

Comprehensive Analysis for Product Claims Concerning Leptoprin®-SD

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Abstract. A new generation of health supplements is ushered in with the introduction of Leptoprin®-SD, an exciting combination of ergogenic methylxanthines and a proven agent for promoting weight loss through a novel mechanism that does not require ephedrine, ma huang or any similar material. Used for weight loss, Leptoprin-SD has been shown in clinical research to delay gastric emptying, which is promoted as the primary reason why subjects lost over ten pounds of weight in 45 days. Used as an ergogenic aid, Leptoprin-SD contains a proprietary mixture of methylxanthines, derived from sources around the world, that have been shown to dramatically improve measures of vigilance, performance, mood, and cognition. In addition, Leptoprin-SD contains the specific amount of the amino acid L-tyrosine shown in research and patented documentation to be instrumental in enhancing sympathomimetic-induced appetite suppression. Leptoprin-SD also exerts an action on inflammatory cytokines, linked to obesity and cardiovascular disease, through the inhibition of pro-inflammatory prostaglandins. Finally, Leptoprin-SD contains calcium for added weight management benefits.

INTRODUCTION

With the continued turmoil over the use of ephedra, the scientific community has intensified the search for an effective weight-control compound that will also provide the energy people expect from a “diet pill.” Capitalizing on recent advances in the understanding of weight management and energy enhancement, a new super ergogenic (energy-producing) weight loss compound has been created, called Leptoprin®-SD.

Leptoprin-SD primarily combines a documented weight loss mixture, a broad spectrum ergogenic, an anti-inflammatory compound, a source of calcium, and an amino acid with a unique ability to enhance the suppression of appetite induced by the ergogenic mixture.

The proprietary weight loss mixture comprises three exotic herbs: *Ilex paraguayensis* (I), *Paulinia cupana* (P) and *Turnera diffusa* (T). This compound has been shown to significantly delay gastric emptying and to produce significant weight loss in humans, without changes in diet or exercise.

Additional weight loss activity is provided through the ability of at least one ingredient in Leptoprin-SD to inhibit the activity of prostaglandins that induce pro-inflammatory cytokines shown in recent research to be involved in the etiology of obesity.

The presence of calcium in

Leptoprin-SD reflects the findings of a great deal of research on the weight loss promoting activity of this mineral.

The proprietary ergogenic mixture comprises several sources of trimethylxanthines including several methylxanthine-containing herbs. These methylxanthines have been shown to dramatically increase energy availability in humans. L-tyrosine is also part of this mixture.

Therefore, this compound can be consumed for either one of two purposes or both: 1) increased energy; and 2) weight loss. Each of these goals will be discussed in the following paragraphs.

I. WEIGHT LOSS

WEIGHT LOSS LINKED TO DELAYS IN GASTRIC EMPTYING

It has been suggested that the stomach plays an important role in regulating delivery of energy and nutrients to the intestinal tract for absorption. When the rate of gastric emptying is dramatically slowed down, food energy intake is limited and severe wasting results. When the gastric emptying rate is accelerated, ‘dumping’ of stomach contents into the small intestine occurs, with consequent disturbances of blood volume and rapid swings in blood glucose and insulin as well as intes-

tinal hurry and diarrhea. Within the ‘normal’ range of gastric emptying, however, there is room for altering gastric emptying time in such a way to promote healthy weight loss.

In 2001, a ground-breaking European study was published that revealed that the delay of gastric emptying through the consumption of an all natural compound may serve as an entirely new method for weight control. The study had two parts. In the first part, gastric emptying was observed using ultrasound scanning in seven healthy volunteers following the consumption of either placebo or the active IPT compound. The active product prolonged gastric emptying time by about 53% compared to the placebo.

The second part of study evaluated the ability of the active IPT compound in Leptoprin-SD to produce weight loss. If gastric emptying reduces caloric absorption and reduces glucose levels following the meal, these factors should make an impact on body weight over time. In this double-blind, placebo-controlled phase of the experiment, mild to moderate overweight patients were instructed to take capsules with a large glass of water 15 minutes before the main meals, and they were asked to take great care not to change their normal dietary or exercise habits. The effect on body weight after 45 days of treatment

was assessed. Several of the subjects continued active treatment for 12 months; measurements were taken each month.

At the end of 45 days, the Active groups showed a mean decrease in body weight of about 11 pounds (5.1kg) while the placebo group experienced an almost meaningless decrease of less than a pound (0.3kg).

The subjects taking the IPT compound who continued for a total of 12 months experienced no rebound but were able to successfully maintain their initial weight loss.

While there is little doubt that the active compound delays gastric emptying, the precise mode through which such delay would act is not clear. The administration of glucagon-like peptide-1 at the beginning of a test meal has been shown to retard gastric emptying, but had little effect on energy consumption, eating rate, and plasma levels of insulin or glucagon. However, it did produce a prolonged period of reduced feelings of hunger and desire to eat following the meal. This effect could in turn have a substantial impact on the amount of snacking going on or the amount of food eaten at the *next* meal.

Experience with the Active IPT compound in Leptoprin®-SD subsequent to the trial reported here has shown that failure to eat following administration results in little effect on subsequent hunger. Hence, the act of eating appears to be integral to successful utilization of Leptoprin-SD. This fact has prompted consideration of a possible role of Leptoprin-SD in the inhibition of the so-called "hunger hormone," ghrelin. This hormone is secreted a few minutes before anticipated meals and increases one's feelings of hunger. Ghrelin levels return to baseline gradually during the course of eating. While the role played by delayed gastric emptying cannot be discounted, it is possible that Leptoprin-SD exerts its primary metabolic impact on weight control through the regulation of ghrelin. Plans are currently underway to examine this mechanism experimentally.

Arguing in favor of the role of gastric emptying in weight loss is research that shows that the consumption of a special, patented, micronized and purified fiber, known to produce weight loss, has been shown to delay gastric emptying and increase the sensation of satiety.

CALCIUM

Calcium's role as a weight loss adjunct has been firmly established in the scientific literature. It has been shown that low levels of dietary calcium intake increase the calcitropic hormones which in turn stimulate lipid (fat) storage and at the same time inhibit the ability of the body to breakdown stored fats and return them to general circulation for use or disposal. The weight loss contribution of dietary calcium is so impressive that a scientist has concluded that increasing calcium among the United States population "has the potential to effect a substantial reduction in the prevalence of obesity."

REDUCING PROSTAGLANDINS

Perhaps the most significant area of fat management research in recent years involves the role of the immune system. There appears to be a solid link between inflammation and obesity. Leptoprin-SD exerts a strong effect on the production of the inflammatory cytokines produced in adipose tissue. These are substances that can adversely affect the metabolism of sugars and insulin and can also increase C-reactive protein, a prominent marker for heart disease. Low-grade inflammatory throughout the body leads to a continual production of these cytokines. Some proteins produced by the immune system, such as certain complement proteins, have actually been shown to increase fat storage. It is likely that one component of diet failure involves uncontrolled inflammatory processes that feed on one another and continue to erode the body's ability to reduce fat stores. Leptoprin-SD, simply by its ability

to inhibit the production and activity of prostaglandins, could be expected to reduce the damage done by inflammatory cytokines.

A significant bonus effect achieved through the ability of Leptoprin-SD to affect prostaglandin metabolism is an actual reduction in the body's ability to recruit new fat cells. Reducing fat cell number equates to less fat storage, less cytokines, less damage to insulin metabolism and a lowered risk of heart disease.

II. ENERGY

Plants that contain methylxanthines have been accepted for centuries as mediators of energy. Long distance runners in Africa and South America achieved these ends by chewing the medicinal parts of plants containing methylxanthines while running to help their bodies turn stored fat into the fuel they needed to keep up the pace. In modern times, these methylxanthines have been extracted and synthesized to produce more compact and easily accessible compounds for maintaining energy levels at required levels. The unique Leptoprin-SD formula combines several sources of methylxanthines in perhaps the most powerful form ever. It is meant to be used by people wanting and needing a high level of energy production, and for weight management. It is not designed to be used indiscriminately, however, and adherence to label directions is recommended for best results. Let's see why.

A good deal of the research on the ergogenic effects of methylxanthines has shown that methylxanthines exert their ergogenic properties in two ways. First, they energize the central nervous system through a fairly direct process. This results in the nearly immediate increase in mental clarity often observed following the consumption of even moderate amounts of methylxanthines. Second, and most important for meeting the exaggerated needs of people involved in prolonged physical or mental exertion, methylxan-

thines stimulate lipolysis in fat cells.

Lipolysis is the process whereby stored body fat is converted into forms the body uses for short term and long term energy production. Technically speaking, lipolysis is the process whereby stored triglycerides are broken down into free fatty acids and then mobilized into the blood stream where they circulate and are taken up and metabolized by all other cells of the body to produce ATP, the energy currency of the cell.

Recently, the armed forces of the United States and Canada have become seriously interested in the possible application of methylxanthines as a method for increasing the performance of soldiers under acute and chronic stress. When people are exposed to several stressors, mental and physical performance are substantially degraded. The military was the first to recognize the serious lack of procedures for counteracting this problem. Astute students of military history, however, would have noticed that plant materials containing xanthines have often been used by military personnel to ward off sleepiness while on guard duty and to maintain vigilance under combat situations lasting for several days without relief.

In one of the most rigorous experimental investigations of the possible role of xanthines to offset severe acute stress, researchers at the U.S. Army Research Institute of Environmental Medicine, in conjunction with scientists from Tufts University and Pennington Biomedical Research Laboratory, examined whether moderate doses of trimethylxanthine would reduce adverse effects of sleep deprivation and exposure to severe, multifactor, environmental and operational stress on mental performance. In this study, US Navy Sea-Air-Land (SEAL) trainees received either placebo or trimethylxanthine capsules after 3 days of sleep deprivation and continuous exposure to other stressors, including running, lifting, paddling, swimming, calisthenics and other rigors inflicted during the appropriately named "Hell Week" period of

training.

As might be expected, sleep loss and exposure to other severe stressors resulted in a profound deterioration in all aspects of cognitive function assessed. Measured against placebo, the trimethylxanthine-treated group experienced a significant improvement in visual vigilance, reaction time, repeated acquisition, self-reported fatigue and sleepiness, with the greatest effects on vigilance, reaction time and alertness. Interestingly, marksmanship, a task that could be affected by shakiness or jitteriness, was not affected by trimethylxanthine. The effects of the trimethylxanthine peaked at a little over an hour but persisted for up to 8 hours following administration. Of the doses used, the higher doses (200 or 300mg) yielded the best results. The researchers concluded that even under the most adverse conditions, these moderate doses of trimethylxanthine can improve cognitive function, including vigilance, learning, memory and mood state. What makes this study so valuable are the extreme conditions under which the trial was conducted. SEAL candidates are already some of the toughest, most stress-resistant people on the planet. Only about one in four soldiers who enter the training graduates. After weeks of intense, difficult training designed to identify individuals who can withstand the adverse effects of extreme stress, candidates must face the rigors of Hell Week during which they engage in continuous 24-hour activities, physical and mental challenges, environmental stress (especially cold-induced stress), and constant psychological pressure.

Other studies have yielded similar results. For example, in a study carried out under the Defense R&D of Canada, a group of civilian and military personnel were enlisted in a trial to examine the duration of methylxanthine's ergogenic effect and whether it differs between users and non-users of the substance. In this trial, patients were required to ride to exhaustion on a stationary bicycle, following consumption of

5mg/kg trimethylxanthine. In the end, the compound allowed the subjects to exercise for about 1/2 hour longer and the non-users benefited slightly more than the users (about 5 minutes). Not only the duration, but the magnitude of response was greater. The energizing effect achieved through trimethylxanthine ingestion has been demonstrated in several other studies.

Mode of Action

While there is rhetoric about the value of methylxanthines in augmenting thermogenesis stimulated by ephedra, this effect is actually achieved through a slightly different process than the increase in ergogenesis or energy that is derived more directly from methylxanthine consumption without ephedra. Ephedra stimulates the production of the neurotransmitter norepinephrine (NE). Xanthines increase the half-life of circulating NE by inhibiting the enzymes that break NE down. (Xanthines inhibit phosphodiesterase activity in cells and increases cyclic AMP accumulation in muscle and fat cells; these actions not only support NE function but contribute to xanthines' own metabolic activity.) In the absence of increased NE, xanthines exert other kinds of metabolic enhancement and this activity is the focus of the current paper.

As mentioned at the outset, xanthines exert two primary actions that can account for the observed enhancement of mental and physical performance. Methylxanthines as a group are universally recognized for their ability to augment central nervous system function. This probably accounts for much of the immediate effect on mental clarity, learning, vigilance, etc. However, the quick effect on the nervous system would only be expected to last for a few minutes in the absence of added fuel in the form of glucose and, indirectly, from increased free fatty acid concentration throughout the rest of the body.

It has been repeatedly demonstrated that ingestion of xanthines

enhances fat metabolism. This is achieved by altering the effectiveness of the fat cell's ability to release stored fats, and by increasing the muscle cell's ability to take advantage of the increasing supply of fat-derived fuel. A consequence of increased fat utilization by the muscle cell is a net increase in the amount of glycogen spared. Because glycogen is spared, quick glucose uptake by the brain is feasible. (Glucose is the main fuel of the brain; if glycogen stores are depleted, fuel reserves for the brain disappear, which can result in mental confusion — that methylxanthines produce mental clarity argues in favor of glycogen sparing under increased metabolic conditions.)

In other words, ingestion of methylxanthines prior to periods of exercise or stress enhances the mobilization of fatty acids that are then used as the major energy source during endurance, exercise or chronic stress. This leaves the glycogen (quick energy) available for use when needed.

Xanthines achieve their lipolytic effect by increasing the activity of an enzyme known as hormone sensitive lipase, by stimulating fat cell receptors that signal lipolysis, and by inhibiting enzymes that inhibit lipolysis. All of these properties have been recognized by researchers as possibly instrumental in increasing endurance, performance time and delaying fatigue. Hence, the effects of xanthines in this arena have been repeatedly examined, with the overall consensus being favorable to the initial hypotheses.

Parentetically mentioned above was the importance of glycogen in brain functioning. But there is also an important role played by glycogen in endurance training. Effective endurance performance requires an optimum use of stored glycogen in muscle and liver. Glycogen storage capacity in the body is severely limited (about 400g in an 80kg healthy male). Therefore the chief causes of fatigue during prolonged endurance exercise are hypoglycemia (low

blood sugar) and depletion of stored glycogen.

The increase in fatty acid availability as a result of ingestion of xanthines reduces the rate of glycogen depletion and improves endurance. Consuming xanthines prior to exercise performance or stressful circumstances would have the net effect of helping to maximize the amount of circulating free fatty acids available for usage at the appropriate moment and sparing the sensitive glycogen stores from rapid depletion.

In a very real sense, methylxanthines should be viewed collectively as a "lipolytic food." As part of the diet of an athlete or anyone in need of acute energy surplus, a lipolytic food would stimulate lipolysis and/or fat oxidation at rest, under stress or during exercise. In one study, the administration of trimethylxanthines 60 minutes prior to exercise resulted in an increase in free fatty acid concentration, increased lipid metabolism and decreased muscle glycogen utilization. The rate of fat utilization for energy output correlated with an increase in the concentration of free fatty acids. Glycerol concentration was actually elevated following exercise, suggesting that methylxanthines enhance lipolytic activity in body fat stores.

To summarize the cellular level chemistry, through a reduction in phosphodiesterase activity stimulated by NE, which in turn increases NE activity, xanthines enhance cyclic AMP and hormone sensitive lipase activity in skeletal muscle and fat cells, with a net increase in circulating free fatty acids.

To summarize the physiological effects, xanthines act as a lipolytic food, 1) increasing the concentration of serum free fatty acids during the early phases (up to an hour) of exercise, thereby maintaining higher fatty acid concentrations during moderate intensity endurance exercise, which becomes the main source of energy for skeletal muscle, and 2) sparing glycogen which is therefore

available for energy production during the latter stages of exercise.

To summarize the net behavioral advantages, ingestion of xanthines leads to improved performance, both mentally and physically, with the strongest effect felt after about 1 hour, declining gradually over the next few hours.

The usefulness of xanthines is not restricted to any particular sex or age group. Indeed, it has been shown that the elderly experience a decreased ability to mobilize fat in response to exercise. In this age group, research has found that xanthine augments fat mobilization as it does in the young, but to a lesser degree. In other words, the elderly need all the help they can get and methylxanthines should be a great aid.

L-TYROSINE

Some xanthines are classified as indirect-acting sympathomimetics, meaning that they cause nerve cells to release norepinephrine and/or dopamine which then act on nerve receptors. Sympathomimetics have appetite suppression ability. Thus, in addition to ability of xanthines to increase lipolysis and ergogenesis, they are also instrumental in reducing appetite. L-tyrosine has been shown in research and patent documentation to significantly extend the appetite suppression attributable to the consumption of both direct- and indirect-acting sympathomimetics.

CONCLUSIONS

The use of xanthines as ergogenic aids has received considerable attention in recent decades, following on the heels of several centuries of use for improving the performance of tribal runners, trained athletes, military personnel and the population at large: from the habit of chewing gooroo nut on hundred mile long runs through the jungle to the increasing needs of marathon athletes; from ancient herbal decoctions to modern drugs;

from the enhancement of exercise to the enhancement of weight loss; throughout history, xanthines have dramatically improved the lifestyles of millions.

We support the term “lipolytic food,” coined by a noted scientist in the field of xanthine chemistry, to describe the primary healthful role of xanthines. In this capacity, ingestion of xanthines allows the body to meet unusual (or even usual) energy demands, whether inflicted by environmental contingencies or arising from any form of athletic endeavor.

As can be seen from the information provided in this review, every effort has been made to make Leptoprin®-SD the most effective weight management tool ever created. Leptoprin-SD not only combines several sources of xanthines with the

proprietary herbal mixture IPT in order to give the user the widest possible rationale for use, but includes several other compounds designed to enhance, extend and magnify the weight control properties of this product. Whether weight management or energy management is your goal, Leptoprin-SD represents the very best options available anywhere.

NOTE: As an added bonus, Leptoprin-SD contains a patented herbal extract shown to significantly improve the bioavailability of nutritional substances with which it is combined. Now, for the first time, the biological usefulness of the active materials in Leptoprin-SD is enhanced beyond their normal digestive limitations.

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