

WHITE PAPER:

**“Weight Loss Products and Health Factors:
Exciting Recent Findings”**

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The Weight Gain Problem

The prevalence of overweight and obesity in America has increased dramatically over the past five decades, today identified as a significant public health issue. The total prevalence of overweight and obesity increased from about 45% in 1960 to almost two thirds of our population in 2004. (National Center for Health Statistics, 2006). In 2008, the Centers for Disease Control (CDC) Behavioral Risk Factor Surveillance System determined the prevalence of overweight (bmi 25.0-29.0) and of obesity (bmi 30+) to be 36.6% and 26.6%, respectively. These figures represent a similar rate of overweight as reported by the CDC in 2002 (37%) but the reported prevalence of obesity increased by almost 21% in that six year period.

The escalating rate of obesity is of particular concern when one considers that obesity is a primary factor associated with increased risk of heart attack, stroke, several cancers, osteoarthritis and musculoskeletal injuries. There is also a direct relationship between obesity and a number of metabolic disorders including type II diabetes, hypertension, and dyslipidemia (Wallace JP and R. Shala. 2009). Persons with obesity generally exhibit altered metabolic functioning as evidenced by increased levels of insulin at rest and response to increasing glucose with decreased insulin sensitivity. It appears that insulin functioning may be a primary mechanism involved in the development and preservation of obesity.

While thyroid disorders and genetic factors do contribute to obesity, the vast majority of cases result from sedentary lifestyles and excessive caloric intake. However, the caloric balance between expenditure (activity) and daily intake is not consistent with increasing levels of obesity. For example, the insulin dysfunctions associated with overweight and obesity effectively limits the circulatory patterns necessary for productive exercise. Insulin resistance restricts the production of nitric oxide which is vital for relaxation of smooth arterial muscle and increased

blood flow into active skeletal muscle (Leland et al, 1999). Without effective capillary bed saturation, exercise output is hampered thereby reducing caloric output. Reduced levels of vasodilation elevate peripheral resistance placing increased stress on cardiac mechanisms. Thus, it is clear that the condition of obesity presents significant particular challenges far beyond the traditional caloric balance model.

It is estimated that Americans currently spend over \$58 billion on various weight loss products and programs annually with growth of this market estimated at over 6% through 2010. (MarketData). The prevalence of overweight and obesity worldwide has resulted in the growth of over the counter weight-loss products into one the largest categories of nutritional supplements. However, the financial success of these products has generally not been matched by proven efficacy.

While various strategies are effective in significant short term weight loss (at least 10% bodyweight), losses in weight are maintained long-term in only about 20% of cases. (Wing 2005) Commonly, temporary weight loss is followed by regaining the weight (and unfortunately a bit more) and when repeated produces a 'yo-yo-ing' of losing and regaining body weight which over time results in further metabolic dysfunction. Many persons do not succeed with weight loss due to unrealistic expectations. Despite common marketing claims to the contrary, it is not possible to sustain and maintain significant long term weight loss without including exercise and nutritional programming. Recent research has suggested that resistance training provides distinct benefits, including increased lean body mass, as part of a total weight loss program. (Donnelly 2009) Otherwise, the traditional long duration, low intensity exercise strategy for weight loss requires more than thirty minutes of exercise virtually every day if coupled with caloric restriction with considerably greater duration of exercise needed without caloric restriction.

Weight Loss Products

Research indicates that effective weight loss maintenance requires both moderate nutritional adaptations and increased activity consisting of both aerobic and anaerobic exercise components with effectiveness potentially enhanced with OTC weight loss products. It has been suggested these products may provide a safe means to reduce to some degree the reduced training and exercise efficiency that goes with the overweight/obese conditions. Nutritional support may provide improved capacity for exercise and the effectiveness of the total weight loss program. Popular products commonly consist of one or more of the following categories:

1. *Appetite Suppressants* reduce caloric intake
2. *Nutrient Blockers* (carbohydrates or fat) disturb the digestive process thereby reducing nutritional uptake of ingested calories
3. *Thermogenic Factors* include various dietary supplements used to stimulate weight loss via increased metabolic rate (consumption of energy) as evidenced by increased body temperature. Thermogenic weight loss is associated with increased metabolic rate and increased cardiac stress (increased heart rate and blood pressure). Many of these agents increase metabolic stresses by stimulating the sympathetic nervous system, which might place some individuals at increased health risk. It is important to note that increased sympathetic nerve activity directly increases vasomotor activity such as constriction of arterial smooth musculature. Ironically, most stimulant thermogenic factors actually increase peripheral pressure (evidenced by increased blood pressures) thereby reducing blood flow into the capillary bed and limiting the ability to exchange nutrients. Central cardiorespiratory stimulation may produce uncomfortable acute responses such which decreases product tolerance thereby limiting the effectiveness of the total weight loss

program. Stimulant thermogenic agents have, in several cases, been associated with high rates of serious side effects such as heart attack, stroke, liver damage and in some cases death which led to the removal of products from the marketplace. Most notably, the weight loss pharmaceutical Fen-phen was recalled by the FDA in 1997 due to increased risk of heart valve complications and pulmonary hypertension and in 2004 the FDA banned ephedra after it was found to be associated with significant gastrointestinal, psychiatric and autonomic side effects (Shekelle et al, 2003). The recent May 2009 recall of one of the most successful OTC weight loss products (due to reported liver risk and one reported death) has prompted an enthusiastic drive to develop effective non-stimulant thermogenic products for the weight loss market. Additionally, some manufacturers have sought out product components that specifically provide nutritional support for enhanced functioning of the metabolic processes that are commonly limited in persons with obesity, such as altered insulin sensitivity.

Recent Research Findings

Recently at the 2009 meeting of the International Society of Sports Nutrition, Dr. Chad Kerksick presented the findings of a weight loss study which he coordinated in his laboratory at the University of Oklahoma. The well designed study examined the effects of a commercial weight loss product (WipeOut™) in 24 sedentary men and women as they participated in an initial eight week exercise program with moderate nutritional control. All subjects participated in the same exercise program which consisted of both resistance training (2 sets of 12 repetitions, seven large muscle group exercises) and cardiovascular training (30 minutes of stationary cycling) and the same nutritional control plan (recommendations for dietary control and a daily protein drink suggested as a meal replacement) (UltraMet Low Carb™, Champion Nutrition). Before and after the eight week program, all the participants underwent measurement of body weight and

composition, physical fitness, resting vital signs as well as blood testing to determine lipid panels, values of fasting glucose, and markers of liver stress. Participants were randomly assigned in a double blind fashion to either a group that received the weight loss product (WL) or to a group receiving a placebo (PL) thereby providing a controlled means to examine the effects of WL in sedentary overweight and obese persons (BMI=30.6) as they also participated in a balanced exercise program with moderate nutritional control. Subjects in the WL and PL groups were directed to take two doses of the respective supplement per day.

Not unexpectedly by following an initial exercise and dietary control program, subjects in the WL and PL groups displayed similar reductions in mean body weight (2.3 and 2.1 lbs, respectively) with like increases of lean body mass (both 1.6 lbs) and parallel statistically significant decreases in body fat mass and percentage (-1.8 , -1.7% for WL, PL), $p < 0.001$). The bench press and leg press test values also increased significantly overall ($p < 0.001$), with no significant differences between the WL and PL groups. These findings are in accordance with prior studies which have reported the effects of exercise and basic nutritional control in combination with a weight loss product in a modest number of sedentary overweight persons over a relatively short period of time.

Close inspection of the study data reveals interesting apparent effects of this weight loss product on resting vital signs as well as the values of blood lipids, fasting serum glucose, and markers of liver stress. Generally, these measurements are performed in such studies to examine for potential negative side effects of the weight loss products as indication of product safety. However in this case not only were there no indications of increased health risks, there were several measurements which actually indicated improvements in these health risk factors within the WL group.

First, both the WL and PL groups exhibited somewhat similar, statistically non-significant, positive changes in resting heart rate following the eight week program (WL↓6.4, PL↓4.9lbs). However, the WL group displayed a statistically significant reduction ($p<0.01$) in resting systolic blood pressure (129.5 to 115.7 mmHG) whereas the PL group displayed a more modest non-significant reduction from 124.5 to 119.8 bpm ($p=0.15$). The WL group also displayed a trend for statistically significant ($p=0.06$) reductions in resting diastolic blood pressure (↓5.3 mmHG) while the PL group displayed an increase in diastolic pressure of 2.3 mmHg. As weight loss products are commonly associated with increased blood pressures, the appreciable reductions in resting pressures observed in the WL group are especially striking. These findings, along with similar reductions in resting HR in WL and PL, suggest that the WL product resulted in reduction of peripheral pressures.

Secondly, the changes in fasting serum glucose in the WL group (↓3.7 mg/dL) were significantly different ($p<0.05$) from those of the PL group (↑3.2 mg/dL). These findings are quite impressive as reduced fasting glucose levels suggest improved glucose clearance. As both the WL and PL groups participated in the same exercise conditioning program, the difference between groups in glucose change scores suggests that some aspect of the WL supplement enhanced the uptake of glucose such as improved insulin sensitivity. As insulin resistance has been found to be a critical factor in the development of preservation of obesity, these findings are particularly encouraging.

Finally, analysis indicated a strong trend ($p=0.09$) that the changes in total cholesterol displayed by the subjects in the WL group (↓4.8 mg/dL) were statistically different from those of the PL group (↓1.0 mg/dL). Total cholesterol is a primary risk factor of cardiovascular disease which is prevalent in the obese and overweight populations. The finding of a trend for greater

total cholesterol reductions in the WL group again suggests that the weight loss product produced positive changes in primary factors of health risk.

The findings of the Kerksick study indicate that the use of a commercial weight loss product (WipeOut™) by sedentary overweight/obese persons during participation in an exercise program with moderate dietary control provided apparent improvements not only loss of body weight but also in several markers of health risk including resting blood pressures, fasting glucose levels, and values total cholesterol beyond those exhibited with the same exercise and diet control alone. It is also interesting to note that nutritional intake analysis indicated a significant shift in carbohydrate intake (3.9 to 3.0 g/kg) ($p=.06$) matched by a significant increase in mean protein intake (1.1 to 1.4 g/kg) ($p<0.05$). Calorically, this represents a 23% decrease in carbohydrate consumption and 27% increase in protein intake. The PL group displayed similar but non-significant shifts in carbohydrate and protein intake. Similar shifts in dietary composition correlate with significant improvements in certain indices of health and body composition in long-term studies.

The unique nature of improved values in health risk factors with a commercial weight loss product prompts consideration of the product components.

The weight loss product examined in the Kerksick study was WipeOut™ (Champion Nutrition) which includes the following key ingredients including several factors not commonly used in weight loss products.

Lysine l-carnitine fumarate is a bonded form of lysine, l-carnitine and fumarate produced by Sigma-Tau HealthScience and marketed by Champion Nutrition as Thermosine™. The Kerksick investigation is the first to examine this carnitine variation but it is well established that carnitine

shuttles fatty acids into the inner matrix of the mitochondria where they undergo beta oxidation to produce energy. The process of escorting the long chain fatty acids, such as triglycerides, is pivotal in long term weight loss and maintenance. Fumarate serves as an intermediate substrate in the Citric Acid Cycle providing an additional energy source. As a precursor to carnitine, the essential amino acid Lysine may assist in the replenishment of carnitine levels.

Citrus Aurantium (bitter orange) is a citrus tree and its fruit that has been used in herbal medicine for its actions as an appetite suppressant and stimulant. Citrus aurantium contains synephrine which is thought to act as a specific beta-agonist by stimulating beta-3 receptors associated with adipose tissue with reduced effect on cardiovascular functioning (e.g. blood pressure). Citrus aurantium has been suggested as a safe alternative to ephedra. However as synephrine has similar stimulatory effects as caffeine and ephedrine, citrus aurantium appears to be a promising diet product ingredient but not the primary component.

7-Keto® DHEA is an active metabolite of DHEA that shares the well established thermogenic, neurological and immunological effects of DHEA without risk of being metabolized into either testosterone or estrogen. 7-Keto® DHEA has been shown in controlled studies to enhance the weight loss produced with dietary control and exercise programming.

Theobromine HCL is an alkaloid in the same chemical family as caffeine. Theobromine has less action as a central nervous system stimulant than caffeine but has a greater stimulatory effect on the heart. In addition to use as a heart stimulant, theobromine has been used clinically as a vasodilator and as a diuretic.

Cayenne is a hot, red chili pepper that contains the chemical capsaicin, which has been attributed with strong vasodilatory effects. Cayenne has also been suggested to reduce plaque accumulated within blood vessels and blood cholesterol levels.

Caffeine exerts stimulatory effects as an antagonist of adenosine receptors. Adenosine activation of these receptors suppresses neural activity, as in central nervous system fatigue. Blocking the adenosine receptor activation produces a stimulatory effect on the central nervous system effect. Caffeine is used commonly to reduce physical fatigue with enhanced mental alertness and focus, particularly in settings with ongoing stress. Caffeine is one of the most, if not the most, common ingredient in weight loss products.

Green Tea Extract is derived from green tea which contains caffeine, commonly more caffeine than in coffee as well as two caffeine metabolites, theophylline and theobromine. The effects of theophylline are stronger than those of caffeine while theobromine exerts weaker effects than caffeine. Green tea also contains polyphenols, specifically epigallocatechin gallate (EGCG) which is thought to produce a thermogenic effect and fat oxidation in addition to that attributed to the caffeine content. It is believed that there may be some interaction between some green tea extract ingredients (including caffeine) same produces greater metabolic activity.

DMAE, or dimethylaminoethanol, is an organic compound related to the amino acid choline that stimulates the synthesis of the acetylcholine. It has been shown that DMAE increases alertness with a positive effect on mood state. As the effectiveness of weight loss and maintenance is commonly reduced by low mood states associated with prolonged caloric restrictions and exercise training, enhanced mood may allow for increased exercise adherence.

Conclusion: Proposed shift in weight loss paradigm

The escalating prevalence of overweight and obesity and the poor success rate of various weight loss programs necessitate the development of novel approaches to this problem. Lack of physical activity and excessive caloric intake over time disturb metabolic functioning evidenced by at least three easily evaluated indices: 1) altered insulin resistance, which over time leads to restricted blood flow into skeletal muscle at rest and during exercise; 2) increases in systolic and diastolic blood pressures, which lead to cardiovascular and kidney syndromes or pathologies; 3) decline in healthy lipid parameters, which lead to increased risk of cardiovascular disease. As these three indices degrade, exercise productivity is dramatically hampered thereby limiting weight loss and maintenance.

The findings of a recent controlled study suggest that use of a commercial weight loss product (WipeOut™) in sedentary overweight/obese persons in combination with participation in an exercise program and moderate dietary control resulted in apparent improvements in each of three markers of increased health risk described above including resting blood pressures, fasting glucose levels, and values of total cholesterol. As far as this author can determine, this is the first time an OTC weight loss supplement has been shown to positively influence these markers. The study also found a significant reduction (23%) in ad-libitum consumption of carbohydrate and a significant increase (27%) in ad-libitum consumption of protein in the group receiving WipeOut™.

It is suggested that properly designed weight loss products may provide a clear health advantage to the obese individual, including improved functioning of the physiological systems that have declined with sedentary lifestyles and poor dietary habits, such as insulin dysfunction. This approach may provide overweight persons with increased exercise capacity along with

improved health levels, both of which will contribute to improved outcomes of weight loss and maintenance programs.

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