Enhancing Metabolic Thermogenesis with Botanicals to Promote Metabolic Homeostasis

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Discussion

METABOLIC DYSFUNCTION

Metabolic dysfunction is recognized as a major contributor to preventable ill health, chronic disease, and death.[1,2] Obesity is currently considered to have reached epidemic proportions.[3] More than one-third of US adults are considered obese[1], while about 17% of those two to 29 years of age are obese.[4] Obesity-related conditions include heart disease, stroke, and certain cancers.[1] Obesity is often associated with metabolic disorders including type 2 diabetes, which is the second leading cause of preventable death in the US.[2]

Metabolic syndrome is recognized as a complex condition that includes six diagnostic criteria: hyperglycemia, insulin resistance, central obesity, hypertension, elevated triglycerides, and decreased HDL-C (high-density lipoprotein cholesterol).[5,6] Long-term stress, chronic inflammation, and cellular oxidative stress all contribute to the formation of metabolic imbalance including overweight and obesity.[3,7] Excessive fat accumulation is currently understood as a state of chronic, low-grade systemic inflammation that negatively impacts adipokine secretion and insulin resistance, adversely influences metabolism, and leads to multiple diseases.[8-10]

Obese adipose tissue shows dynamic changes in cellular function and composition.[8] Because of frequent lack of patient compliance with dietary, exercise, and lifestyle modifications, research exploring alternative strategies is abundant. Key targets include modification of metabolic efficiency, increasing thermogenesis, and enhancing thyroid function as ways to modulate healthy metabolic function.

METABOLIC HOMEOSTASIS

Metabolic homeostasis occurs when there is a balance between energy intake and energy expenditure and when metabolic function is optimal. This is supported by a healthy diet, exercise, and lifestyle. Three components of daily energy expenditure that influence our metabolic homeostasis include basal metabolic rate, diet-induced thermogenesis, and energy expended through physical activity.[11]

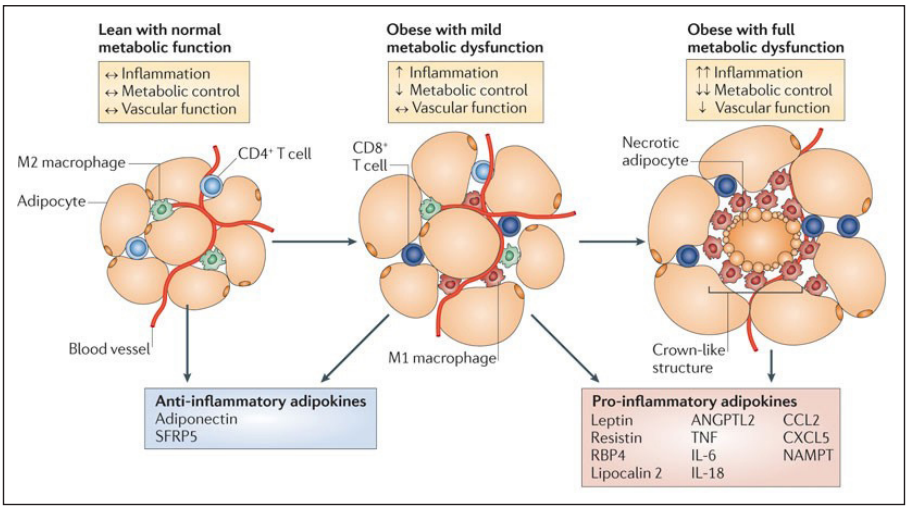
Obligatory thermogenesis, essential for all metabolic processes, maintains core temperature and basal metabolic rate. Facultative or adaptive thermogenesis is activated to produce extra heat on demand and can include both shivering (involving skeletal muscle) and nonshivering (in adipose tissue) forms.[12] Adaptive thermogenesis, governed by multiple mechanisms, increases energy expenditure and protects against hypothermia, obesity, and diabetes.[3,7] Decreased adaptive thermogenesis contributes to obesity.[13]

As part of the HPAT (hypothalamic-pituitary-adrenal-thyroid)-axis, the thyroid plays a key role in metabolic homeostasis. Thyroid hormones increase obligatory thermogenesis through stimulation of numerous metabolic pathways and influence adaptive thermogenesis through interactions with the sympathetic nervous system (SNS).[14-16]

The SNS plays a key role in maintaining energy homeostasis through hormonal and neuronal control. This complex regulatory system selectively activates specific tissues and systems to regulate fat metabolism, lipolysis, and thermogenesis. The SNS innervates white adipose tissue (WAT) and influences regulation of total body fat. Recent human studies find that SNS activation occurs in response to overeating to help maintain normal body weight while low sympathetic activity contributes to fat accumulation.[17,18]

ADIPOSE TISSUE

Adipose tissue, which used to be considered as an inert storage organ for fat, is now recognized as a metabolically dynamic endocrine organ. Adipose tissue synthesizes



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numerous biologically active compounds that modulate metabolic homeostasis and is found to be part of a complex network that regulates numerous biological functions.[2,9] Adipose tissue synthesizes and secretes hormones that influence nutrient uptake, regulation of obesity, insulin resistance, and inflammation.[2,9] Brown and white adipose tissue are highly studied as possible targets for the treatment of obesity and diabetes along with the more recently discovered beige adipose tissue.[3,7,9]

White adipose tissue, now recognized as an endocrine organ that regulates multiple activities including insulin sensitivity, may represent the largest endocrine tissue in humans.[3,9] Found throughout the body, it insulates and protects the viscera, organs, and tissues and plays a key role in maintenance of body temperature.[9]

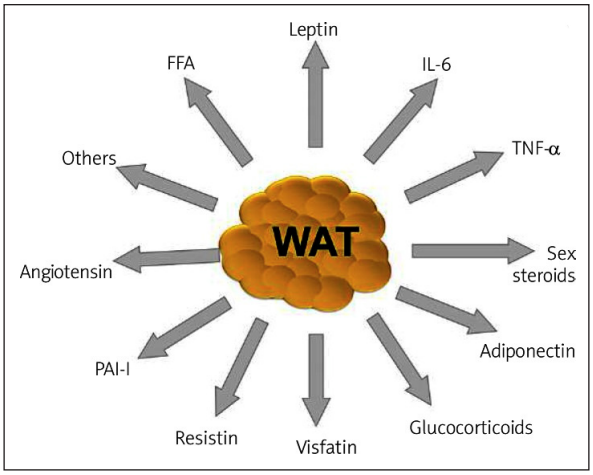
Specializing in adaptive thermogenesis, brown adipose tissue (BAT) stores energy in lipid form and generates heat to maintain body temperature.[3,7] BAT contains lipid droplets, an extensive vascular supply, and numerous mitochondria.[3] The vascular system delivers lipids to BAT for storage and oxidation and then carries the heat generated through oxidation in the mitochondria throughout the body.[9]

BAT mitochondria contain a specialized protein called uncoupling protein-1 (UCP-1).[3,9] Research finds that in adult humans, WAT can be infiltrated with brown adipocytes expressing UCP-1. Clusters of these UCP-1 expressing adipocytes, referred to as a third type of adipose tissue known as beige (or brite), are researched for their role in thermogenesis.[3,7,9] Some studies suggest that BAT may be regulated by thyroid hormone[16], which stimulates thermogenesis in concert with the SNS.[19] Typically, thermogenesis in brown fat deposits is regulated by catecholamines secreted by sympathetic nerve endings in BAT.[3]

ROLE OF BOTANICALS

Select adaptogenic botanicals can work through the HPAT-axis to enhance allostasis and provide foundational support to help normalize and restore metabolic processes. Used long-term, adaptogenic botanicals can help promote a beneficial endocrine response and function. Adaptogens also protect against stress-induced endocrine changes that cause metabolic shifts resulting in weight gain.

The botanicals outlined in this paper promote healthy metabolism of lipids to address conditions of overweight and obesity. Through promoting adaptive thermogenesis, these herbs encourage a healthy ratio of physiological energy storage to energy output. When combined with appropriate lifestyle, exercise, and dietary changes, they help support metabolic homeostasis, healthy weight, and long-term health.



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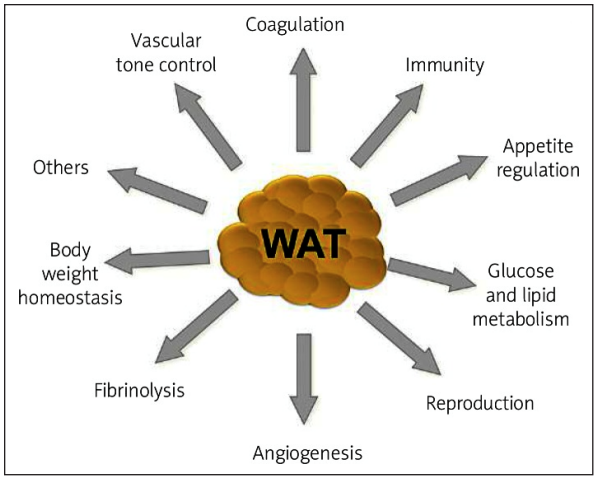

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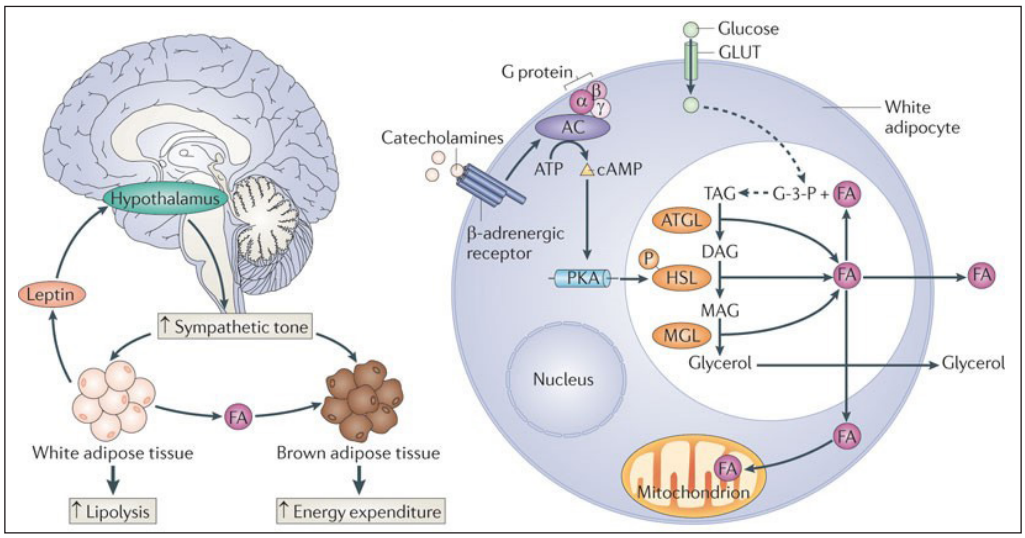
Leptin Promotes Lipolysis and Energy



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Enhancing Metabolic Thermogenesis with Botanicals to Promote Metabolic Homeostasis

Green Coffee Bean (*Coffea arabica*)

Green coffee bean (GCB) contains an array of polyphenols with potent antioxidative activity. One of these, chlorogenic acid, is found to benefit both glucose and lipid metabolism.[20] Chlorogenic acid is found to exert a positive influence on fat accumulation and insulin resistance through down-regulating genes involved in adipogenesis and inflammation in visceral adipose tissue.[21] In human studies, GCB was found to significantly reduce body weight, body mass index, and body fat percentage in human subjects taking GCB compared to those receiving placebo.[20]

Coleus forskohlii

Coleus forskohlii, native to India, is traditionally used in Ayurvedic medicine to treat conditions of the cardiovascular, respiratory, gastrointestinal, and central nervous systems.[22] Its diterpene isolate, forskolin, is highly studied for its ability to increase intracellular cAMP (cyclic adenosine monophosphate) levels. Forskolin is a

potent activator of adenylyl cyclase, the enzyme specific for production of cAMP, which is active in cellular metabolic processes.[22-26] Cyclic-AMP plays an indispensable role in diverse cellular functions related to weight management.[26-29] It promotes lipolysis, regulates dietary thermogenesis, raises the metabolic rate, and increases utilization of body fat.[22] Forskolin is found to stimulate lipolysis in vitro and in animal and human studies through activation of adenylate cyclase and increase of cAMP.[26]

Forskolin exerts antioxidant and anti-inflammatory activity.[26,29] Forskolin is found to enhance beta-cell function, the release of insulin, and to benefit fasting glucose levels.[29] Forskolin is shown to stimulate release of thyroid hormones and to increase thyroid hormone production. It is also found to stimulate secretion of digestive agents including hydrochloric acid, pepsin, amylase, and pancreatic enzymes.[26]

Phaseolus vulgaris

Phaseolus vulgaris is found to inhibit the digestive enzyme alpha-amylase and thus slow digestion of complex carbohydrates.[30-32] This approach is utilized in the management of excess weight and obesity to benefit weight loss and help lower post-prandial glucose levels.[30,31]

In a 30-day study (randomized, double-blinded and placebo-controlled), slightly overweight volunteers were given *Phaseolus vulgaris* extract along with a high carbohydrate diet. They showed greater reduction of body weight, body mass index, fat mass, adipose tissue thickness, and waist/hip/thigh circumference, and maintained lean body mass better than placebo subjects.[32]

Hijiki Seaweed (*Sargassum fusiforme*)

Fucoxanthin is a carotenoid found in brown seaweeds such as Hijiki.[10] Fucoxanthin is noted for its antioxidant, anti-inflammatory activity and is shown to exert anti-obesity and antidiabetic influence.[10]

The anti-obesity influence of fucoxanthin is thought to act through multiple pathways. In animal studies, fucoxanthin is found to significantly lower body weight and body fat accumulation including that of WAT (white adipose tissue).[10] Fucoxanthin demonstrates the ability to oxidize fat and release energy through adaptive thermogenesis in WAT through breaking apart the UCP-1 (uncoupling proteins).[33] In animal studies, fucoxanthin is found to reduce body weight and percentage of WAT.[34]

It is also found to improve plasma adipokine levels, down-regulate lipogenic enzymes, and up-regulate fatty acid oxidation and uncoupling protein gene expression in visceral adipose tissues. This range of activity suggests that fucoxanthin acts to modulate lipid metabolism in fat tissues.[10]

Bladderwrack (*Fucus spp.*) and/or Kelp (*Ascophyllum spp.*)

Cultures around the world use seaweeds for culinary and medicinal purposes due to their high nutrient content. The Japanese use around 88 species of seaweed for culinary and medicinal purposes. Seaweed is rich in minerals, vitamins, and lignans. It contains carotenoids, polyphenols, and polysaccharides.[34] Inclusion of seaweed in the diet is well-known to benefit overall health. Epidemiological studies report a correlation between higher dietary seaweed ingestion and decreased prevalence of chronic disease.[34]

Many types of seaweed are studied for their ability to reduce obesity and help maintain healthy body weight. Seaweed is found to help delay gastric clearance and enhance nutrient absorption.[34] Fucus and Ascophyllum species are brown seaweeds, which provide a rich source of bioactive polysaccharides (including alginate and fucoidan) and polyphenols (such as phenolic acids, flavonoids, stilbenes, and lignans). These compounds are found to modulate enzyme activity and lipid digestion.[35] Research finds that fucoidan acts to lower lipid accumulation in adipocytes.[36] Extracts of Ascophyllum and Fucus species are found to slow digestion and absorption of dietary fat through inhibition of lipase.[34,35]

Fucus spp. (Bladderwrack) is traditionally noted for its iodine content, which is present as di-iodotyrosine (DIT), a precursor of T3 (tri-iodothyronine) and thyroxine (T4). Bladderwrack is used in traditional herbal medicine as a botanical of choice to support normal thyroid function when used appropriately.[37-39]

Green Tea (*Camellia sinensis*)

Tea (*Camellia sinensis*) is a true botanical treasure with a 5,000-year history as a beverage and medicine in the Chinese culture. In modern times, tea is one of the most widely consumed beverages in the world. Green tea is well-known to possess digestive, diuretic, stimulant, and health-promoting qualities. In Chinese, Japanese, and other Asian cultures the tea ceremony celebrates quietude and contemplation. Even in daily use, tea is revered for its ability to promote calmness and clarity. Tea is also known to exert anti-inflammatory influence, enhance health, support weight loss, and to alleviate metabolic syndrome among other benefits.[40]

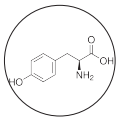
Using ancient methods, black, green, oolong, and pu'erh teas are all produced from varieties of *Camellia sinensis*. Green tea is produced by steaming the fresh leaves which preserves the highly-prized polyphenols. Comprising 30% to 40% of the green tea leaves, these polyphenols include the flavonoids

known as flavonols and flavanols (catechins).[40-44] Tea catechins are potent antioxidants.[40] EGCG (epigallocatechin-3-gallate) is the main form of tea catechins. Green tea also contains quercetin, kaempferol, and the alkaloids caffeine and theobromine.[40] All these factors impart significant anti-inflammatory and antioxidant activity.[41-44] Tea polyphenols benefit cell cycle regulation and are found to be cell-protective.[45,46]

Studies find the thermogenic action of Green tea is greater than that of its caffeine content alone. The catechin compounds in tea are found to modulate the expression of enzymes essential for lipid metabolism. They are found to inhibit proliferation and differentiation of adipocytes and to lessen the formation of oxidized LDL.[47] Green tea catechins are found in animal and human studies to improve weight control, lower cholesterol levels, and exert antidiabetic influence with amelioration of insulin resistance and improvement in insulin sensitivity, glucose tolerance, and increased fat oxidation.[48]

Both Green tea extract (GTE) and EGCG are found to significantly reduce weight gain and adipose tissue. They are also found to help reduce blood glucose and insulin levels and increase insulin sensitivity.[40] GTE is found to enhance healthy body composition through modulatory influence on multiple pathways.[47,49-51] GTE is also found to promote significant reduction of body weight and body fat, and to increase energy expenditure.[51] Combined with a low-energy diet, GTE is found to help limit weight gain.[51] Studies find that GTE activates thermogenesis, increases the metabolic rate, and stimulates lipid oxidation.[47,49]

EGCG is found to stimulate thermogenesis and fat oxidation possibly through inhibition of the enzyme that degrades norepinephrine.[18,51] EGCG is found to exert anti-angiogenic activity. Research finds that modulation of angiogenic factors helps prevent obesity because adipogenesis is highly correlated with angiogenesis during the development of adipose tissue growth and development of fat mass. This process of angiogenesis is mediated by leptin along with other factors. EGCG is found to inhibit production of VEGF and other factors influencing this process.[51-54]



N-Acetyl-L-Tyrosine

This conditionally essential amino acid is incorporated into many proteins. Tyrosine exerts a wide influence in the nervous system, thyroid, and other functions. Tyrosine is an essential precursor for synthesis of the thyroid hormone thyroxine and for a number of neurotransmitters including dopamine and norepinephrine.[55,56] Because of its influence on the nervous system, tyrosine is considered to possess adaptogenic qualities that enhance the body's ability to adapt to stress at multiple levels.[55,56] N-acetyl-L-tyrosine, which is converted in the body to L-tyrosine, is highly soluble in water and considered a bioavailable form of tyrosine.

Ginger (*Zingiber officinale*)

This world-renowned and well-loved herb has been used as cooking spice, herbal remedy, and revered medicine for centuries. A daily household remedy for digestive upset, ginger is valued as an anti-nausea remedy and digestive carminative. Ginger exerts a thermogenic influence, acting as a gentle diffusive stimulant on circulation and is used to warm the system during cold weather. Herbalists use Ginger to enhance the effectiveness of other herbs in a formula because it benefits digestion of the herbs. Its active ingredients include many volatile oils.[57,58]

Ginger demonstrates powerful antioxidant[59-61] and anti-inflammatory activity[62,63] and is found to modulate lipid peroxidation.[64] The pungent taste of ginger is attributed to its gingerols, which are known to influence thermogenesis.[18,51]

Black Pepper (*Piper nigrum*)

Black Pepper (BP) is widely known for its ability to enhance the bioavailability of herbs and nutrients. In Chinese and Ayurvedic medicine it is added to formulas to aid digestion and to carry herbs throughout the body. Traditionally, BP is known to stimulate metabolism, generate body heat, and enhance nutrient absorption.[18,51,65]

Black Pepper berries are carefully harvested and sun-dried. Their extract is standardized to 95% piperine, a powerful and highly-researched compound. One way that piperine is thought to enhance bioavailability is through influencing the cellular biomembrane and intestinal enzymes.[66-68] Piperine is known to be antioxidative, antimutagenic, antibacterial, and hepato-protective.[67,72]

Piperine is found to reduce levels of pro-inflammatory mediators including COX-2, IL factors, and TNF (tumor necrosis factor). It also supports healthy glutathione and SOD (super oxide dismutase) levels.[69-70] It is found to inhibit VEGF and to modulate cytokine and growth factor responses.[71]

Piperine, the pungent constituent of BP, is thought to act on the capsaicin receptor with the ability to enhance energy metabolism.[65] In animal studies, piperine is found to suppress body fat accumulation, and to help decrease body weight and visceral fat.[65] Piperine is found to influence thermogenesis through various pathways including through the SNS.[18,51]

For more information on any of the ingredients listed here, including extensive research or individual monographs compiled by Donnie Yance, please email info@naturaedu.com.

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