 281-360-7282
Fax: 713-583-8615
archmorebotanical@gmail.com
www.archmorebotanical.com

Formulation Overview and Ingredient Summary

Burn was designed to be an easy to consume encapsulated product to support weight management. It combines botanical and nutritional ingredients to support more efficient energy expenditure and fat burning to improve overall body composition. These ingredients include *Garcinia cambogia* and *Coleus forskohlii,* two unique and well-suited botanical ingredients for weight loss. It also includes extracts from green coffee bean and green tea to improve metabolic rate without having an energy "crash" that you sometimes find with artificial caffeinated products. Finally, it includes extracts from capsicum and Vitamin D3 to improve thermogenesis and support a nutritional balance needed for weight loss.

Many of these botanicals have very harsh flavor profiles that make them nearly impossible to include in beverages at efficacious doses. Javita has chosen to use scientifically confirmed effective dosage levels to achieve optimal results. This necessitated the encapsulation of this formula- so taste would not be a factor. Javita took extra measures to insure the proper processing and encapsulation of the ingredients follow dissolution standards necessary for the optimal absorption of these nutrients.

- Formulation includes unique botanical and nutritional ingredients that work synergistically to support weight management
    - *Garcinia cambogia* provides naturally occurring hydroxycitric acid (HCA)
        - Inhibits the conversion of carbohydrates to fat in the body
        - Increases available energy for calorie burning
        - Increases serotonin levels to reduce emotional overeating
    - *Coleus forskolli c*ontains forskolin
        - Increases cAMP for improved energy expenditure
        - Activates the enzyme adenylate cyclase which can stimulate lipolysis in fat cells
    - Green Coffee Bean Extract for increased energy
    - Green Tea Extract with EGCG to promote efficient energy metabolism
    - Capsicum to activate thermogenesis for fat and energy burning
    - Vitamin D3
        - Normally deficient in metabolic syndrome which can prevent weight loss

Phone: 281-360-7282
Fax: 713-583-8615
archmorebotanical@gmail.com
www.archmorebotanical.com

***Garcinia cambogia*- overview**

Garcinia cambogia, also known as Malabar tamarind, has been consumed by peoples 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 when food sources are scarce. 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.

Phone: 281-360-7282
Fax: 713-583-8615
archmorebotanical@gmail.com
www.archmorebotanical.com

***Coleus forskohlii*- overview**

Coleus forskohlii is a small herbaceous plant in the mint family that grows throughout the Indian subcontinent, Sri Lanka, Nepal and Thailand. Although used by natives for years to assist in ailments such as cardiovascular disease and breathing disorders, it wasn't until 1974 that a compound was extracted from the roots and identified for its numerous benefits in the body. This compound is called forskolin. In cellular trials, it was shown to increase cyclic AMP, the critical energy making process of cells and the driving force for burning fat and energy in our bodies.

Recently, this compound has gained acclaim for its ability to assist in weight management, particularly by improving body composition. Clinical trials have shown weight loss in severely obese individuals as well as moderately overweight individuals. Improvements in body composition and reductions in blood pressure have also been reported. As hypertension can be caused by metabolic disorder, lowering blood pressure while losing weight is a key asset of *Coleus forskohlii*.

This rise in popularity has prompted researchers to investigate the safety of this compound as well as the herb as a whole. In general, this forskolin has been shown to produce significant results with minimal clinical side effects. It has even been tested as a combination product with other known weight management botanicals, such as capsicum (red pepper), and the benefits were additive. Through the inclusion of *Coleus forskohlii* in this formulation, Burn can help improve the energy and fat burning efficiency of the body.

Phone: 281-360-7282
Fax: 713-583-8615
archmorebotanical@gmail.com
www.archmorebotanical.com

Green Coffee Bean Extract- overview

Green coffee beans are the same coffee beans used to make your morning cup of coffee, yet they have not yet been roasted. They are sent through an extraction process instead to concentrate various compounds, in particular methylxanthines such as caffeine. By extracting instead of roasting, the taste of the green coffee bean is dramatically different than that of a roasted bean, allowing it to be delivered in different dosage forms than coffee, namely juices, fruit cocktails, supplements, and powdered beverages.

The major benefits from the green coffee bean extract lie in the concentration of caffeine. Caffeine is a natural stimulant that can provide an immediate feeling of energy and also enhance metabolic rate. By speeding up this process, more energy can be burned from fat already stored already in the body.

Although there has been a controversy over whether green coffee directly improves weight management, there have been some small trials done that indicate it may assist in preventing weight gain and possibly lower blood pressure. These studies are preliminary, and more work needs to be done in this area. However, as a component to a complex supplement, such as Burn, green coffee bean can help improve energy levels during calorie restriction, increasing weight loss efforts like exercising.

Most of the safety concerns associated with green coffee concern the caffeine content itself. For those negatively affected by caffeine, care should be taken when consuming the product. However, in most consumer and clinical trials, no adverse safety events have been seen with the consumption of green coffee extract.

Phone: 281-360-7282
Fax: 713-583-8615
archmorebotanical@gmail.com
www.archmorebotanical.com

Green Tea Extract with EGCG- overview

Green tea has been consumed for more than 4,000 years, with its origins believed to be in China. Due to the popularity of this beverage and the rich traditional aspect of its consumption, more than 600 different cultivars are currently in circulation. These varietals all contain various concentrations of beneficial compounds; Javita selected an extract standardized for a high concentration of EGCG to be used in Burn. EGCG stands for epigallocatechin-3-gallate and is the ester of epigallocatechin and gallate.

Although centuries of historical use have deemed this botanical safe for human consumption, the discovery of EGCG has prompted much research to be conducted for its health benefits. Among these are antioxidation, energy balance, and energy metabolism.

EGCG has been shown to provide cardio and cellular protection for those cells experiencing oxidative stress. This stress may be the result of environmental stressors or the stress one encounters that cause fatigue, i.e. mental stress, physical stress, or aging. By protecting against oxidative damage, EGCG assists the body in combating fatigue on the cellular level.

In studies demonstrating the antioxidant benefit of EGCG, it was also noted that EGCG plays an instrumental role in regulating energy metabolism. This helps improve energy levels by more efficiently using natural energy reserves already present in the body. But it also improves energy over longer periods of time due to better energy regulation and use on the cellular level.

Phone: 281-360-7282
Fax: 713-583-8615
archmorebotanical@gmail.com
www.archmorebotanical.com

Capsicum- overview

Capsicum is the genus for red and chili peppers and contains several compounds called capsinoids that give these fruits their spicy taste. Among these capsinoids are capsaicin, capsiate, and dihydrocapsiate. In the body, these compounds can activate thermogenesis, the heat given off with the burning of certain types of fat stores. Thermogenesis can help reduce body weight and body fat.

Phone: 281-360-7282
Fax: 713-583-8615
archmorebotanical@gmail.com
www.archmorebotanical.com

Vitamin D3- overview

Vitamin D3 is a vitamin that our bodies are able to manufacture through sun exposure. However, sunscreens and a more sedentary, indoor lifestyle have dramatically reduced the amount of Vitamin D we are making by up to 99%. This means that the vast majority of individuals are Vitamin D deficient. Studies have linked Vitamin D deficiency with obesity, citing the need for this critical vitamin to manufacture compounds that aid in satiety and appetite control. Vitamin D also helps with the absorption of other weight management compounds, such as calcium. Calcium in necessary when losing weight to preserve muscle mass. And improving muscle mass can also help burn fat more efficiently during exercise. Combined with the other effective nutrients in Burn, Vitamin D3 plays a critical role to improve body composition.

Phone: 281-360-7282
Fax: 713-583-8615
archmorebotanical@gmail.com
www.archmorebotanical.com

Formulation Efficacy- A Detailed Review of Available Studies

Research suggests multiple mechanisms by which *Garcinia cambogia*, *Coleus forskohlii*, and Capsicum affect the body with regards to weight management. Outlined below are those conclusively defined in published available literature. As these natural ingredients continue to gain popularity in the world market, further funding will be available for research, and additional mechanisms of action may become known. At the time of publication of this white paper, these are the most commonly known mechanisms:

- *Garcinia cambogia*
  - Competitively inhibits citrate lyase to prevent the formation of fat cells
  - Increases energy
  - Increases serotonin levels to reduce emotional overeating
- *Coleus forskohlii*
  - Increases cAMP for improved energy expenditure and lipolysis
- Capsicum
  - Increases thermogenesis for improved fat burning

Green coffee bean and green tea were included in this formulation due to their synergistic effects. Their weight management benefits will be outlined together but will encompass:

- Increase energy through stimulation of the central nervous system
- Regulating energy metabolism through antioxidation
- Protect cells from stressors that may cause fatigue

Vitamin D3 is naturally deficient in most cases of metabolic disorder, such as obesity and overweight. Including it in this formulation will have benefits for those deficient but may also assist in weight loss due to a balance in other nutrients necessary for weight loss.

Phone: 281-360-7282
Fax: 713-583-8615
archmorebotanical@gmail.com
www.archmorebotanical.com

***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 [1]. 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 [2].

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 [3].

Researchers wanted further conclusive evidence of this disruption in lipogenesis, or the formation of fat cells, and were able to achieve it. By measuring electron densities of the molecules as HCA is introduced to human ATP-citrate lyase, they were able to determine that hydroxycitric acid causes the protein to bind in a different orientation, effectively leaving the molecular ring open and unable to form new molecules. This effectively disrupts the lipogenesis pathway, leading to the reduction in fat cell formation [4].

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 [5].

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 [6].

Athletes are constantly in search of ways to improve their endurance and performance. It is theorized that if lipid oxidation can be increased, there will be more available energy for improving endurance. Therefore, supplements that are known to increase lipid oxidation and metabolism have been reviewed to determine their benefit in this capacity. In a 2016 review of these natural supplements including garcinia, they determined that this herb, along with several others, does indeed promote fat metabolism which could have endurance benefits for athletes. However, more studies conducted in the athletes themselves should be carried out to provide conclusive results for this market [7].

A pleasant side effect of HCA is the decrease in oxidative stress, inflammation, and insulin resistance associated with obesity and metabolic syndrome [8].

<u>Mechanism of Action: Increases serotonin to diminish emotional overeating</u>

With obesity being a global health epidemic, billions of dollars and countless hours of research have been spent to determine the cause. A significant factor increasing the occurrence of obesity is overeating due to emotional stress, 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 have 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, providing relief from the stressor even if only for a short period of time. This is known as stress- or emotional-overeating [9].

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's been hypothesized that an increase in serotonin production should help quiet the 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 [10].

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 [11]. This two-prong approach shows the neurological benefits of HCA for managing weight through the reduction of emotion overeating and increasing satiety [12].

In a more recent animal trial involving garcinia, researchers showed that food intake was significantly reduced just one hour after consuming garcinia, indicating that the animals felt full even though less calories had been consumed. This quick acting natural product may help reduce calories when consumed just prior to the largest meals because of this immediate effect [13]. More research needs to be done to determine if this same benefit can be seen in humans.

Phone: 281-360-7282
Fax: 713-583-8615
archmorebotanical@gmail.com
www.archmorebotanical.com

Garcinia cambogia: a review of negative outcomes from clinical trials

Although the majority of 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 [14].

However, a later study noted a flaw in the study design which eliminated the positive results others 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 [15]. 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 [16].

Phone: 281-360-7282
Fax: 713-583-8615
archmorebotanical@gmail.com
www.archmorebotanical.com

***Coleus forskohlii*-efficacy**

Mechanism of Action: increases cAMP to promote fat burning

Coleus forskohlii is a small herbaceous plant in the mint family (Lamiaceae) that grows throughout the Indian subcontinent as well as Sri Lanka, Nepal, and Thailand. It has a long and diverse history of use by the people of southern Asia: from heart disease, chest pain, and blood pressure disorders to breathing problems and asthma. It wasn't until 1974 that a compound was extracted from the tuberous roots and identified for its numerous benefits in the body. This compound is called forskolin and is a diterpene found exclusively in this species' roots.

In cellular trials, forskolin has been shown to increase cyclic adenosine monophosphate, or cAMP. This is the critical energy making function of cells and the driving force for burning fat and energy in our bodies. It increases cAMP and cAMP-mediated functions through the activation of the enzyme adenylate cyclase [17]. This effect on cAMP influences a number of other functions including vasodilation, bronchodilation, alleviating intraocular pressure, etc. But probably the most crucial for the purposes of Burn is the role it plays in stimulating lipolysis of fat cells [18]. Both cellular and animal trials have demonstrated this effect, with more recent studies confirming similar results in humans as well.

Mechanism of Action: increases cAMP to suppress appetite and prevent weight gain

In an animal trial, *Coleus forskohlii* extract (CFE) was administered to rats fed different diets: normal pellet diet (control), a cafeteria-type diet (shown to cause obesity), and a cafeteria-type diet plus CFE. Those animals given the cafeteria diet without CFE became obese, while those animals in the cafeteria-type group plus CFE showed marked improvements in body composition, including a reduction in weight gain. The researchers felt that the CFE assisted with appetite suppression due to reduced calories voluntarily consumed by the animals while taking the extract. In addition, researchers concluded that CFE might be beneficial for those battling dyslipidemia caused by poor food choices [19].

To determine if similar results occur in humans, a small clinical study was conducted on overweight women. CFE was administered twice daily to these women for eight weeks. The average weight lost at the end of the trial was 10 pounds, with an eight-percent reduction in body fat. Blood pressure was also

lower in all women during the trial. No adverse effects were reported, indicating *Coleus forskohlii* extract is safe and effective for losing weight and body fat [20].

Similar results have been seen in larger clinical trials. Henderson, et.al. studied the effects of CFE on body composition in twenty-three overweight women, but also examined hematological profiles. CFE was administered twice daily for twelve weeks. Following the study, researchers noted that those receiving CFE did not gain additional weight even while following the same diet. Although not a direct catalyst for weight loss, this study concluded that CFE helped mitigate weight gain normally seen when calories are not restricted [21]. Since the target consumer for Burn will be striving to lose weight, a restricted calorie diet is recommended; therefore, CFE is an ideal ingredient to help propel weight loss efforts.

A more recent clinical study further demonstrates the positive benefits CFE can have for weight management. In a study published in 2015, thirty participants were given either CFE or placebo and advised to follow a restricted calorie diet. Following the twelve-week study duration, both groups experienced significant reductions in waist and hip circumference and increases in HDL cholesterol levels (beneficial cholesterol). These are both indictive of the positive benefits of a calorie-restricted diet. However, the CFE group also had favorable improvements in insulin concentration and resistance [22]. Since blood sugar irregularities tend to be an unfortunate consequence of metabolic syndrome, they may be mitigated through the use of *Coleus forskohlii* extract.

Green Coffee Bean Extract - efficacy

Mechanism of Action: increases energy through stimulation of the central nervous system

Caffeine is a methylxanthine used to stimulate the central nervous system, and is a major nutrient found in green coffee beans. Caffeine is the world's most widely consumed psychoactive substance for its positive energy effects with minimal side effects. It functions in numerous ways in the central nervous system, including acting as an antagonist at the level of the adenosine receptors. This allows caffeine to increase energy metabolism throughout the body: in the brain this has resulted in improved memory, alertness, and minimizes anxiety-related and physiological and behavioral responses through its action on serotonin neurons [23, 24]. For weight management, this stimulation of the central nervous system increases metabolic rate. This allows the burning of more fat stores through the action of lipolysis.

Although not a direct weight management tool, caffeine may transiently affect appetite as shown in clinical trial [25]. But more likely is that it enhances lipid metabolism through AMP-activated protein kinase (AMPK) activation [26].

In addition, caffeine is usually consumed without the central nervous system developing a great tolerance to the compound; thus, caffeine will continue to provide stimulation to the central nervous system even when consumed regularly. Some dependency and withdrawal systems, however, have been noted in clinical trials, although the benefits on the central nervous system continue to be experienced [27].

Phone: 281-360-7282
Fax: 713-583-8615
archmorebotanical@gmail.com
www.archmorebotanical.com

Green Coffee Bean Extract- A Review of Negative Outcomes from Clinical Trials

There has been a study conducted on green coffee bean to determine its effects on protein and energy utilization. In this animal experiment, various botanicals including green coffee were administered, and protein digestibility and digestible energy were measured. Green coffee bean was one of many botanicals that had slightly negative effects on these values. However, researchers noted that the observed effects may have been in part due to the anti-nutritional effects of tannin, a compound present in whole green coffee beans [28]. The green coffee extract used in Burn has been processed to remove the majority of tannins; therefore, these deleterious results on protein digestibility should not be observed in consumers.

Phone: 281-360-7282
Fax: 713-583-8615
archmorebotanical@gmail.com
www.archmorebotanical.com

Green Tea Extract with EGCG- Efficacy

Mechanism of Action: assists in regulating energy metabolism

In an animal trial to determine the metabolic response to EGCG from green tea, researchers tested the concentration of EGCG in adipose (fat storage) tissue after oral administration. After chronic EGCG dosing, fatty tissue deposits were significantly decreased. Researchers concluded that EGCG assisted in regulating the metabolism of these fat stores in the body. They hypothesized that this was accomplished through its powerful antioxidative effects [29].

In a separate trial conducted by different researchers, similar results were seen in terms of energy metabolism; however, these researchers did not attest to the antioxidative effect of EGCG for the regulation of energy metabolism but rather to the effect EGCG has on the growth of certain species of gut microbiota. These particular microbiota are associated with a pattern of short chain fatty acids which may be responsible for this regulation of energy metabolism [30]. A much earlier study had similar conclusions; they found that fat oxidation, and thus energy metabolism, was due to a reduction in digestibility of fat caused by EGCG. This could have been due to the gut microbiota or by increased fat and nitrogen excretion seen in a later study [31,32]. Regardless of the underlying cause, all research teams asserted to the powerful benefit EGCG has on regulating and improving energy metabolism and thus reducing fat stores in the body.

Although energy expenditure had been seen in several studies previously, researchers in one particular study wished to show energy expenditure via a different mechanism than fat oxidation and metabolism. They chose to measure shivering intensity during a cold exposure period. In this scenario, they proved that EGCG, when combined with caffeine, significantly increased energy expenditure compared to placebo in healthy adults exposed to cold, thus reducing shivering activity. This was a novel approach to demonstrate EGCG's effect on energy metabolism [33].

This increase in energy expenditure was also seen when exercise was increased in subjects. In a counter-balanced, crossover design study, twelve healthy individuals performed a cycling exercise at a moderate rate and were supplemented at various points with green tea extract or placebo. Average fat oxidation rates were significantly higher in the green tea group than with placebo, and the contribution of fat oxidation to total energy expenditure was also significantly higher. Researchers concluded that green

tea extract increases fat oxidation during moderate-intensity exercise better than exercise alone [34]. A similar study noted that EGCG also improved endurance capacity and increased muscle lipid oxidation, a benefit for those wishing to improve endurance and performance [35].

Finally, an increase in energy expenditure from a combination of EGCG and caffeine was noted in a short-term, randomized, placebo-controlled, double-blind, cross-over study. Healthy subjects were monitored for 24-hour-energy-expenditure, substrate oxidation, and blood pressure before and after EGCG-caffeine administration. Although there was no significant change in systolic blood pressure after 24-hours, there was a significant increase in 24-hour energy expenditure with this combination product [36]. This demonstrates the more immediate results that will be felt with the combination formula found in Burn.

Mechanism of Action: antioxidation for cellular protection

Although not mutually exclusive from energy metabolism, it should be noted that the antioxidant potential of EGCG has cellular benefits as well. This is important in an energy product, since much energy loss may be caused by oxidative stress. By reducing and reversing this damage, energy increases due to more efficient cellular processes. In an in vitro study, researchers used eight proteins associated with energy metabolism as biomarkers for oxidative stress. When EGCG was administered as a pretreatment prior to a stressor, all of the detrimental effects of the stressor were reversed. They concluded that EGCG protects against oxidative stress and to reduce cell injury [37]. These results were recreated using cells from different regions of the body, showing the protective antioxidation from EGCG to be universal [38].

Outside the scope of weight management and energy, EGCG also improves cognitive function because of this antioxidation. In a clinical trial, several oxidative stress markers were evaluated following administration of this catechin. It was shown that cognitive deficit, nitric oxide metabolites, and reactive oxygen species were completely reversed by EGCG administration. Researchers attested to the powerful neuroprotective potential of this compound, attributing the benefits to its antioxidative potential [39].

Phone: 281-360-7282
Fax: 713-583-8615
archmorebotanical@gmail.com
www.archmorebotanical.com

The protective effects of EGCG were also found to be comparable with caloric restriction, a well-established dietary intervention proven to slow the aging process. By having a similar effect, EGCG may assist with the detrimental side effects of aging, namely fatigue and mental decline [40].

Phone: 281-360-7282
Fax: 713-583-8615
archmorebotanical@gmail.com
www.archmorebotanical.com

Capsicum- efficacy

Capsicum annum peppers, commonly referred to as red or chili peppers, are consumed either dried, cooked, or even raw to confer spice on a recipe. The heat provided by this pepper comes from certain compounds in the fruit and seeds called capsinoids. Certain capsinoids have been studied for their ability to stimulate thermogenesis, or heat, a metabolic process that warms the body. Through this heat production, energy stored as fat can be burned. This may help in weight loss.

Recent findings suggest that a certain type of fat, known a brown adipose tissue, is the fat that is burned by the body in response to the cold. When metabolized or burned off, brown adipose tissue generates heat, warming the body. However, in modern times, this particular type of fatty tissue is rarely burned and is a potential contributor to weight gain in western cultures. Capsicum has the ability to stimulate the burning of brown adipose tissue, particularly when combined with *Coleus forskohlii*, improving overall body composition [41]. This is an active area of recent research in humans.

Phone: 281-360-7282
Fax: 713-583-8615
archmorebotanical@gmail.com
www.archmorebotanical.com

Vitamin D3- efficacy

As obesity and overweight have been on the rise in the Western world, many studies are looking at this particular body composition to determine cause as well as cure. It has been determined that in most cases, Vitamin D is deficient in these types of bodies. Vitamin D is critical for the regulation of skeletal metabolism as well as calcium and phosphate homeostasis. In particular, calcium is necessary to maintain muscle mass which assists in losing weight. When Vitamin D is deficient, calcium can not be absorbed properly, which leads to muscle loss. In these cases, weight loss is not able to be achieved.

In a review of the therapeutic role Vitamin D plays in weight loss and fitness, researchers noted that supplementation with vitamin D coupled with exercise or mild caloric restriction improves markers of fitness and reduces exercise-induced inflammation. They also noted from previous studies that cholesterol levels are lowered when Vitamin D is sufficiently supplemented in overweight individuals [42].

Phone: 281-360-7282
Fax: 713-583-8615
archmorebotanical@gmail.com
www.archmorebotanical.com

Safety

- Burn was designed to achieve results when taken according to package recommendations. Recommended dosage is two capsules twice per day. This dosage maintains safety parameters set by Javita as outlined in clinical research.
- All safety studies cited in this paper are relevant to the dosages recommended for Burn
- Adverse safety and toxicity trials are also reviewed for reference where applicable

Phone: 281-360-7282
Fax: 713-583-8615
archmorebotanical@gmail.com
www.archmorebotanical.com

***Garcinia cambogia*- safety**

Garcinia cambogia, also known as the Malabar tamarind from which HCA is extracted and supplied in Burn, 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, researchers 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 [43]. Researchers also 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 [44]. 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.

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 [45].

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 it actually reduces markers of inflammation in the brain, intestines, kidney and serum [46].

As *G. cambogia* (HCA) along with several other natural products have gained immense momentum in recent years particularly among adolescents, a review was conducted to see if this particular market was abusing these herbs with negative side effects. Reports to Poison Control from 2003 to 2014 were reviewed to assess how often *G. cambogia* is abused by adolescents and what type of negative outcomes were seen. Although 84 cases were found for abuse of natural product herbs by adolescents, only 7 involved the use of Garcinia. Of these cases, they were ruled minor with minimal or no negative effect and were ultimately ruled "non-toxic" or "minimally toxic", most of which did not result in even an office visit to a health care professional [47].

Adverse Events in Clinical Trials: A Review of Garcinia cambogia and HCA

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 [48].

However, researchers conducted a more recent study to evaluate the specific effect of *Garcinia extract* on serum sex hormones in overweight human subjects. In this double-blind, placebo controlled trial, it was 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. They concluded that as dosages commonly recommended for human consumption, *Garcinia cambogia* extract (HCA) does not affect serum sex hormone levels and blood parameters [49]. These dosages are significantly higher than those used by Javita even when multiple products are consumed containing G. cambogia following daily dosage guidelines.

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 [50].

Phone: 281-360-7282
Fax: 713-583-8615
archmorebotanical@gmail.com
www.archmorebotanical.com

***Coleus forskohlii*- safety**

Research has shown efficacy for the compound forskolin derived from the roots of *Coleus forskohlii*. This compound has shown benefits with minimal adverse events. In clinical trials, no adverse events were reported. However, because of the benefits seen for lowering blood pressure and improving blood flow, care should be exercised by those individuals taking blood pressure medication and blood thinners. *Coleus forskohlii* may enhance the effects of these drugs in an undesired way. Do not begin taking *Coleus forskohlii* without consulting your primary care physician if you are currently on these or any prescription drug.

In terms of adverse events, one group of researchers determine the potential for stimulating fatty liver conditions in mice who were administered forskolin by modifying triglyceride production. While these findings could be cause for concern, no other group of researchers has duplicated the results. That does not discount them, but means that other issues could be playing a role, such as diet, animal handling conditions, etc. It should be noted that this effect has not been seen in human clinical trials to date. In clinical trials where blood parameters were measured, no increases in triglyceride production were noted. More research needs to be conducted in this arena before firm conclusions can be made [51].

It should also be noted that at the time of this white paper, the published monograph for *Coleus forskohlii* outlined no adverse events or safety concerns with the use of this botanical at the recommended human doses. Burn was formulated to be in compliance with these doses [52].

Phone: 281-360-7282
Fax: 713-583-8615
archmorebotanical@gmail.com
www.archmorebotanical.com

Green Coffee Bean Extract- safety

Green coffee beans are the starting point from which all roasted coffee originates. Therefore, there is a significantly long history of use for this beverage and much information regarding its main chemical compound: caffeine. As green coffee itself does not appear to pose major health concerns nor serious adverse effects, the focus of this safety evaluation will be on the caffeine itself.

Caffeine is regularly consumed by most adults at an intake level of 200mg per day, according to the FDA. At these moderate consumption levels, naturally occurring sources of caffeine are not associated with adverse effects, according to the FDA Commissioner [53]. Because of the multiple ways it is dosed, however, caffeine has been classified by the FDA as both a drug and a food additive; therefore, it carries some warnings and advisements from the FDA.

Caffeine is a diuretic; therefore, consuming it with water helps to maintain a proper water balance in the body to avoid dehydration. It is recommended to take Burn with at least an 8 oz glass of water to help balance the water that may be lost due to the caffeine itself.

Large amounts of caffeine may be harmful during pregnancy; therefore, women who are pregnant or planning to get pregnant should speak with their health care professional prior to using any product containing caffeine.

Caffeine affects individuals differently depending on their body composition. Therefore, individuals sensitive to caffeine should reduce or refrain from consuming caffeine-containing beverages.

Caffeine is not intended for use by children. Consult your health care professional before administering any caffeine-containing product to a child.

Phone: 281-360-7282
Fax: 713-583-8615
archmorebotanical@gmail.com
www.archmorebotanical.com

Green Tea Extract and EGCG- safety

Over 4,000 years of documented historical use have shown the safety of green tea as a beverage. However, with the extraction and concentration of the tea to supply the main catechin, EGCG which is utilized in Burn, more stringent safety evaluations have been conducted.

In a double-blind, placebo-controlled, randomized trial on women with breast cancer, a high dosage of green tea extract was well tolerated by more than one thousand participants. There were no significant differences in the percentage of women with adverse events in the placebo group versus the extract group. Those who did experience side effects reported minor nausea or dermatologic symptoms, and these were transient [54].

An initial animal study was conducted to evaluate low and high doses of EGCG on liver and kidney tissues over a 6-month period. Both the low and high doses were well-tolerated by the animals without causing tissue damage or dysfunction to either the liver or kidneys. This was determined using both histopathological and biochemical observations [55]. Similar results were recreated in humans, where researchers used a randomized, double-blind, placebo-controlled format to evaluate EGCG in over eighty female test subjects. At a comparable dosage to Burn, EGCG did not cause any adverse effect on liver function biomarkers even when consumed daily for 12 weeks [56].

A different type of safety study was conducted to determine the effects EGCG has on sperm survival and metabolism. In this study, various levels of EGCG were administered to sperm in vitro. All levels increased sperm motility, viability, and phosphorylation of proteins controlling cell survival, indicating a beneficial effect on sperm survivability and functionality [57].

Phone: 281-360-7282
Fax: 713-583-8615
archmorebotanical@gmail.com
www.archmorebotanical.com

Capsicum- safety

Capsicum contains compounds called capsinoids which have thermogenic properties but also give the fruit its spiciness. Only very small amounts are needed of these compounds to produce thermogenesis. Therefore, normal side effects to spicy foods, such as heartburn or indigestion, should not occur from ingesting the recommended doses of this compound. In toxicology tests, capsicum was found to be safe for both topical and internal use at recommended dosage with little to no irritation or adverse clinical effects [58].

Phone: 281-360-7282
Fax: 713-583-8615
archmorebotanical@gmail.com
www.archmorebotanical.com

Vitamin D3- safety

It is virtually impossible to overdose or have a negative side effect from Vitamin D3, according to most medical professionals. In a 4-year double-blind, placebo-controlled trial, more than 5,000 adults were given either 100,000IU of vitamin D (ten-times the RDA) or placebo daily. There was no statistical difference between adverse events reported, concluding that even at high doses, Vitamin D is safe for long term use [59].

In rare cases, Vitamin D overuse could cause an imbalance in blood calcium levels could occur. This could result in constipation, nausea, confusion, kidney stones, and potentially an irregular heart rhythm. Should these symptoms occur, discontinue use, and consult your healthcare professional immediately.

Phone: 281-360-7282
Fax: 713-583-8615
archmorebotanical@gmail.com
www.archmorebotanical.com

Usage Guidelines

Obesity and overweight are conditions that negatively impact millions of people in the civilized world. They may be caused by various health factors or by dietary and lifestyle choices. Regardless of the cause, they have the same serious health implications if left untreated. Every individual should strive to be their healthiest to increase longevity and improve wellbeing. This starts with reducing excess body weight, which can significantly reduce the risk for obesity-related diseases. Burn may help in this process.

Burn was formulated to produce benefits when two capsules are taken twice daily. It is recommended to take this product on an empty stomach before your two largest meals, ideally breakfast and lunch. Since the product does contain caffeine, taking it late in the day or before bed may negatively affect sleep patterns and is not recommended.

By taking this product according to the package recommendations, one should experience the positive benefits as outlined in this white paper. Results will differ between individuals, as no two bodies act identically when faced with the same stimulus. However, the general results should include

- a decrease in body weight and/or body fat
- an increase in available energy
- a feeling of fullness or a suppression of the appetite itself.

As noted in this white paper, safety studies were conducted using dosages of these natural ingredients much higher than those provided in Burn. Except in rare circumstances or where contraindicated, this amount should be safe for adult use.

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.

Phone: 281-360-7282
Fax: 713-583-8615
archmorebotanical@gmail.com
www.archmorebotanical.com

Citations

1. Heymsfield SB, et. al. Garcinia cambogia (hydroxycitric acid) as a potential antiobesity agent: a randomized controlled trial. JAMA 1998 Nov 11;280(18):1596-600
2. Marquez F, et. al. 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. Roy S, et. al. 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
4. Acta Crystallogr D Struct Biol. 2017 Aug 1;73(Pt 8):660-671
5. Roy S, et. al. 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
6. Preuss HG, 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.
7. J Nutr Sci Vitaminol (Tokyo). 2016;62(3):141-61
8. Asghar M, et. al. 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
9. Singh M. Mood, food, and obesity. Front Psychol. 2014; 5: 925
10. Roy S, et. al. 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
11. Bagchi M, et. al. 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
12. Downs BW, et. al. Bioefficacy of a novel calcium-potassium salt of (-)-hydroxycitric acid. Mutation Research. 2005;579(1-2):149-162
13. Yimam, M, et.al. Evaluation of natural product compositions for appetite suppression. J Diet Suppl. 2018 Feb 14:1-19
14. Heymsfield SB et. al. Garcinia cambogia (hydroxycitric acid) as a potential antiobesity agent: a randomized controlled trial. JAMA. 1998 Nov 11;280(18):1596-600
15. Chuah LO. et. al. Updates on antiobesity effect of Garcinia origin (-)-HCA. Evid Based Complement Alternat Med. 2013;2013:751658
16. Sullivan AC, et. al. Inhibition of lipogenesis in rat liver by (-)-hydroxycitrate. Arch Biochem Biophys. 1972 May; 150(1):183-90
17. Metzger H, Lindner E. The positive inotropicacting forskolin, a potent adenylate cyclase activator. Arzneimittelforschung 1981;31:12481250
18. Okuda H, Morimoto C, Tsujita T. Relationship between cyclic AMP production and lipolysis induced by forskolin in rat fat cells. J Lipid Res 1992;33:225-231
19. Hebbani, Nagarajappa, Shivaprasad. Effect of Coleus forskohlii extract on cafeteria diet-induced obesity in rats. Pharmacognosy Res. 2014 Jan-Mar; 6(1): 42–45. doi: 10.4103/0974-8490.122916 PMCID: PMC3897007 PMID: 24497741
20. Badmaev V, et. al. Diterpene forskolin: a possible new compound for reduction of body weight by increasing lean body mass. Townsend Lett 2001;June:115
21. Henderson, et. al. Effects of Coleus Forskohlii Supplementation on Body Composition and Hematological Profiles in Mildly Overweight Women. Journal of the International Society of Sports Nutrition. 2(2): 54-62, 2005.
22. Loftus HL, et. al. Coleus forskohlii Extract Supplementation in Conjunction with a Hypocaloric Diet Reduces the Risk Factors of Metabolic Syndrome in Overweight and Obese Subjects: A Randomized Controlled Trial. Nutrients. 2015 Nov 17;7(11):9508-22. doi: 10.3390/nu7115483
23. Nazario LR, et. al. Caffeine protects against memory loss induced by high and non-anxiolytic dose of cannabidiol in adult zebrafish (Danio rerio). Pharmacol Biochem Behav. 2015 Aug;135:210-216
24. Abrams JK, et. al. Serotonergic systems associated with arousal and vigilance behaviors following administration of anxiogenic drugs. Neuroscience. 2005;133(4):983-97
25. Panek-Shirley LM, et. al. Caffeine Transiently Affects Food Intake at Breakfast. J Acad Nutr Diet. 2018 Jul 16. pii: S2212-2672(18)30768-8. doi: 10.1016/j.jand.2018.05.015
26. Rothenberg DO, Zhou C, Zhang L. A Review on the Weight-Loss Effects of Oxidized Tea Polyphenols. Molecules. 2018 May 14;23(5). pii: E1176. doi: 10.3390/molecules23051176
27. Nehlig A, Daval JL, Debry G. Caffeine and the central nervous system: mechanisms of action, biochemical, metabolic and psychostimulant effects. Brain Res Brain Res Rev. 1992 May-Aug;17(2):139-70
28. Eggum B. The influence of dietary tea, coffee and cocoa on protein and energy utilization of soya-bean meal and barley in rats. Br J Nutr. 1983 Sep;50(2):197-205
29. Moreno MF et. al. Metabolic profile response to administration of epigallocatechin-3-gallate in high-fat-fed mice. Diabetol Metab Syndr. 2014 Aug 12;6(1):84
30. Unno T et. al. Effect of dietary supplementation of (-)-epigallocatechin gallate on gut microbiota and biomarkers of colonic fermentation in rats. J Nutr Sci Vitaminol (Tokyo). 2014;60(3):213-9
31. Klaus S et. al. Epigallocatechin gallate attenuates diet-induced obesity in mice by decreasing energy absorption and increasing fat oxidation. Int J Obes (Lond). 2005 Jun;29(6):615-23

32. Friedrich M et. al. Acute effects of epigallocatechin gallate from green tea on oxidation and tissue incorporation of dietary lipids in mice fed a high-fat diet. Int J Obes (Lond). 2012 May;36(5):735-43
33. Gosselin C, Haman F. Effects of green tea extracts on non-shivering thermogenesis during mild cold exposure in young men. Br J Nutr. 2013 Jul 28;110(2):282-8
34. Venables MC et. al. Green tea extract ingestion, fat oxidation, and glucose tolerance in healthy humans. Am J Clin Nutr. 2008 Mar;87(3):778-84
35. Murase T et. al. Green tea extract improves endurance capacity and increases muscle lipid oxidation in mice. Am J Physiol Regul Integr Comp Physiol. 2005 Mar;288(3):R708-15
36. Bérubé-Parent S et. al. Effects of encapsulated green tea and Guarana extracts containing a mixture of epigallocatechin-3-gallate and caffeine on 24 h energy expenditure and fat oxidation in men. Br J Nutr. 2005 Sep;94(3):432-6
37. Chen WC, et. al. Molecular identification for epigallocatechin-3-gallate-mediated antioxidant intervention on the H2O2-induced oxidative stress in H9c2 rat cardiomyoblasts. J Biomed Sci. 2014 Jun 9;21:56.
38. Casanova E. Epigallocatechin gallate counteracts oxidative stress in docosahexaenoxic acid-treated myocytes. Biochim Biophys Acta. 2014 Jun;1837(6):783-91
39. Biasibetti R, et. al. Green tea (-)epigallocatechin-3-gallate reverses oxidative stress and reduces acetylcholinesterase activity in a streptozotocin-induced model of dementia. Behav Brain Res. 2013 Jan 1;236(1):186-93
40. Meng Q, et. al. Regulating the age-related oxidative damage, mitochondrial integrity, and antioxidative enzyme activity in Fischer 344 rats by supplementation of the antioxidant epigallocatechin-3-gallate. Rejuvenation Res. 2008 Jun;11(3):649-60
41. de Lima Viera-Brock, P, et.al. Thermogenic blend alone or in combination with whey protein supplement stimulates fat metabolism and improves body composition in mice. Pharmacognosy Res. 2018 Jan-Mar; 10(1): 37-43
42. Slusher AL, et.al. A therapeutic role for vitamin D on obesity-associated inflammation and weight-loss intervention. Inflamm Res. 2015 Aug;64(8):565-75. doi: 10.1007/s00011-015-0847-4. Epub 2015 Jul 4
43. 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
44. Marquez F, et. al. 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
45. Chuah LO, et. al. In vitro and in vivo toxicity of Garcinia or hydroxycitric Acid: a review. Evid Based Complement Alternat Med. 2012; 2012: 197920
46. Clouatre DL, Preuss HG. Hydroxycitric acid does not promote inflammation or liver toxicity. World J Gastroenterol. 2013 Nov 28;19(44):8160-2
47. Biggs, JM, et. al. Abuses and misuse of selected dietary supplements among adolescents: a look at poison center data. J Pediatr Pharmacol Ther. 2017 Nov-Dec;22(6):385-393
48. Saito M, et. al. 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
49. Hayamizu K, et. al. Effects of Garcinia cambogia extract on serum sex hormones in overweight subjects. Fitoterapia. 2008 Jun;79(4):255-61
50. Preuss HG, 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
51. Umegaki, K., et. Al. Induction of fatty liver by Coleus forskohlii extract through enhancement of de novo triglyceride synthesis in mice. Toxicology Reports 1 (2014) 787-794
52. Coleus forskohlii Monograph. Alternative Medicine Review Volume 11, Number 1 March 2006
53. Caffeine in Food and Dietary Supplements: Examining Safety. Remarks by Dr. Margaret Hamburg, FDA Commissioner. To a meeting of the Institute of Medicine, Food and Nutrition Board and Board on Health Sciences Policy. National Academy of Sciences, Washington, DC. April 5, 2013
54. Dostal AM, et. al. The safety of green tea extract supplementation in postmenopausal women at risk for breast cancer: results of the Minnesota Green Tea Trial. Food Chem Toxicol. 2015 Sep;83:26-35
55. Meng Q, et. al. Regulating the age-related oxidative damage, mitochondrial integrity, and antioxidative enzyme activity in Fischer 344 rats by supplementation of the antioxidant epigallocatechin-3-gallate. Rejuvenation Res. 2008 Jun;11(3):649-60
56. Mielgo-Ayuso J, et. al. Effects of dietary supplementation with epigallocatechin-3-gallate on weight loss, energy homeostasis, cardiometabolic risk factors and liver function in obese women: randomised, double-blind, placebo-controlled clinical trial. Br J Nutr. 2014 Apr 14;111(7):1263-71
57. De Amicis F, et. al. Epigallocatechin gallate affects survival and metabolism of human sperm. Mol Nutr Food Res. 2012 Nov;56(11):1655-64
58. Baskaran Thyagarajan, Vivek Krishnan and Padmamalini Baskaran. J toxicology January 1, 2007 Volume: 26 (1) suppl: 3-106. CAP and Metabolic Diseases: A Mini Review on Preclinical Mechanisms and Clinical Efficacy, Capsaicin and its Human Therapeutic Development Gyula Mozsik, IntechOpen, DOI: 10.5772/intechopen.78353
59. Malihi, Z. et. al. Monthly high-dose vitamin D3 supplementation and self-reported adverse events in a 4-year randomized controlled trial. Clin Nutr. 2018 Aug 4. pii: S0261-5614(18)31248-2. doi: 10.1016/j.clnu.2018.07.034