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THE SCIENCE BEHIND BLADE®

The Solution to the Struggle of Fat Loss

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Body fat can be very stubborn to lose for many reasons. Most bodybuilders and fitness competitors can attest that the process of burning off unwanted fat can sometimes be the most unpleasant phase of fitness training. The reason stems from it being unnatural to willingly remove a rich source of energy from the body. The body is designed to preserve extra calories as fat when nutrients are in abundance and yet conserve those calories when fuel resources are low. This combination of physiological effects makes the process of purposefully losing fat an uphill battle.

It is a naïve and oversimplified view that simply exercising more and eating less is an effective recipe for fat loss, based on the "energy in" versus "energy out" principle. The premise of this idea is that net body mass is a simple equation based on the balance on how much energy is consumed as food, and how much energy is burned during exercise. The flaw in this principle is based on an incomplete understanding on what all contributes to "energy out". Exercise definitely contributes to energy expenditure, but it actually plays a smaller portion than expected. This is where Blade® can assist.

Energy Expenditure Comes in Several Forms

There is a minimum rate of energy expenditure the body uses every day just to keep the body functioning and cells alive, called the basal metabolic rate (BMR). Surprisingly, this rate is not always constant as it can be modified daily, seasonally, and even environmentally. It is the most prominent variable for energy expenditure, and modifying this will have a dramatic influence on overall energy expenditure. What the BMR does not account for are the effects of any feeding or any movement.

The second influence on energy expenditure is the thermogenic effect of foods. This accounts for the energy required to ingest, digest, absorb and store the nutrients in the diet. Considering the amount of activity that is required for this process, a considerable amount of energy is expended during feeding. The final influence is the amount of non-exercise activity. Activities of daily living make major unconscious contributions to the overall energy expenditure. Environmental factors and lifestyle in a large part dictate the extent of non-exercise activities, but the sympathetic nervous system plays a sizable role in non-exercise energy expenditure.

While the "energy in / energy out" principle is true in theory, understanding how to manipulate the "energy out" portion of the equation is quite complex with the overall metabolism seemingly going in the opposite direction as intended. For instance, with dieting alone, the lack of food causes a drastic increase in a hormone called Ghrelin. The elevation of Ghrelin is responsible for not only the increase in appetite but also a decrease in metabolism, energy expenditure, and fat oxidation, resulting in the conservation of fat. The reduction of food intake also diminishes the thermogenic effect of feeding as expected. Worst of

all however, is the decline in sympathetic nervous system (SNS) activity. This is the sensation of feeling sluggish, empty, tired, lazy and unmotivated to do any physical activity. This decline in SNS activity is responsible for the dramatic loss of non-exercise activity and also the guilt behind missing workout days **(see Figure 1)**.

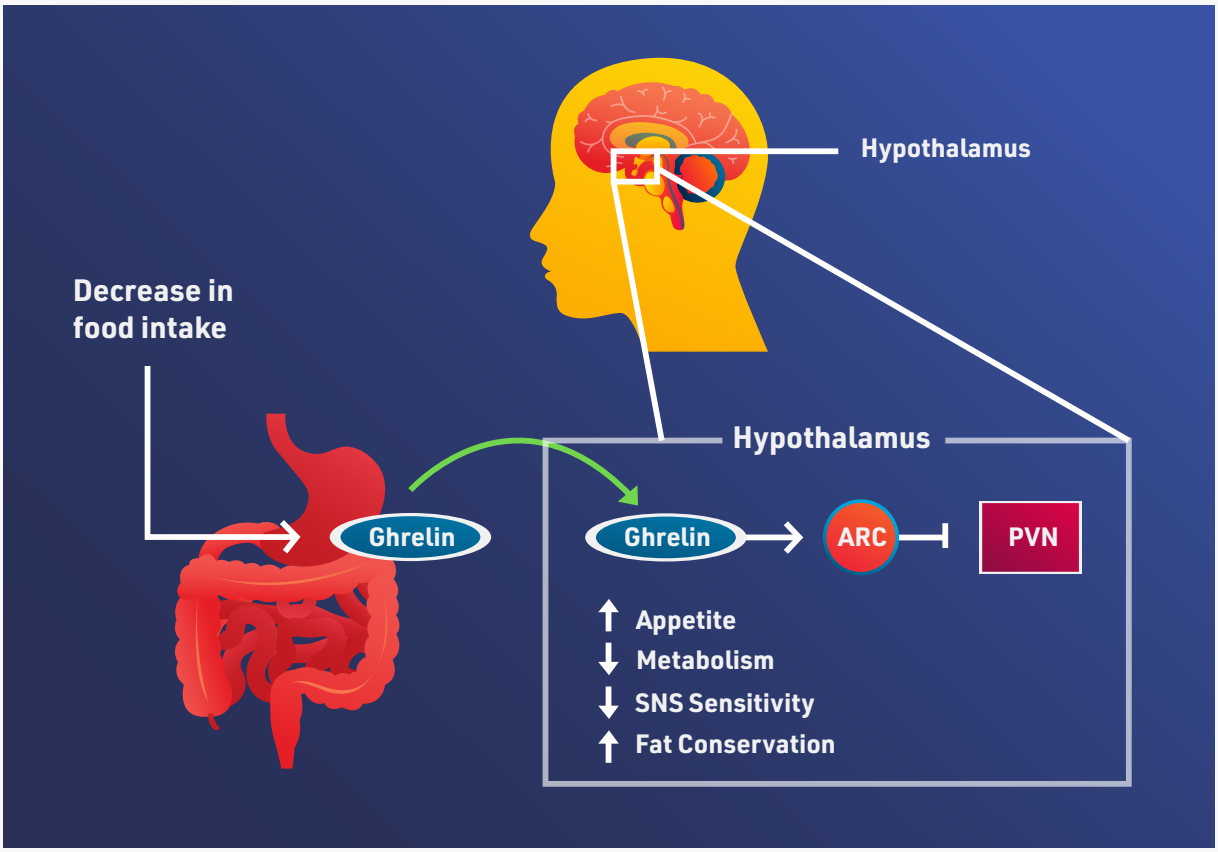

Figure 1. Dieting causes an increase in Ghrelin release from the gut into the blood that crosses the blood brain barrier and into the hypothalamus. Ghrelin activates the NPY/AgRP neurons in the arcuate nucleus (ARC) which in turn inhibit the MC4 receptors in the paraventricular nucleus (PVN), which is responsible for satiety and energy balance. Dieting therefore results in increased appetite, lower rates of metabolism, lower SNS sensitivity and fat conservation.

Through supplementation with Blade®, these variables can be addressed to assist with a diet plan to make fat loss effortless and more substantial. The ingredients in Blade® have been scientifically and clinically shown to be a positive factor in fat loss on five fronts. When combined together, these five mechanisms synergistically allow for the ultimate environment to achieve maximal fat loss.

1. Increased Lipolysis

The very first place to start with fat loss is breaking down the fat tissue where it resides in the fat cells. The process of lipolysis is the enzymatic breakdown of fat stored as triglycerides into individual free fatty acids (FFA). This process is the rate-limiting step for the removal of unwanted fat and is governed by SNS activity. Typically, SNS activity leads to the production of the hormones epinephrine and norepinephrine (N.E.) that bind to β-adrenergic receptors in fat cells to trigger a cascade of signals to result in an increase in lipolysis **(Figure 2)**. Therefore, using ingredients that have been shown to enhance SNS activity, N.E. availability, or increase lipolysis are beneficial for this purpose.

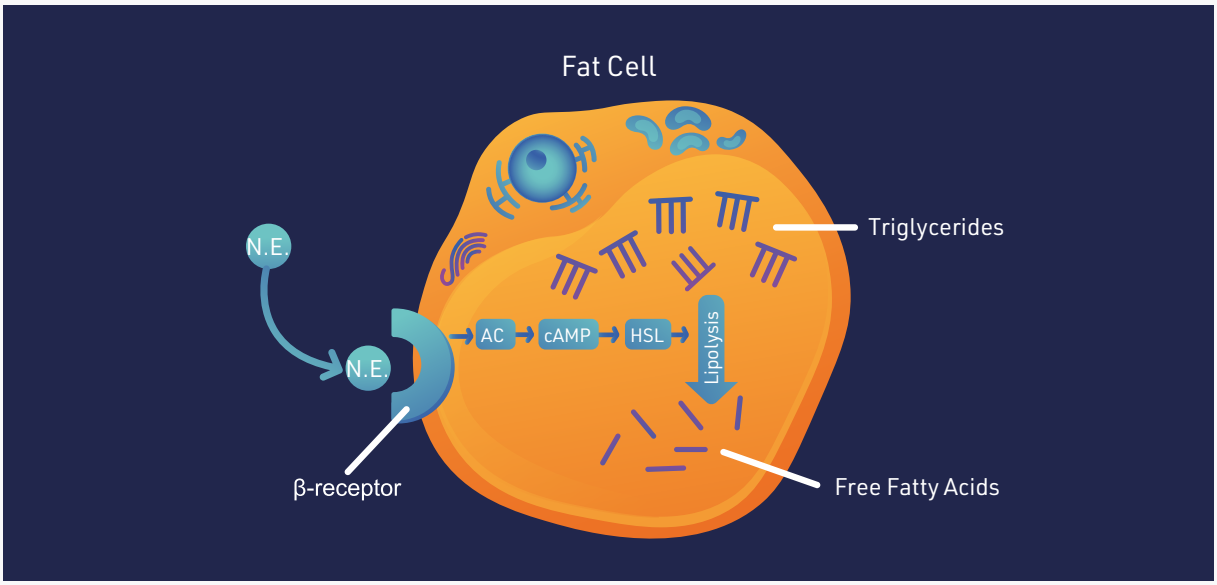

Figure 2. Norepinephrine (N.E.) stimulates the breakdown of fat (lipolysis) through the β-adrenergic signaling pathway (AC: Adenylate cyclase, cAMP: cyclic adenosine monophosphate, HSL: hormone sensitive lipase).

Green tea extract is another ingredient that increases the concentration of N.E. but by another mechanism. A subclass of green tea flavonoids called tea catechins have been shown to have long lasting effects on the inhibition of the enzyme that degrades N.E. called COMT. Research with green tea extract show that inhibition of COMT can allow N.E. to stay elevated for at least 24 hours. Green tea extract on its own has been shown to increase N.E. concentration levels by 37%.

Capsiate is a natural capsinoid from CH-19 sweet peppers. Structurally similar to capsaicin, it binds to the same receptors that capsaicin does to activate the SNS to produce an increase in N.E. that has been shown clinically to yield an 89% increase in free fatty acids.

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Caffeine also activates multiple pathways to induce lipolysis. Firstly, caffeine competes with a compound called adenosine. Adenosine acts on α1-receptors to induce drowsiness by decreasing the release of N.E. Caffeine effectively increases N.E. by inhibiting this pathway. Caffeine plays an additional role in prolonging the effect of lipolysis by inhibiting an enzyme that interferes with the β-adrenergic signaling pathway.

Advantra Z® takes a more direct approach. Using an extract from the bitter orange known as Citrus aurantium. Advantra Z® is standardized to the active ingredient, p-synephrine. Among several beneficial features, p-synephrine can independently and directly bind to β-receptors to induce lipolysis.

The combination of each of these ingredients results in the fast acting, long lasting, and dramatic increases in N.E. concentrations through synergistic mechanisms to provide the highest possible increase in lipolysis.

2. Enhanced Lipid Transport and Oxidation

Freeing up fatty acids is the rate-limiting step for fat burning but does not actually burn any fat. If left unprocessed, individual FFA can resynthesize into triglycerides if they are not quickly burned (oxidation). Fat oxidation is a long and complex process that occurs primarily in the mitochondria of muscles. However, the mitochondrial membrane is completely impermeable to fatty acids. Using a series of transporters, carnitine is an indispensable carrier of FFA across the mitochondrial membrane. Improving the pool of muscle carnitine through supplementation of L-carnitine can allow for enhanced FFA transport into mitochondria and thus lead to greater fat oxidation.
The influence of green tea extract alone is capable of increasing fat oxidation by 35%, leading to an average of 26.8g of fat oxidation over a 24-hour period. The combination of L-carnitine and green tea ensures that a maximal quantity of free fatty acids make it into the mitochondria, and the fat burning process is continually turned on for 24 hours.

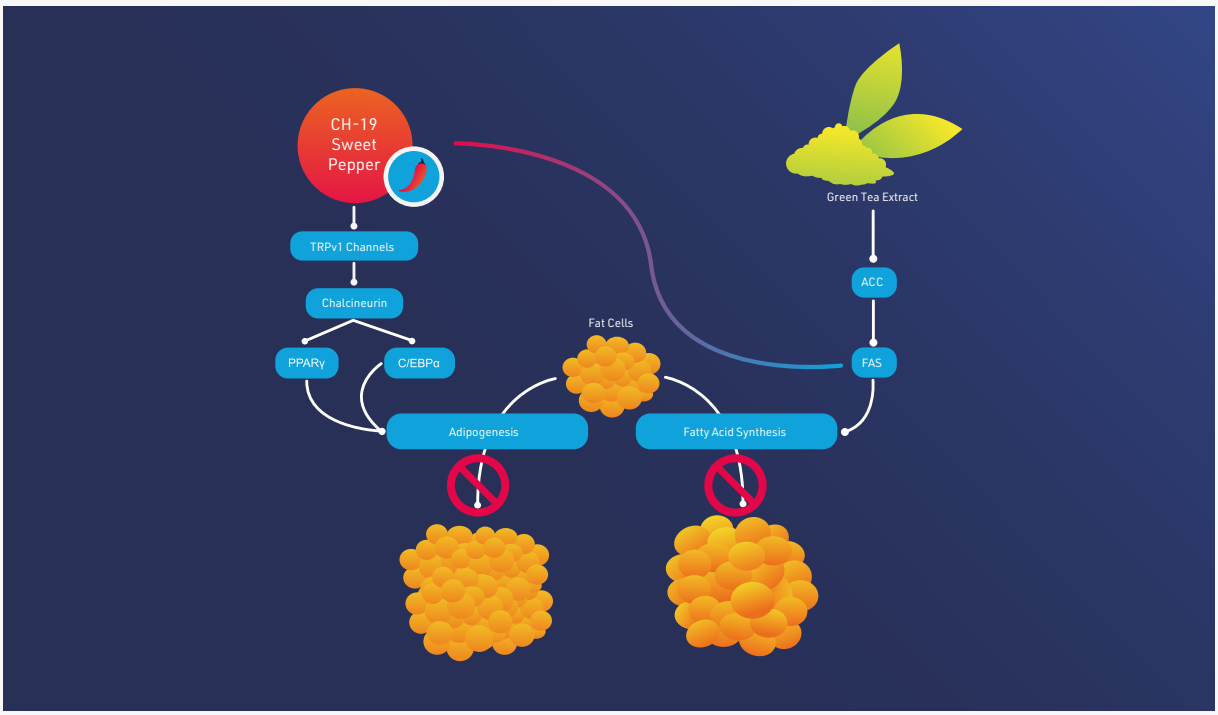

Figure 3. CH-19 sweet pepper and green tea extract inhibit independent cell signaling pathways to inhibit adipocyte production (adipogenesis) and fat-cell growth (fatty acid synthesis).

3. Decreased Adipogenesis and Fatty Acid Synthesis

Attacking the already existing fat is important for fat loss, but it is crucial to attenuate the deposits of new fat. The synthesis of fat can occur on two major levels: the production of new fat cells (adipogenesis) and the growth of fat cells caused by the synthesis of fatty acids within them (fatty acid synthesis). Suppressing the adipogenesis and/or fatty acid synthesis will help contribute to a leaner physique.

The regulation of these processes can be complex. Specific transcription factors known as PPARγ and C/EBPα primarily promote adipogenesis. Simply put, negatively effecting PPARγ or C/EBPα will help reduce the production of new fat cells. As illustrated in **(Figure 3)**, Capsiate activates a capsaicin receptor called TRPv1 that ultimately inhibits adipogenesis through the inhibition of PPARγ and C/EBPα.

The process of fatty acid synthesis is initiated and committed by the enzyme Acetyl-CoA-Carboxylase (ACC), which is then carried out by the enzyme Fatty Acid Synthase (FAS). Inhibition of either of these two enzymes will suppress the accumulation of fat into fat cells. Green tea extract can inhibit ACC and thus suppress the committed step of fatty acid biosynthesis. Specifically, the research data indicates that one specific tea catechin, named Epigallocatechin gallate (ECGC) is responsible for this effect. Furthermore, capsiate has been shown to reduce fatty acid synthesis through the reduction of FAS activity. Collectively, these studies show improvements over a 9 day period that inhibit the increases in adipocyte number by 34% and total triglyceride content by 54%.

4. Increase in Overall Metabolic Rate / Thermogenesis

Manipulating overall energy expenditure in the absence of chronic exercise is not easy. However, certain compounds can help improve energy expenditures by either improving BMR or exploiting a tissue that is mostly dormant in the body called brown adipose tissue (BAT). BAT is a type of fat tissue but is not to be confused with the undesirable fat targeted to be lost. BAT is a highly metabolic tissue that functions by burning calories for heat (thermogenesis) rather than for activity. This means that simply increasing BAT activity can help burn fat without requiring an increase in activity at all. For many years, it was believed that only infants had BAT and humans lost BAT after becoming adults, but recent evidence shows that adults still have adequate BAT that can be used to burn through excess energy. BAT uses a specialized set of proteins called uncoupling proteins (UCP) that are responsible for the conversion of energy to heat. The following ingredients in Blade® have been associated with thermogenesis.

Caffeine is a potent thermogenic compound that has been repeatedly shown to improve the basal metabolic rate by at least 6% for the first 4 hours after consumption. Caffeine is also documented to increase fat metabolism by 42%.

Green tea extract has also been shown to stimulate BAT thermogenesis, especially when combined with caffeine to a degree greater than caffeine alone. It is proposed that the catechin-polyphenols of the green tea are responsible for stimulating thermogenesis at various control points. In result, green tea extract has been shown to increase total energy expenditure by 4.5% during waking hours alone.

Capsiate has been shown in studies to upregulate UCP, while exhibiting an increase in body temperature and energy. In fact, a clinical study of 80 participants who supplemented with capsinoids 30 minutes before morning and evening meals showed that the mechanism of activating UCP was preferential to the abdominal fat region. This particular study observed a significantly greater loss of fat mass in the abdominal region when relative to the overall body fat loss when compared to a placebo group using caloric restriction alone **(Figure 4)**.

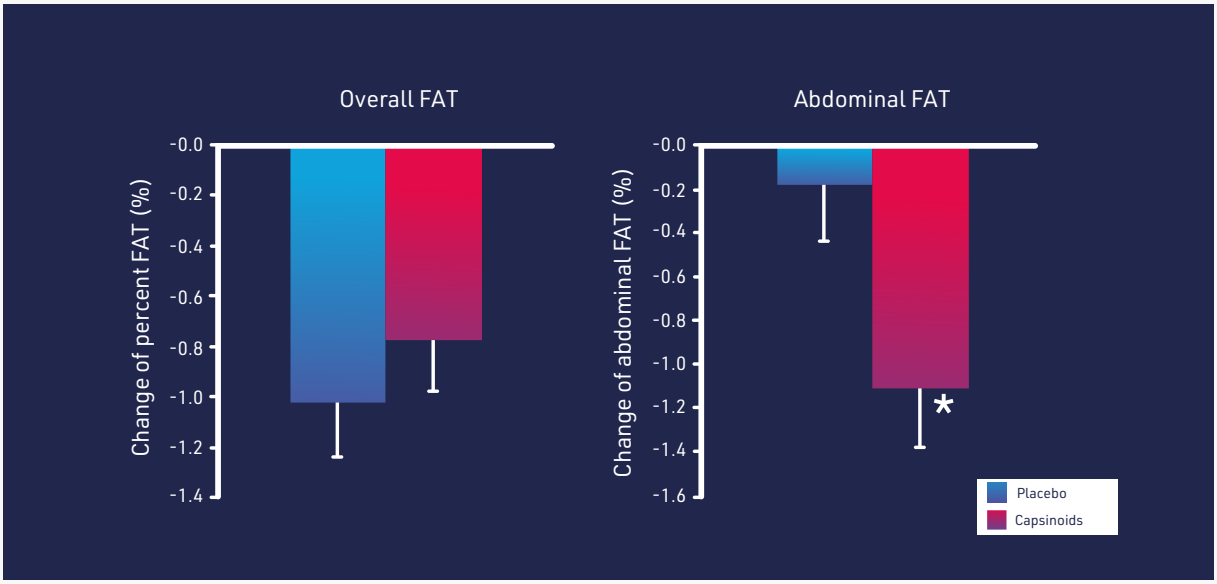

Figure 4. Clinical study with 80 participants indicates that supplementation with capsinoids is significantly associated with significantly greater decreases in abdominal fat loss relative to overall fat loss.

At least nine studies have investigated the effects of p-synephrine on metabolic rate and energy expenditure. All of which showed an increase in resting metabolic rate, energy expenditure and modest increases in weight loss within 6-12 weeks. Due to its mechanism in increasing fat oxidation, improving SNS activity, and overall metabolic rate, research on Advantra Z® has also observed that exercise was perceived as less difficult by over 80% of test participants.The ability to manipulate metabolic rate, non-exercise energy expenditure, SNS activity, and improve upon the desire to exercise is a huge advancement for supplementation. This leaves just one variable left to address.

5. Decreased Appetite

The final component to achieving a lean physique is accounting for the "energy in" portion of the equation. While the mechanisms of Blade® so far can assist with augmenting fat breakdown, improving metabolic rate and increasing SNS sensitivity, the remaining negative characteristic to dieting is the effects of appetite. Without curbing appetite, fat loss still remains to be an uphill battle. Capsiate has been shown to affect eating behaviour on two different levels. Studies show not only a reduction of voluntary calorie consumption by 14%, but a significant trend to crave healthier foods. Evidence suggests that capsiate also increases the "feel-good" hormone called dopamine in the brain, which contributes to making better nutritional decisions during the unpleasant experience of dieting.

CONCLUSION

The formulation of Blade® is the only formula that addresses every possible angle required for a fat loss process. Blade® uses only the most efficient, natural health ingredients that overlap with several attributes relating to targeting fat breakdown, preventing fat gain, improving metabolic rate, increasing the susceptibility for activity, and managing appetite. Simply put, the ingredients in Blade® are backed by science unlike any other fat burner on the market.

Rob Riches
Blue Star Nutraceuticals® Athlete

References

Belza A, Toubro S, Astrup A. The effect of caffeine, green tea and tyrosine on thermogenesis and energy intake. Eur J Clin Nutr. 63; 57-64, 2009.

Birerdinc A, Jarrar M, Stotish T, Randhawa M, Baranova A. Manipulating molecular switches in brown adipocytes and their precursors: A therapeutic potential. Prog Lipid Res. 52; 51-61, 2013.

Bloomer RJ, Canale RE, Shastri S, Suvarnapathki S. Effect of oral intake of capsiacinoid beadlets on catecholamine secretion and blood markers of lipolysis and healthy adults: a randomized, placebo controlled, double-blind, cross-over study. Lipids Health Dis. 9; DOI: 10.1186/1476-511X-9-72, 2010.

Diepvens K, Westerterp KR, Westerterp-Plantenga MS. Obesity and thermogenesis related to the consumption of caffeine ephedrine, capsaicin, and green tea. Am J Physiol Regul Integr Comp Physiol. 292; R77-R85, 2007.

Dulloo AG, Duret C, Rohrer D, Girardier L, Mensi N, Fathi M, Chantre P, Vandermander J. Efficacy of green tea extract rich catechin polyphenols and caffeine in increasing 24-h energy expenditure and fat oxidation in humans. Am J Clin Nutr. 70; 1040-1045, 1999.

Dullo AG, Seydoux J, Girardier L, Chantre P, Vandermander J. Green tea and thermogenesis: interactions between catechin-polyphenols, caffeine and sympathetic activity. Int J Obes Relat Metab Disord. 24; 252-258, 2000.

Galitzky J. Taouis M, Berlan M, Riviere D, Garrigues M, Lafontan M. alpha2-Antagonist compounds and lipid mobilization: evidence for lipid mobilizing effect of oral yohimbine in healthy male volunteers. Eur J Clin Invest. 18; 587-594, 1988.

Grasing K, Sturgill MG, Rosen RC, Trout JR, Thomas TJ, Kulkarni GD, Maines P, Seibold JR. Effects of yohimbine on autonomic measures are determined by individual values for area under the concentration-time curve. J Clin Pharmacol. 36; 814-822, 1996.

Hsu CL, Yen GC. Effects of capsaicin on induction of apoptosis and inhibition of adipogenesis in 3T3-L1 cells. J Agric Food Chem. 55; 1730-1736, 2007.

Imaizumi K, Sato S, Kumazawa M, Arai N, Aritoshi S, Akimoto S, Sakaibara Y, Kawashima Y, Tachiyashiki K. Capsaicinoids-induced changes of plasma glucose, free fatty acid and glycerol concentrations in rats. J Toxicol Sci. 36; 109-116, 2011.

Kao YH, Hiipakka RA, Liao S. Modulation of obesity by green tea catechin. Am J Clin Nutr. 72; 1232-1234, 2000.

Musso NR, Vergassola C, Pende A, Lotti G. Yohimbine effects on blood pressure and plasma catecholamines in human hypertension. Am J Hypertens. 8; 565-571, 1995.

Neal JW, Clipstone NA. Calcineurin Mediates the Calcium-dependent Inhibition of Adipocyte Differentiation in 3T3-L1 Cells. J Biol Chem. 227; 49776-49781, 2002.

Ohnluki K, Haramizu S, Watanabe T, Yaxzawa S, Fushiki T. CH-19 sweet, nonpungent cultivar of red pepper, increased body temperature in mice with vanilloid receptors stimulation by capsiate. J Nutr Sci Vitaminol. 47; 295-298, 2001.

Ratamess NA, Bush JA, Kang J, Kraemer WJ, Stohs SJ, Nocera VG, Leise MD, Diamond KB, Campbell SC, Miller HB, Faigenbaum AD. The effects of Supplementation is p-Synephrine Alone and in Combination with Caffeine on Metabolic, Lipolytic, and Cardiovascular Responses during Resistance Exercise. J Am Coll Nutr 35; 657-669, 2016.

Reinbach HC, Smeets A, Martinussen T, Moller P, Westerterp-Plantenga MS. Effects of capsaicin, green tea and CH-19 sweet pepper on appetite and energy intake in humans in negative and positive energy balance. Clin Nutr. 28; 260-265, 2009.

Rosen ED, Speigelman BM. Molecular Regulation of Adipogenesis. Anny Rev Cell Dev Biol. 16; 145-171, 2000.

Schwartz MW, Woods SC, Porte D, Seeley RJ, Baskin DG. Central nervous system control of food intake. Nature. 6; 661-671, 2000.

Stohs SJ, Preuss HG, Keith SC, Keith PL, Miller H, Kaats GR. Effects of p-Synephrine alone and in Combination with Selective Bioflavonoids on Resting Metabolism, Blood Pressure, Heart Rate and Self-Reported Mood Changes. Int J Med Sci 8; 295-301, 2011.

Stohs SJ, Preuss HG, Shara M. A Review of the Human Clinical Studies involving Citrus aurantium (Bitter Orange) Extract and its Primary Protoalkaloid p-Synephrine. Int J Med Sci. 9; 527-538, 2012.

Stohs SJ, Badmaev V. A Review of Natural Stimulant and Non-stimulant Thermogenic Agents. Phytother Res. 30; 732-740, 2016.

Szallasi A, Blumberg PM. Vanilloid (Capsaicin) Receptors and Mechanisms. Pharmacol Rev. 51; 159-211, 1999.

Tschop M Smiley DL, Heiman ML. Ghrelin induces adiposity in rodents. Nature 19; 908-913, 2000.

Whiting S, Derbyshire E, Tiwari BK. Capsaicinoids and capsinoids. A potential role for weight management? A systematic review of the evidence. Appetite. 59; 341-348, 2012.

Y D Cheung, D B Barnett, S R Nahorski. [3H]Rauwolscine and [3H]yohimbine binding to rat cerebral and human platelet membranes: possible heterogeneity of alpha 2-adrenoceptors. Eur J Pharmacol. 15;84(1-2):79-85, 1982.

C Pimoule, M S Briley, C Gay, H Loo, D Sechter, E Zarifian, R Raisman, S Z Langer. 3H-Rauwolscine binding in platelets from depressed patients and healthy volunteers. Psychopharmacology (Berl). 79(4):308-12, 1983.

T R Norman, N M Kimber, F K Judd, G D Burrows, I M McIntyre. Platelet 3H-rauwolscine binding in patients with panic attacks. Psychiatry Res. 22(1):43-8, 1987.

N B Shepperson, N Duval, R Massingham, S Z Langer. Pre- and postsynaptic alpha adrenoceptor selectivity studies with yohimbine and its two diastereoisomers rauwolscine and corynanthine in the anesthetized dog. J Pharmacol Exp Ther. 219(2):540-6, 1981.

J C Doxey, A C Lane, A G Roach, N K Virdee. Comparison of the alpha-adrenoceptor antagonist profiles of idazoxan (RX 781094), yohimbine, rauwolscine and corynanthine. Naunyn Schmiedebergs Arch Pharmacol. 325(2):136-44, 1984.

B Szabo, L Hedler, K Starke. Peripheral presynaptic and central effects of clonidine, yohimbine and rauwolscine on the sympathetic nervous system in rabbits. Naunyn Schmiedebergs Arch Pharmacol. 340(6):648-57, 1989.

M F Callahan, M Beales, G A Oltmans. Yohimbine and rauwolscine reduce food intake of genetically obese (obob) and lean mice. Pharmacol Biochem Behav. 20(4):591-9, 1984.

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