POSITION ON WEIGHT LOSS

INTRODUCTION TO WEIGHT LOSS PRODUCTS



Support Document

Introduction

- Dieting to lose weight without financial motivation is challenging for most everyone and generally ends with a weaker structure and much of the weight regained within the first year¹⁻⁵
- Therefore, for weight/body fat reduction, dotFIT recommends exercise (some sort of significant physical activity) and calorie restricted meal planning based on a safe desired rate of loss¹⁰
- Participants should avoid loss of lean body mass and fill unavoidable nutrient gaps caused by the necessary restricted food intake required to produce a calorie deficit for weight loss by using appropriate supplementation including at a minimum, a multivitamin and mineral formula (MVM)^{4,10,24-31}
- Appropriate Supplementation has been shown to:
 - ✓ Fill gaps, preserve LBM, lessen/ease the workload to avoid plateaus and/or surrender, increase daily energy & total energy expenditure (TEE) and manage appetite until lifestyle conforms. 4,10,24-31









Two Essential Items:

- 1. Individualized Complete MVM
 - √ Kid's, Active, Women's, Vegan or Over 50
- 2. Protein (Diet & Protein Rich Meal Replacement) choice of:
 - ✓ LeanMR, WheySmooth, Natural Whey, BestPlantProtein, Pre/Post Workout & Meal Replacement Formula

JOB 2 – MAKE IT HAPPEN AS EASILY, QUICKLY & HEALTHFULLY AS POSSIBLE – INSTANT GRATIFICATION LEADS TO QUICKER ADDICTION TO FITNESS

TEMPORARY ADDITIONAL SUPPLEMENTS FOR GETTING OVER THE DIET HUMP, TIME CONSTRAINTS, MULTIPLE FAILURES SPECIALTY FAT LOSS SUPPLEMENTS

- WEIGHT LOSS & LIVER SUPPORT
- CARB REPEL
- UPDATED THERM ACCEL THERMACCEL

MAKING OR UPDATING A PRODUCT – PLUGGED INTO THE RAPIDLY EVOLVING SCIENCE OF FEEDING THE BODY









Daily Research Leads to Evolving Formulas to Meet Evidence-based Guidelines

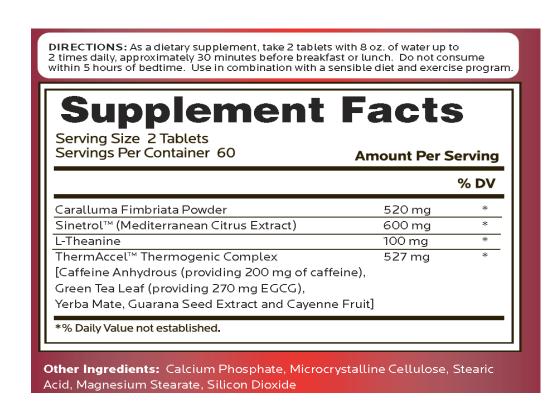
- Product Goal (non-clinical/medicinal)
 - ✓ Health, weight/fat control, performance, muscle gain
 - ✓ Peer review journals/web/Medline only real time data
- Rationale for ingredient(s) selection
 - ✓ Overview of structure and function (how they work in the body)
 - Individually/synergistically
 - ✓ Mechanisms of action
 - Helps determine symbiotic relationships true unique dotFIT discipline
 - ✓ Human studies to determine safe and effective forms, dosing & synergy consideration
 - Research all studies: effective, negative, null; both animal and human
 - Capture human results to determine forms, dosage amounts & timing
- Creation of the PDSRG Document formulates the final product

THERM ACCEL GOAL **RATIONALE KEY POINTS ThermAccel TYPICAL USE**

BALANCED ENERGY OR BETTER STIMULANT EFFECT







ThermAccel
4th Edition

Controlled Stimulant Formula to Increase Metabolism & Daily Activities + Support Appetite



New formula

Supplement Facts

Serving Size: 2 Tablets

Servings Per Container: 60

DIRECTIONS: As a dietary supplement, take 2 tablets with 8 oz. of water up to 2 times daily, approximately 30 minutes before breakfast or lunch. Do not consume within 5 hours of bedtime. Use in combination with a sensible diet and exercise program.

Ingredient	Amount Per Serving
Caralluma Fimbriata Powder	520 mg
Sinetrol™ (Mediterranean Citrus Extract)	600 mg
L-Theanine	100 mg
ThermAccel™ Thermogenic Complex	931 mg
[Caffeine Anhydrous (providing 200 mg of caffeine), Green Tea Leaf (providing 270 mg EGCG), Yerba Mate, Guarana Seed Extract and, Cayenne Fruit (100K Scoville Heat Units [SHU])	

BALANCED ENERGY OR BETTER STIMULANT EFFECT



Goal

➤ Increase daily calorie burn without forcing more work, reduce diet induced appetite increases and avoid plateaus*

Rationale²⁻³³

- In order to continue weight/fat loss when natural/adaptive plateaus occur* and diet is generally healthy, more deliberate work and/or less food, which in turn causes increased hunger, is the only remedy unless:
 - ✓ 1) calories burned can be increased without adding more exercise or the needed added work is involuntary/spontaneous because of increased energy levels and/or
 - ✓ 2) appetite can be controlled during further caloric restriction.
 - ✓ Thermogenic blends have demonstrated the ability to accomplish #s 1 & 2 and few natural plant extracts have had success for #2
- These combined and potentially additive effects should ease the workload and mitigate hunger to allow continued weight reduction with less hardship

*You burn 100-150 calories/day less at 10% weight loss



3- PRONG APPROACH OVERVIEW



Thermogenic complex with caffeine, yerba mate,* guarana,* green tea extract polyphenol (EGCG) and capsaicin that have independently and combined demonstrated total daily energy expenditure (TDEE) enhancements and fat oxidation increases compared to placebo^{20-22,34-43}

- ➤ Sinetrol (polyphenols), which is a combination of non-stimulant polyphenols that also contributes, but through different mechanisms, to increases in fat oxidation i.e. partitioning energy usage³²
- Caralluma fimbriata, a plant-based appetite suppressor shown to have effects on weight loss^{25,33}

^{*}Synergistic with caffeine

INGREDIENTS & MECHANISM'S OF ACTION



Thermogenic Blend - Max Daily Dose of 2-tabs, twice daily

2-tabs contain:

- Caffeine (200 mg): increases metabolic rate and fat oxidation through: 1) stimulation of adenosine receptors, (a blockade that may also increase dopamine levels) causing a buildup of cAMP with increased cell activities; 2) sympathetic activation of the CNS; 3) inhibition of phosphodiesterase (PDE) to maintain higher cAMP leading to increase lipolysis, heat production and liver satiety signals^{20,26,38-41,48-76}
- ➤ Green tea extract (270 mg EGCG): Increases EE and fat oxidation via inhibiting the enzyme COMT* (degrades epinephrine and norepinephrine while caffeine stimulates both); 2) activation of AMPK** through affecting the ratios of AMP/ADP/ATP (suppressing gluconeogenesis and lipogenesis and enhancing lipolysis) and signaling the gene expression of proteins that play a role in thermogenesis and beta-oxidation^{29,41,53,68,75,82-84,86-95,99-111,115,116,119}

^{*}Catechol-O-methyltransferase participates in the degradation catecholamine transmitters

^{**}Adenosine monophosphate-activated protein kinase

Caffeine & EGCG Additive Effects^{20,31,40,84,65,124-126}

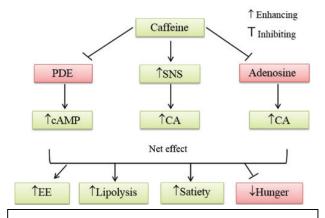


Figure 1 Caffeine Targets in Supporting Weight Loss

PDE- phosphodiesterase

SNS- sympathetic nervous system

cAMP- 3,5-cyclic-adenosine monophosphate

CA- catecholamines **EE**- energy expenditure

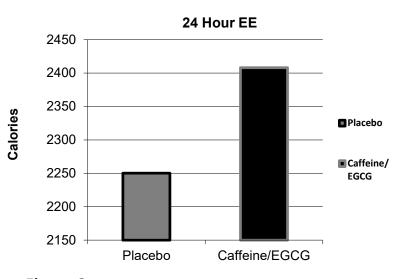


Figure 2: Dullo et al. showed at least a 10% increase in 24-hour EE or equivalent to 157 more calories burned in the caffeine/EGCG group (Average subject's weight was 173 lbs).⁵³

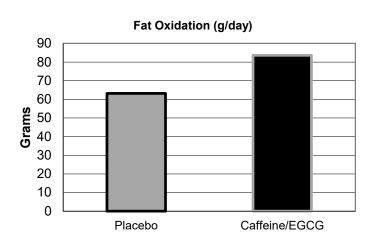


Figure 3: In the same study, approximately 20 more grams of fat was oxidized daily by the supplemented group.⁵³

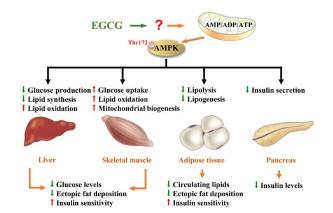


Figure 4: Yang et al. hypothesis on the role of AMPK in metabolic regulation by EGCG.⁸⁸

"EGCG is proposed to <u>active AMPK through affecting the ratios of AMP/ADP/ATP</u>. The activated (phosphorylated) AMPK regulates metabolism in different organs toward the direction of reducing (\downarrow) gluconeogenesis, fatty acid synthesis, insulin secretion and ectopic fat deposition in muscle and liver. These are accompanied by increased (\uparrow) insulin sensitively and the oxidation of glucose and fatty acids". The lower part of the figure was modified from Long et al.⁸⁹

Also helps blocks COMT to keep CA higher

AMP-activated protein kinase (AMPK) plays a key role as a master regulator of cellular energy homeostasis

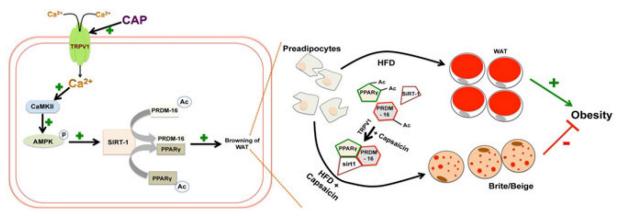
INGREDIENTS & MECHANISM'S OF ACTION



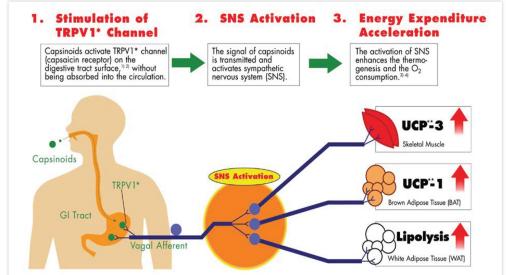
2-tabs contain:

Capsaicin (17 mg= 100κ scoville Heat Units*): increases EE and lipid oxidation, and reduces appetite by increasing thermogenesis through 1) stimulation of transient receptor potential (TRP) channels enhancing BAT, which by activation of the SNS increases calorie burning to produce heat through the uncoupling of oxidative phosphorylation mediated by UCP1, and 2) improves lipid metabolism^{30,34,127-132,135-153}

Browning of white adipose tissue



Model describing the mechanism of action of capsaicin (CAP). Intracellular Ca2+ rise via TRPV1 channels stimulated by CAP activates CaMKII/AMPK, which phosphorylate and activate SIRT-1. This causes deacetylation of PPARy and PRDM-16 and facilitates their interaction to promote browning of WAT. From P. Baskaran et al.¹⁴⁸



Mechanism of Action by which Capsinoids Accelerate Energy Expenditure¹⁴¹

*Average size cayenne pepper contains 30-50K SHUs







2-tabs contain:

- ➤ L-Theanine(100 mg): increases GABA* levels to deliver anti-stress effects including balancing caffeine stimulation²⁰⁰⁻²¹³
 - ✓ Study reviews show caffeine combine with L-theanine had the greatest positive effect on outcome measures (cognitive and mood)²¹⁴⁻²²² "due to balancing caffeine's overstimulation"
- Caralluma Fimbriata (500 mg): appetite support through 1) hypothalamic/nootropic actions including SSRI** activity and 2) ability to inhibit activity of enzymes involved in carbohydrate digestion/absorption^{23-25,179-199}
- Sinetrol (600 mg): improve overall lipolytic activity via inhibiting cAMP-PDE (maintaining higher levels of cAMP) and enhancing fat oxidation and related gene expression (favorable energy partitioning)^{32,155-178} including reducing the activity of Catechol-O-methyltransferase (COMT)

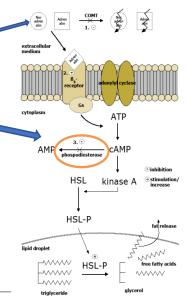
^{**} Selective serotonin reuptake inhibitors: class of drugs used as antidepressants in treatment of depressive disorder/anxiety disorders



^{*}Gamma-Aminobutyric acid

Sinetrol (Bioactive flavonoids Naringenin & Neohesperidin)

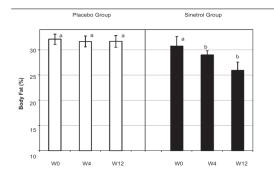
Works through inhibition of PDE and stimulation of fat oxidation genes and other genes/areas shown to enhance lipid metabolism including related apoptosis, energy partitioning & hormone sensitive lipase; and reducing COMT activity 32,155,156,166



Inhibition of Phosphodiesterase [PDE-4]

- → Catabolism of triglycerides into Free fatty acids (FFA) + Glycerol
- → Release of FFA + Glycerol in the bloodstream
- → Direct fat burning action

Sinetrol vs Placebo



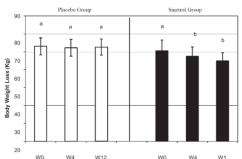


Table 1. Effect of placebo and SINETROL on BMI, body weight & body fat in 20 volunteers after 4 & 12 weeks of treatment 155

Groups	BMI		Body weight evolution (kg)			Body fat evolution (%)		
	Initial	Variation (%) after 12 weeks	Initial 0 weeks (W0)	After 4 weeks (W4)	After 12 weeks (W12)	Intial 0 weeks (W0)	After 4 weeks (W4)	After 12 weeks (W12)
Placebo SINETROL ^S	28.570.7 ^a 28.172.45 ^a	-0.2 7 0.5 ^a -2.2 7 0.9 ^b	73.074.8 ^a 70.576.0 ^a	72.2 7 4.7 ^a 67.5 7 5.2 ^b	72.6 7 4.5 ^a 64.9 7 4.5 ^b	32.071.0 ^a 30.771.9 ^a	31.671.0 ^a 29.070.8 ^b	31.671.0 ^a 25.971.0 ^b

Measuring free fatty acid release from adipocytes, the researchers found that SINETROL significantly stimulated lipolytic activity via the polyphenols inhibition actions on cAMP-phosphodiesterase (PDE) in a range of 6-fold greater than the placebo.

As shown in Table 1, the treatment subjects, compared to placebo, **body fat significantly decreased with a difference of 2.53% and 5.6% after 4 and 12 weeks, respectively**. Additionally, **the body weight decreased with a significant difference of 6.6LB and 12.3 LB after 4 and 12 weeks, respectively**.

THERMACCEL USAGE







Typical Use

- Anyone without adverse events to stimulants and seeking to accelerate weight loss, avoid plateaus and ease the journey, including helping control appetite
- People who need a serious multiple pronged approach to weight control including a strong but controlled stimulatory effect to help increase metabolism
- Do not use if taking heart medications
- Do not use with other stimulants. Keep a minimum of 4-hours between other stimulants including caffeine
- Discontinue after reaching body fat reduction goal or when lifestyle is under control to continue to the desired body composition goal without assistance
- Maximum dose: take four (4) tablets daily, two (2) at breakfast and two (2) with lunch with at least eight (8) ounces of fluids.
 - ✓ If sensitive to caffeine, start with 2-tabs daily in 1-tab doses and move to 2-tab max dose twice daily if comfortable

BALANCED ENERGY OR BETTER STIMULANT EFFECT



Summary of Unique/Key Points

- The combined ingredients of ThermAccel have the ability to significantly increase metabolic rate and potentially daily activities (total calorie burn) while balancing the stimulatory effects of caffeine related herbs, and suppress appetite through multiple mechanisms.
 - ✓ i.e. ingredients may have additive effects in mutual and exclusive pathways
- This combination may allow the user to avoid or overcome typical plateaus related to early weight loss without the normal obligatory increase in activity or decrease in food intake required to continue desired weight/fat reduction.
- ➤ With weight loss prescription drugs being deemed to have too many negative side effects (including being pulled off the market²²³) with minimal results,^{15,224,225} there is high interest in products like ThermAccel and other natural sources for assisting in weight management^{15,124,129,149,152,226-228}

Unique, synergistic and potential additive effects

