

# **MD+ Metabolic Version V**

## **Metabolic, Hormonal, and Immune Optimizer**

By improving the metabolic, hormonal and immune environment Metabolic improves body composition and performance, and increases energy levels and well-being.



Metabolic version V is formulated to help regulate and optimize metabolic, hormonal and immune processes that can be disrupted by exercise, dieting, stress and aging.

By improving the metabolic, hormonal and immune environment Metabolic improves body composition, helps get rid of body fat, especially cellulite, increases energy levels and well-being, and provides anti-aging benefits.

As well, Metabolic, because of its effects on optimizing the body's hormones, is useful in dealing with insulin, thyroid, growth hormone and sex hormone dysfunction that occurs secondary to stress, weight loss and aging.

<https://metabolicdiet.com/product/metabolic-version-v-new/>

Revised October 3, 2021, by Mauro Di Pasquale, B.Sc. (Hons); M.D.

### **Metabolic can help with:**

1. Weight and fat loss
2. Improving body composition
3. Decreasing the effects of dieting, stress and aging on the hormonal system
4. Improving insulin, thyroid, pituitary and adrenal functioning
5. Improving hormone levels and sexual functioning in both men and women
6. Improving energy, cognition and mood
7. Boosting the immune system
8. Anti-Aging and longevity
9. Increasing wellbeing and quality of life

The information below on the new Metabolic version V is in near final draft form and will be expanded and revised over the next several months. For now, this latest information will give you the flavor of just what Metabolic version V will do for you in helping you achieve your health, anti-aging, body composition and performance goals.

## Table of Contents

<b>Metabolic can help with:</b>	1
<b>Covid-19 Pandemic and Metabolic</b>	2
<b>Metabolic version V Nutritional Panel</b>	3
<b>Changes in Metabolic Version V, the latest version of Metabolic</b>	4
<b>Ingredients in Metabolic that support weight and body fat loss and optimize body composition and performance</b>	4
L-Carnitine	6
Taurine	7
Neurotransmitter Precursors	7
Calcium, Magnesium, Potassium and Vitamin D	8
<b>Anti-Stress and Adaptogenic Effects of Metabolic</b>	9
<b>Neurohormonal Effects of Metabolic</b>	10
<b>Hormonal Optimization</b>	10
Adrenal Support	10
DHEA	11
Exogenous DHEA versus Increasing Endogenous DHEA Production	12
Drug Tested Athletes	12
Maca Root	13
Growth Hormone	13
Insulin	13
Thyroid	15
Metabolic and LipoFlush Combo	16
<b>References</b>	17

## Covid-19 Pandemic and Metabolic

As you can see from the Supplement Panel below, and in the text of this information paper, Metabolic contains several dozen ingredients that boost the immune system and help protect us from opportunistic infections, including Covid-19, as well as helping us heal from them if we become infected.

The ingredients in Metabolic are many and include Vitamin A, Vitamin B6, Vitamin B12, Folate, Vitamin C, Vitamin D, Vitamin E, niacin, zinc, selenium, magnesium, taurine, curcumin, quercetin, lipoic acid,

astaxanthin, reduced glutathione, acetyl-L-carnitine, and many other flavonoids, polyphenols and extracts.

As an example, recent studies found that an adequate supply of zinc, selenium, and vitamin D is essential for resistance to other viral infections (including Covid-19), immune function, and reduced inflammation.<sup>12</sup>

## Metabolic version V Nutritional Panel

Supplement Facts:			Serving Size: 6 Tablets	Servings Per Container: 30	
	Amount Per Serving	% Daily Value		Amount Per Serving	% Daily Value
Vitamin A (as Retinyl Palmitate)	2000 IU	40%	Forskohlin	50 mg	*
Vitamin B2 (as Riboflavin)	10 mg	600%	CDP Choline	250 mg	*
Vitamin B3 (as Niacinamide & Inositol Hexanicotinate)	20 mg	100%	Rhodiola Rosea Extract	250 mg	*
Vitamin B6 (as Pyridoxal-5-Phosphate)	10 mg	500%	L-Taurine	250 mg	*
Vitamin B12 (as Methylcobalamin)	100 mcg	1667%	Conjugated Linoleic Acid (CLA)	225 mg	*
Pantothenic Acid (as D-Calcium Pantothenate)	20 mg	200%	Panax Ginseng Root Extract	200 mg	*
Vitamin C (as Ascorbic Acid)	250 mg	415%	Suma Root Extract	200 mg	*
Vitamin D3 (as Cholecalciferol)	400 IU	100%	Mucuna Pruriens (15% L-Dopa)	200 mg	*
Magnesium (as Magnesium Phosphate)	200 mg	50%	Gum Guggul Extract (resin)	160 mg	*
Manganese (as Manganese Sulfate)	2 mg	100%	Gugullsterones	16 mg	
Molybdenum (as Amino Acid Chelate)	150 mcg	200%	Schizandra Chinensis Extract	150 mg	*
Zinc (as Zinc Citrate)	10 mg	67%	Bacopa Monnieri Extract	150 mg	*
Chromium ( as Amino Acid Chelate)	50 mcg	42%	Gymnema Sylvestre Extract	150 mg	*
Potassium (as Potassium Phosphate)	99 mg	3%	Ginkgo Biloba Extract	150 mg	*
Iodine (from Kelp)	300 Mcg	200%	L-Glutathione (Reduced)	20 mg	*
Selenium (as L-Selenomethionine)	25 mcg	35%	Astaxanthin	5 mg	*
Bioperine (Piper Nigrum)	5 mg	*	<b>Metabolic Proprietary Complex 4050 mg *</b>		
Calcium Pyruvate	667 mg	*	Betaine, Beta Alanine, Arginine Alpha-Ketoglutarate, L-Citrulline Malate		
Garcinia Cambogia Extract	500 mg	*	Raspberry Ketones, ATP, Creatine Monohydrate, L-Glycine, L-Alanine,		
Hydrocitric Acid (HCA)	250 mg	*	L-Lysine, Phosphatidylserine, Phosphatidylcholine, Ocimum Sanctum,		
L-Tyrosine	400 mg	*	Astragalus Membranaceous Root Extract, Chlorella Powder, Avena Sativa,		
DMAE Bitartrate	300 mg	*	Panax Notoginseng, Grape Seed Extract, Inosine, Curcumin, Ginger Root		
Ashwagandha Root Extract	300 mg	*	Powder, Maca Root, Banaba Leaf Extract, L-Theanine, Vinpocetine. *		
L-Carnitine	250 mg	*			
Coleus Forskohlii Root Extract	250 mg	*	* Daily Value not established.		

Other Ingredients: Microcrystalline Cellulose, Hypromellose, Silicon Dioxide.

Metabolic normalizes and optimizes metabolism and macronutrient utilization (the use of fats, carbs and protein). It also has significant effects on the body's hormonal balance. For example, it increases levels of growth hormone and testosterone (in both men and women), decreases cortisol levels, increases insulin sensitivity, and optimizes thyroid hormone levels and function.

These effects increase weight and fat loss while maintaining or even increasing muscle mass. As well, the hormonal environment created by Metabolic will allow cellulite, that stubborn dimpled fat, to be oxidized along with the rest of the body fat.

The ingredients in Metabolic function synergistically to increase the anabolic and fat burning effects of exercise, and to combat fatigue, wear and tear on the body, stress and hormonal dysfunction. Because of its effect on metabolic rate and on muscle mass and fat loss it can be used by both men and women.

## **Changes in Metabolic Version V, the latest version of Metabolic**

The dose is 6 tablets instead of 4. Each bottle has 180 tablets instead of 120 tablets.

The amounts of several ingredients in prior version of Metabolic have been increased.

As well, dozens of ingredients have been added to increase the effects of Metabolic on health, body composition, and fat loss, and for optimizing metabolic, hormonal, and immune function, including:

**Acetyl-L-Carnitine, Alpha Lipoic Acid, Astaxanthin, Astragalus, Adenosine Triphosphate (ATP), Avena Sativa, Betaine, Beta Alanine, CDP Choline, Chlorella, Conjugated Linoleic Acid (CLA), Creatine Monohydrate, Curcumin, Ginger Root, Ginkgo Biloba, Grape Seed Extract, Inosine, L-Alanine, L-Citrulline Malate, L-Glutathione (reduced), L-Glycine, L-Lysine, L-Taurine, L-Theanine, Molybdenum, Panax Notoginseng, Pantothenic Acid, Raspberry Ketones, Rhodiola Rosea, Schizandra Chinensis, Selenium, Vitamin B12, Vitamin B2, Vitamin B3, Vitamin B6, and Vitamin C.**

## **Ingredients in Metabolic that support weight and body fat loss and optimize body composition and performance.**



All of the ingredients in Metabolic are meant to work together either additively or synergistically to achieve a homeostatic state in case of aberrations in your metabolism. As well, the ingredients are meant to go beyond normalization and help you lose weight, lose body fat, and improve your body composition, both directly and through their effects on the hormonal, immune, and central nervous systems.

Some of the ingredients in Metabolic are specifically included for their effects on weight and fat loss and body composition (mostly to lose body fat while maintaining or even gaining muscle mass). Some others are meant to deal with the body's counterproductive response to a drop in calories, the mainstay of any effective diet. And still others are meant to adjust the body's hormonal and immune responses to various stressors, whether due to chronic stress, dieting or aging, that can affect weight loss and body composition, and wellbeing.

Some of the ingredients do double or triple duty in that they affect one or more of the pathways I've described, and sometimes more as far as helping the body to fight off and prevent various dysfunctions and disorders.

For example, Metabolic contains **pyruvate**, a product of metabolism arising from carbohydrates and protein. Several studies have shown that pyruvate may aid weight and fat loss and improve body composition and exercise performance.<sup>34567</sup> As well, it increases insulin sensitivity, improves plasma lipids, has significant antioxidant effects, and may even inhibit the growth of certain cancers.<sup>89101112</sup>

Another example is **hydroxycitric acid (HCA)**, which has been shown to block the enzyme that converts carbohydrates into body fat.<sup>13</sup> Technically HCA competitively inhibits the extramitochondrial enzyme ATP-citrate-lyase, which catalyzes the cleavage of citrate to acetyl-CoA and oxaloacetate, a key step in lipogenesis. HCA also has thermogenic and appetite suppressant properties that are useful for weight and fat loss.

Laboratory research suggests that **garcinia cambogia** extract or **HCA** may be an effective compound for promoting weight loss. It is believed that HCA acts in several different ways. It is an effective appetite suppressant, and also limits the production of cholesterol and fatty acids in the body. It is also believed to raise body temperature to act in a thermogenic manner. HCA has also recently been shown to suppress weight regain.

HCA is not one of the new kids on the block. Over the last 30 years there has also been a lot of research on HCA and its effects on fat metabolism, with even the early research looking at its effects on fat metabolism.<sup>14</sup>

Theoretically, because HCA decreases the 2-carbon pool necessary for the formation of fat, and increases certain enzymes that promote fat oxidation, it should increase fat oxidation and decrease fat formation. In fact, several studies have shown that these effects do occur. For example, in one study, HCA and other tricarboxylic acids were shown to inhibit fatty acid synthesis from body glycogen without affecting protein synthesis.<sup>15</sup> Studies have also shown that HCA has appetite suppressant effects, especially if taken prior to meals.<sup>16</sup>

Even though its use in weight loss is supported by animal studies, where it appears to act (by a mechanism which is not yet clear, although some studies have implicated a serotonin connection) by reducing food intake, much of the research on the effects of HCA on appetite and body composition has been inconclusive and in some cases showed no effects, especially in humans. As well, there's been a lack of studies that show significant long lasting effects on weight loss and total fat formation and oxidation.

Over the past few years, however, this situation has changed. A recent study on humans has shown that 2 weeks of taking as little as 300 mg of HCA three times a day reduced 24 hour energy intake in obese humans with no increase in hunger.<sup>17</sup>

Another recent study has shown that HCA has sustained long-term effects in rats on various parameters of weight loss and hunger.<sup>18</sup> An interesting finding in this study is that the fat content of the diet seemed to be important for the long-term suppressive effect of HCA on feeding. HCA had little effect on rats that were on a very low fat diet.

The bottom line is that HCA has the potential to decrease appetite and weight and fat loss and, along with a proper diet, exercise and other targeted nutritional supplements, should be part of any serious weight and fat loss regimen.

## L-Carnitine

L-carnitine is mainly known for shuttling fatty acid acyl units into mitochondria so that beta oxidation of these acyl units provides acetyl units to fuel the TCA cycle and through oxidative phosphorylation to increase ATP production. In this respect, L-carnitine functions much like a gas pump in that it puts fuel in the gas tank so that your car engine can use it to provide energy to run the car. LC also acts to maintain mitochondrial function and suppresses oleic acid-mediated MPT through acceleration of beta-oxidation.<sup>19</sup>

But L-carnitine (LC) is much more than just the shuttle mechanism to get fatty acids into mitochondria and facilitate beta oxidation, it also functions in the opposite direction when there's an overload of acyl and acetyl units in the mitochondria that can result in mitochondrial dysfunction and insulin resistance.<sup>20</sup> LC thus acts more like a regulator of mitochondrial function both by providing nutrients that can be used efficiently and removing nutrients that are clogging up the mitochondrial machinery.

Studies have shown that the more fat is shuttled into the mitochondria and used as fuel, the more L-carnitine is needed. So, unless the body's metabolism is primed epigenetically to deal with utilizing fat as a primary fuel, and that also means a sufficient amount of LC to deal with the use of fat as a primary fuel (i.e. avoiding a relative carnitine insufficiency which can also be caused by aging and vegetarian diets), the result can be high rates of incomplete fat oxidation and intramuscular accumulation of fatty acylcarnitines, byproducts of lipid catabolism produced under conditions of metabolic stress including exercise.<sup>2122</sup>

Although it seems counter intuitive given LC role in fat metabolism, LC also increases insulin sensitivity and is a regulator of glucose metabolism and may be used to counter the metabolic syndrome and help treat type II diabetes.<sup>2324</sup>

A recent study found that the combination of L-carnitine, alpha lipoic acid, and betaine, **all in Metabolic**, had beneficial effects on health and body composition.<sup>25</sup> As well, LC is essential for proper muscle function and some studies have shown that carnitine supplementation improves exercise performance.<sup>26</sup>

LC has antioxidant properties directly but also ramps up endogenous antioxidant systems including glutathione, catalase, and SOD. The dual action decreases the effects of ROS produced with higher intensity resistance and aerobic exercise. L-carnitine also decreases the production of some of the pro-inflammatory cytokines and has anti-inflammatory and immunomodulating effects.<sup>272829</sup>

A pilot study showed that the use of **hydroxycitrate (HCA)**, **L-carnitine** and **pyruvate (all in Metabolic)** to obese subjects resulted in a remarkable rate of body-fat loss and thermogenesis,<sup>30</sup> which pointed to an uncoupling of fatty-acid oxidation – that is the energy from the burning of fat was thrown off mostly as heat, and thus took some fat out of the metabolic equation.

The increased flux, combined with the activation of fatty acid oxidation induced by the trio increases fat breakdown and the oxidation of fatty acids, along with an increase in uncoupling protein. The overall result is an increase in fat breakdown and an increase in heat production from the metabolism of fat.

## Taurine

Taurine ((2-aminoethane-sulfonic acid), a sulfur-containing amino acid is the second most abundant amino acid in the body, the most abundant free amino acid found in skeletal muscle tissue, the heart and brain. It's also one of the most abundant amino acids in most organs in the body. Although it's one of the few amino acids not directly used for protein synthesis, it can indirectly increase protein synthesis.

Taurine has a myriad of beneficial functions in the body, including the musculoskeletal and central nervous system, from development to cytoprotection in all age groups.<sup>313233</sup> Because of its potent antioxidant and cytoprotective properties it may be useful for combating the adverse effects of physical and psychological stress, improving body composition and physical and mental performance, and decreasing the adverse effects of aging.<sup>34,35,36,37</sup>

Taurine has many properties that can enhance the training effect, including its abilities to increase growth hormone, protect joints, and protect the liver, as well as its antioxidant and anabolic effects.<sup>38</sup> Taurine has also been shown to have insulin like effects and to help control cell volume. The volumizing effect on muscle cells is felt to lead to an increase in protein synthesis.

Over the years, oral taurine administration has been shown to help muscle cramping in patients with liver cirrhosis and myotonic dystrophy. Several studies have suggested that it may also help to alleviate muscle cramps occurring during and after exercise.

For the full current information on taurine go to [https://metabolicdiet.com/wp-content/uploads/2017/product\\_pdf/Taurine.pdf](https://metabolicdiet.com/wp-content/uploads/2017/product_pdf/Taurine.pdf).

## Neurotransmitter Precursors

One of the problems with trying to lose weight is that the body tries to sabotage your efforts. That's because your body reacts to the imagined threat of starvation by instituting some ages old survival mechanisms, mainly slowing the metabolic rate so you can get by on fewer calories, and increasing hunger so you can take full advantage of any food that you find. Even though you're deliberately trying to lose weight to improve your looks and health, your body looks at the calorie reduction as a sign of impending starvation and adjusts accordingly.

One of the main ways your body does this is by decreasing neurotransmitter levels in the central nervous system resulting in lowered metabolic rate, decreased activity, hunger and fatigue.

Metabolic counters this by providing **tyrosine, DMAE, mucuna pruriens, and various choline compounds** including **CDP choline** and **phosphatidylcholine**, ingredients that increase neurotransmitter function and increase energy, activity and wellbeing as well as decreasing appetite. Tyrosine, an amino acid, is also a precursor for thyroid hormone.

For example, CDP-choline serves as a choline donor in the metabolic pathways for biosynthesis of acetylcholine and neuronal membrane phospholipids, chiefly phosphatidylcholine.<sup>39</sup> The principal components of CDP-choline, choline and cytidine, are readily absorbed in the GI tract and easily cross the blood-brain barrier. CDP-choline supplementation has been researched in animal experiments and human clinical trials that provide evidence of its cholinergic and neuroprotective actions.

**Vinpocetine and bacopa monniera** also have neuroprotective effects, as well as effects on improving neurotransmitter levels.

## Calcium, Magnesium, Potassium and Vitamin D

**Calcium**, while generally considered a key element for maintaining bone density and strength, also has other health benefits including reducing blood pressure,<sup>40</sup> and more importantly for both men and women losing weight, the prevention of any adverse effects of dieting on bone mass and a preventative effect on osteoporosis.<sup>41</sup>

For example, calcium can also help lower your cholesterol.<sup>42</sup> In a recent study it was found that people with cholesterol levels in the high range of 240 to 260 reduced their total cholesterol by 6 percent when they took in an extra 1,800 milligrams of calcium a day. And the best part is that LDL (low-density lipoprotein) cholesterol—the bad cholesterol that's implicated in coronary artery disease, dropped by 11 percent. As well, calcium has recently been inversely associated with the incidence of colorectal adenomas.<sup>43</sup>

But there's more. Calcium has also been shown to modulate the inflammatory response<sup>44</sup> and to increase weight loss. A recent study found that an increase in dietary calcium intake, together with a normal protein intake, increased fecal fat and energy excretion by about 350 calories per day.<sup>45</sup> This observation may help explain why a high-calcium diet produces weight loss, and it suggests that an interaction with dietary protein level may be important.

Several studies have shown that calcium plays a key role in body weight regulation and especially on fat metabolism (with possible effects on lipolysis, fat oxidation, lipogenesis, energy expenditure and appetite suppression) and thus is a useful supplement for those looking to decrease weight and body fat.<sup>46474849505152535455</sup>

For example, Zemel et al. (2002) looked at the effects of calcium supplements on obese adults who were dieting. They found that a high-calcium diet (1200-1300 mg/day) resulted in greater weight and fat loss in humans compared to a low-calcium diet (400-500 mg/day).

Another study published in 2004 found that a high intake of calcium may hinder weight and fat regain.<sup>56</sup> The study found that after putting mice on a low-calorie diet and producing weight and body fat loss, that those on a low calcium diet regained their weight after 6 weeks. However, for those on a high calcium diet it was a different story. They found that the high calcium diets produced significant increases in lipolysis, decreases in fatty acid synthase expression and activity, and reduced fat regain. They also found that increasing calcium through the use of dairy products had significantly greater effects on fat regain.

The bottom line is that increasing calcium intake is a boon to those who want to not only lose weight, but to lose fat, improve body composition, and keep that fat and weight from coming back.

**Magnesium**, besides complementing the effects of calcium on obesity<sup>57</sup> and other functions, also has important effects on its own. Low levels of magnesium promote inflammation<sup>5859</sup> and impact on the body's ability to handle stress.<sup>60</sup> These functions are useful in alleviating the release of pro-inflammatory cytokines, and decreasing both insulin resistance and inappropriate cortisol secretion.

**Vitamin D** (as vitamin D3) is important for augmenting calcium dynamics. However, it also has other important effects,<sup>61</sup> for example on insulin resistance,<sup>62</sup> inflammation<sup>6364</sup> and obesity<sup>6566</sup>

Vitamin D deficiency is associated with rickets and growth retardation in children and osteoporosis and osteomalacia in adults, many acute and chronic illnesses including some cancers, autoimmune diseases, cardiovascular disease, type 1 and type 2 diabetes mellitus, thyroid disorders, infectious diseases and neurocognitive dysfunction and other diseases, as well as infertility and adverse pregnancy and birth outcomes.<sup>67686970</sup>

Vitamin D along with Calcium is intimately involved in skeletal homeostasis. But each does much more. Vitamin D has several vital functions outside this established role. Vitamin D has been shown to have important implications for general, musculoskeletal, cardiometabolic, and immune system health, and cognitive function.<sup>71,72,73,74,75,76,77,78</sup>

Vitamin D deficiency has also been linked to decreases in muscle function, strength, exercise, sports performance and body composition, increases in injuries and inflammation, and an increase in illness along with a decrease in immunity.<sup>79,80,81,82,83,84,85,86,87,88,89,90</sup>

As well, vitamin D is intimately involved in improving body composition, athletic performance, and decreasing the risk of injury.<sup>91,92,93,94,95,96,97,98,99</sup>

Although getting adequate amounts of vitamin D is crucial to health, vitamin D deficiency is relatively common and is a global health problem.<sup>100,101,102</sup> So, checking your vitamin D status is important and if not optimal supplementing with vitamin D is primary to realize all the benefits that it offers.

For current updated information on vitamin D go to [https://metabolicdiet.com/wp-content/uploads/2017/product\\_pdf/VitaminD.pdf](https://metabolicdiet.com/wp-content/uploads/2017/product_pdf/VitaminD.pdf).

**Potassium** helps correct the potassium loss often seen with dieting and in some people under some circumstances. Marginal potassium levels are often seen in women who lose it secondary to their menses and fluid retention.

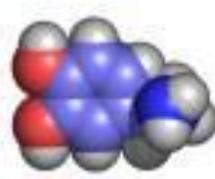
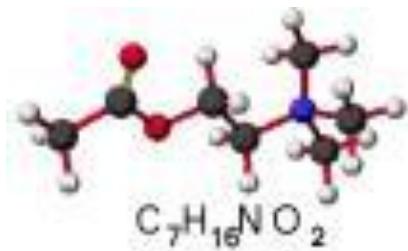
Loss of potassium can lead to fatigue and lethargy, which can decrease well-being and can be counterproductive to dieting.

## Anti-Stress and Adaptogenic Effects of Metabolic

Metabolic contains several ingredients that have a beneficial effect on decreasing stress and the effects of stress on both body and mind, decreasing inflammation and having significant antioxidant effects, including for example a **unique balance of B vitamins, Alpha Lipoic Acid, Ashwagandha, Astaxanthin, Astragalus, Ginkgo Biloba, L-Theanine, Magnesium, Ocimum sanctum, Panax Ginseng, Panax Notoginseng, Rhodiola Rosea, Schizandra Chinensis, and Vinpocetine.**<sup>103,104,105,106,107,108,109,110,111,112,113,114,115,116,117,118,119</sup>

The beneficial effects of the many adaptogens in metabolic is due to several mechanisms including optimizing the hypothalamic-pituitary-adrenal axis, helping to keep the adrenals healthy, decrease morbidity, and decrease the stress response.

## Neurohormonal Effects of Metabolic



There are several ingredients in Metabolic that have multiple properties and that affect various hormonal and other pathways. These ingredients have beneficial effects not only on weight loss, performance, and body composition but on health and feelings of well-being.

For example, **ocimum sanctum** has been shown to have significant antioxidant properties, to regulate thyroid function and to increase insulin sensitivity.<sup>120121</sup>

**CDP-choline** increases growth hormone as well as noradrenaline and dopamine levels in the central nervous system.<sup>122</sup>

Since most of the ingredients in Metabolic serve two or more purposes I'll discuss them under the various neurohormonal systems that are affected by them.

## Hormonal Optimization

Hormonal support is a mainstay of Metabolic and involves not only the hormones themselves but their neuroendocrine regulatory systems. As such, it's much more than simply replacement therapy or a quick fix, it's a way to actually optimize hormonal functioning and regulation in both the short and long terms.

## Adrenal Support

Metabolic contains ingredients that normalize adrenal functioning due to weight loss, stress and aging.

It is well known that plasma levels of dehydroepiandrosterone (DHEA), a steroid hormone secreted the adrenal cortex, reach the maximal values in the third decade of life and then gradually decline with age. On the other hand, cortisol levels tend to increase at the same time. This also tends to occur with prolonged dieting and stress.

DHEA often serves as an antiglucocorticoid and can buffer effects of inflammation and oxidative stress.<sup>123</sup> The decrease in DHEA and increase in cortisol leads to weight gain and increases in body fat especially around the midsection.

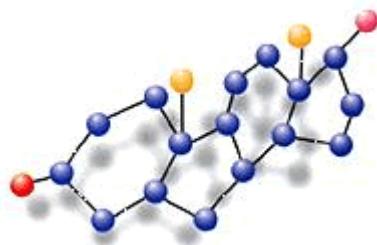
Metabolic thus contains ingredients to support adrenal function and increase endogenous **DHEA** to augment declines in DHEA levels secondary to lifestyle factors, aging and stress resulting in a variety of beneficial effects. Also ingredients such as **vitamin A**, **zinc**, **magnesium**, and **phosphatidylserine** to decrease inappropriate increases in cortisol levels.<sup>124</sup>

**phosphatidylserine** has been shown to not only to reduce levels of inflammatory mediators,<sup>125</sup> but also to dampen the ACTH and cortisol response to physical stress and decrease the reaction of the body to stressors.<sup>126</sup>

This combination of ingredients to increase DHEA and also decrease cortisol results in a lower cortisol/DHEA ratio, which has been proposed as a mechanism that regulates body weight and body fat levels, as well as contributing to feelings of wellbeing.

Other ingredients in Metabolic help to normalize your system and allow you to adapt to stress. For example bacopa monniera extract has adaptogenic properties and has been shown to decrease the effects of stress on the adrenals and on other systems in the body.<sup>127128</sup>

## DHEA



DHEA has potent effects on improving body composition, weight loss and fat loss while at the same time maintaining muscle.<sup>129130131132133</sup>

But DHEA does much more than help regulate body composition.

- Sex hormones are known to play an important role in mood and well-being in both sexes. Because levels of these hormones decline with aging, there is a parallel deterioration of mental function, and DHEA replacement is thought to be of potential benefit.
- Many disorders of aging, such as reduced immunocompetence, obesity, diabetes, and cancers, have been attributed to changes in DHEA based on animal studies and human epidemiological data.<sup>134135136</sup>
- DHEA replacement seems to lead to an improvement in mood and cognition, and a decrease in depression.<sup>137</sup>
- DHEA has antioxidant properties and can reduce this free radical-induced damage.<sup>138</sup>
- DHEA lowers serum insulin levels and increases insulin sensitivity and has been shown to have a role in reducing age-related increases in insulin levels, insulin resistance, and blood glucose.<sup>139140141</sup>

A recent study found that the long term use of 25 mg of DHEA a day resulted in significant improvements in the hormonal profile of early and late postmenopausal women<sup>142</sup> and aging men.<sup>143</sup>

The first study found that 25mg of DHEA taken daily resulted in several favorable changes, including increases in the sex hormones, a reduction in hot flashes and other post climacteric and aging symptoms.

The study with aging men found that 25 mg of DHEA taken over several months resulted in increases in DHEA, DHEAS, androstenedione, total and free testosterone, DHT, progesterone, 17-hydroxyprogesterone, estrone, estradiol, GH, IGF-1 and beta-endorphin levels, while FSH, LH and SHBG levels showed a significant decrease.

What this means is that the DHEA normalized the hormonal profile increasing the levels of important hormones such as DHEA, testosterone, growth hormone and IGF-I. The result was an improvement in mood, fatigue and joint pain.

The authors of the study concluded that “DHEA supplementation certainly has a potential in the prevention and treatment of age-related diseases and physiological decline of endocrine and neuroendocrine functions. The link between DHEA and the aging process, suggested by the age-related withdrawal of this steroid, is supported by the evidence that, in PADAM, the return to young adult DHEA levels is even able to counteract the age-related decline of other endocrine systems such as the somatotropic and gonadal axis and the neuroendocrine system.”

## Exogenous DHEA versus Increasing Endogenous DHEA Production

While using exogenous DHEA can be useful it's better to naturally increase endogenous levels.

Using exogenous DHEA to increase your levels of DHEA in your body is the wrong way to approach the problem of low systemic DHEA levels and to optimize adrenal function.

Instead of helping stimulate DHEA production, the use of DHEA decreases the natural production of DHEA and the precursors and mechanisms that lead to DHEA production, some of which are biologically active and needed for normal physiological functions. As well, once you go off the replacement therapy, your DHEA levels often end up lower than before you started taking the exogenous DHEA.

On the other hand, endogenous (developed within the body) DHEA production and normalizing adrenal function, which involves much more than DHEA, avoids many of the problems associated with exogenous DHEA use. By promoting the natural production of the hormone within the body, the regular feedback mechanisms are not by-passed and do not lead to many of the side effects that can be associated with exogenous hormone use.

In fact, the use of Metabolic to normalize adrenal function and increase endogenous DHEA production ramps up your natural DHEA producing machinery so that even if you stop taking it, your natural levels will be at least as high as before you started, and sometime higher as the body recognizes the higher level as normal and maintains that level naturally.

The bottom line is that whatever your reasons for wanting physiologically increased levels of DHEA, Metabolic is the best way to go.

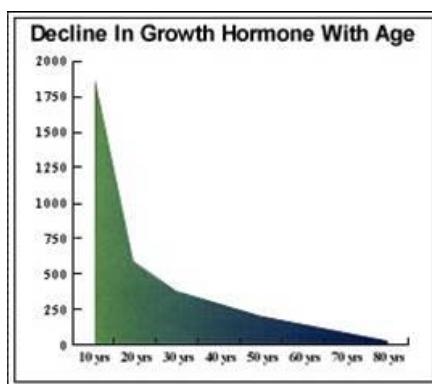
## Drug Tested Athletes

Besides being more effective in increasing DHEA levels and optimizing adrenal function, the use of Metabolic won't result in a positive drug test, as is the case with exogenous DHEA use.

## Maca Root

Lepidium meyenii (maca) is rich in amino acids, iodine, iron, and magnesium. Traditionally maca root has been used in the Andean region for its supposed aphrodisiac and/or fertility-enhancing properties. Modest empirical support exists for its ability to improve male sexual function.

## Growth Hormone



Growth hormone levels in the body are controlled by an intricate network and feedback system involving parts of the brain, the pituitary gland, the liver and other tissues such as muscle. For various reasons GH levels decline rapidly with age so that levels in middle age and later are much lower than levels in the second decade of life.

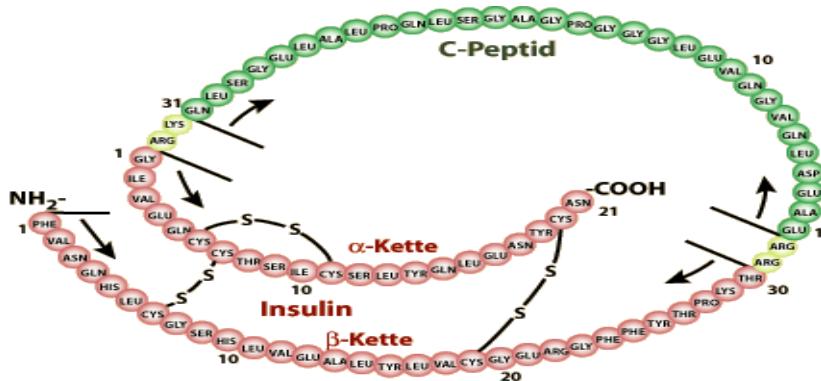
Growth hormone has a potent effect on body composition both directly, by increasing fat loss and maintaining muscle, and through stimulating increased systemic and tissue levels of insulin-like growth factor I (IGF-I).

Various ingredients in Metabolic, including cytidine 5'-diphosphocholine (**CDP choline**), **Velvet bean extract (L-dopa)**, **coleus forskohlii**, **L-tyrosine**, **arginine alpha-ketoglutarate** and **zinc** increase GH secretion and IGF-1 levels, either directly or through increases in dopamine, which together act to increase protein synthesis, decrease muscle breakdown and increase body fat loss.

For example, **CDP choline** has been shown in several studies to have an effect on dopamine metabolism and increase serum levels of GH in man.<sup>144145146</sup>

Especially where a deficiency may be present, supplemental **zinc** has resulted in an increase the secretion of growth hormone and IGF-I.<sup>147</sup> A recent review has shown the beneficial effects of **zinc** on the endocrine system including thyroid hormone, growth hormone, insulin and testosterone.<sup>148</sup>

## Insulin



Insulin resistance is felt to be a causative factor in obesity, the metabolic syndrome, diabetes and a host of other diseases. As well, as insulin resistance increases it results in changes in other hormones that can be detrimental to health and wellbeing.

Measures to increase insulin sensitivity are important in order to reverse the adverse effects of insulin resistance

For example, one of the most frustrating aspects of being overfat is that your body has become conditioned to converting excess calories, especially with high carbohydrate intake, into body fat. Part of the problem with this fat conditioning involves insulin.

The problem is that as you gain more body fat you become more insulin resistance so that you need more insulin to do the same job as when you had less body fat. This increase in insulin decreases your ability to use body fat as fuel, and stores more energy as body fat. The end result is a fatter you. Increasing insulin sensitivity allows fat to be mobilized and burned off.

There are several ingredients in Metabolic that will increase insulin sensitivity, including **chromium, zinc, manganese, vitamin D, gymnema sylvestre** and **banaba leaf extract**.

**Chromium** enhances insulin sensitivity and decreases insulin resistance, and helps you to lose body fat.

Many studies have shown the effects of chromium on insulin and diabetes. Chromium has been shown to decrease fasting glucose levels, improve glucose tolerance, lower insulin levels, and decrease total cholesterol and triglyceride levels while increasing HDL (good) cholesterol levels

Although most diets just barely provide the RDA for chromium, for many it's not enough to make up for daily losses, especially if they exercise. With Metabolic you get another 50 mcg per day (using two doses daily), so that you have all the chromium you need for fat loss purposes.

But not any kind of chromium is OK. For example the most commonly used form of chromium, chromium picolinate, has potential adverse effects associated with its use.<sup>149</sup> The amino acid chelate form of chromium used in Metabolic is a readily absorbable and biologically active form of chromium that enhances insulin sensitivity, without side effects.

Chromium also works synergistically with other ingredients in Metabolic, such as **banaba leaf extract, zinc, vitamin D, and gymnema sylvestre** and all the ingredients that decrease inflammation and the levels of some of the pro-inflammatory cytokines, to optimize insulin metabolism and function.

**Gymnema sylvestre** has been long used as a treatment for diabetes. As well there is some evidence that it may possibly regenerate or revitalize the insulin-producing beta cells of the pancreas.<sup>150151152153</sup>

**Banaba leaf extract** increases insulin sensitivity as well as promoting weight loss.<sup>154155</sup> The active ingredient in banaba extract, corosolic acid, has been shown to have some anti-obesity potential.

It's been shown that there is an improvement in insulin resistance with **zinc** supplementation and that zinc is involved in controlling some of the aspects of obesity.<sup>156</sup> Zinc also improves calcium metabolism and thus the beneficial effects that calcium has on fat metabolism (see below).

**Vitamin A** increases insulin sensitivity. vitamin A intake is associated with enhanced insulin-mediated glucose disposal. \*\*\*\*\* find study

**Manganese** is necessary for the metabolism of proteins and fats. It's also vital for proper immune and central nervous systems functioning, increases insulin sensitivity, has antioxidant properties, and is involved in energy metabolism.

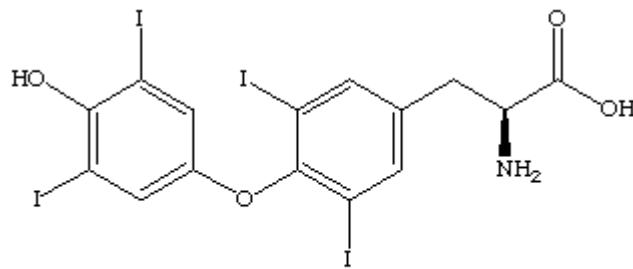
Manganese is a mineral that is required in small amounts to manufacture enzymes necessary for the metabolism of proteins and fats. It also supports the immune system, regulates blood sugar levels, and is involved in the production of cellular energy, reproduction, and bone growth.

Manganese works with vitamin K to support blood clotting, aids in digestion, and as antioxidant, is a vital component of Sodium Oxide Dismutase, a large molecule that is the body's main front-line defense against damaging free-radicals. Working with the B-complex vitamins, manganese help control the effects of stress while contributing to one's sense of wellbeing.

A deficiency in intake of manganese can retard growth, cause seizures, lead to poor bone formation, impair fertility, and cause birth defects. Researchers are also looking at new links between manganese deficiency and skin cancers.

Like magnesium, **germanium** is also involved in the electron transport system and in improving immune function.

## Thyroid



Thyroxine

As we mentioned above, your body reacts to decreasing calorie intake, and what it believes is impending starvation, by putting in place various survival mechanisms.

One of these ways it to decrease your metabolic rate and energy output mainly by decreasing the amount and activity of thyroid hormone.

Metabolic keeps the metabolism from shutting down in response to fewer calories through the action of various ingredients. For example:

1. Phosphates help maintain a higher metabolic rate.
2. Guggulsterones stimulate the thyroid gland
3. L-Tyrosine acts as a precursor to some neurotransmitters and thyroid both acting to decrease the metabolic effects of dieting.
4. Selenium has been shown to be important in the production of thyroid hormone.

Several ingredients in Metabolic optimize and increase thyroid hormone activity and increase metabolic rate. For example, **vitamin D, phosphates, guggulsterones Z and E, ocimum sanctum, iodine from kelp, zinc, and selenium** promote thyroid function, increase the metabolic rate and support thermogenesis.<sup>157</sup> All actions that promote fat breakdown and oxidation.

Studies have shown guggulsterones to have thyroid stimulating activity and increases thyroid efficiency by increasing the conversion of the less active T-4 to the more active T-3.<sup>158159160</sup> The use of guggulsterones has been shown to result in a decrease in body fat, and to also lower cholesterol levels.<sup>161</sup>

Metabolic also contains substantial amounts of natural phosphates, in the form of calcium, magnesium and potassium phosphates, which have also been shown to prevent a decrease in T-3 and increase the BMR.

And there's more good news. The combination of guggulsterones and phosphates has been shown to optimize body composition in adults.<sup>162</sup>

The thyroid gland contains high levels of selenium which is involved in protection of oxidative stress and metabolism of thyroid hormones.<sup>163164</sup>

**Bioperine**, a patented preparation of the black pepper thermogen, piperine, has demonstrated the ability to improve the absorption of nutrients. This result in less degradation of the active compounds; thereby ensuring higher percentages get through to work their magic!

## Metabolic and LipoFlush Combo<sup>165</sup>



Metabolic is formulated to aid in maximizing body composition and to maintain hormonal homeostasis. As such, it's useful as an aid to weight and body fat loss, and can be used on its own or along with LipoFlush. When used together LipoFlush and Metabolic are particularly effective in maximizing body composition and in decreasing body fat, especially cellulite.

When used together with LipoFlush Metabolic adds another dimension to the weight loss, body composition, and health equations by providing an increased impetus to weight and fat loss efforts.

Metabolic is different from LipoFlush in that it attacks weight and fat loss from different directions, and also takes into account the hormonal status of the body, optimizing insulin, thyroid, growth hormone, sex and adrenal hormones.

The result is that Metabolic, besides being an effective weight and fat loss product, also functions to restore optimal hormonal functioning, regardless of whether the hormonal dysfunction is due to dieting, stress or aging.

LipoFlush works incredibly well for weight and fat loss, but combined with Metabolic you'll get even better results. Together they make an effective AM/PM combination.

Metabolic, when used with LipoFlush, is most effective when used in the evening, a time when LipoFlush shouldn't be used as it may give you some problems falling asleep. As such Metabolic is the perfect evening and nighttime companion to LipoFlush and together they're a potent force against weight and fat loss, and are especially useful for reducing cellulite.

### Hormonal Enhancement Combo

Metabolic, along with **TestoBoost** and **GHboost** represent my hormone replacement and optimization combo and together will help optimize hormonal and metabolic health.

## References

- <sup>1</sup> Alexander J, Tinkov A, Strand TA, Alehagen U, Skalny A, Aaseth J. Early Nutritional Interventions with Zinc, Selenium and Vitamin D for Raising Anti-Viral Resistance Against Progressive COVID-19. *Nutrients*. 2020 Aug 7;12(8):E2358. doi: 10.3390/nu12082358. PMID: 32784601.
- <sup>2</sup> Bae M, Kim H. Mini-Review on the Roles of Vitamin C, Vitamin D, and Selenium in the Immune System against COVID-19. *Molecules*. 2020 Nov 16;25(22):5346. doi: 10.3390/molecules25225346. PMID: 33207753; PMCID: PMC7696052.
- <sup>3</sup> Cortez MY, Torgan CE, Brozinick JT Jr, Miller RH, Ivy JL. (.). Effect of pyruvate and dihydroxyacetone consumption on the growth and metabolic state of obese Zucker rats. *Am. J. Clin. Nutr.* 1991; **53**: 847–853.
- <sup>4</sup> Kalman D, Colker CM, Wilets I, Roufs JB, Antonio J. The effects of pyruvate supplementation on body composition in overweight individuals. *Nutrition*. 1999 May;15(5):337-40.
- <sup>5</sup> Ivy JL, Cortez MY, Chandler RM, et al. Effects of pyruvate on the metabolism and insulin resistance of obese Zucker rats. *Am J Clin Nutr* 1994;59:331-7.
- <sup>6</sup> Stanko RT, Tietze DT, Arch JE. Body composition, energy utilization, and nitrogen metabolism with a severely restricted diet supplemented with dihydroxyacetone and pyruvate. *Am J Clin Nutr* 1992; **55**: 771–776.
- <sup>7</sup> Stanko RT, Tietze DL, and Arch JE. Body composition, energy utilization, and nitrogen metabolism with a 4.25-MJ/d low-energy diet supplemented with pyruvate. *Am J Clin Nutr* 1992;56(4):630-5.
- <sup>8</sup> Cicalese L, Lee K, Schraut W, et al. Pyruvate prevents ischemia-reperfusion mucosal injury of rat small intestine. *Am J Surg* 1996;171:97-101.
- <sup>9</sup> Cicalese L, Subbotin V, Rastellini C, et al. Acute rejection of small bowel allografts in rats: Protection afforded by pyruvate. *Trans Proc* 1996;28(5):2474.
- <sup>10</sup> Deboer LWV, Bekx PA, Han L, et al. Pyruvate enhances recovery of rat hearts after ischemia and reperfusion by preventing free radical generation. *Am J Physiol* 1993;265:H1571-6.

- <sup>11</sup> Stanko RT, Mullick P, Clarke MR, et al. Pyruvate inhibits growth of mammary adenocarcinoma 13762 in rats. *Can Res* 1994;54:1004-7.
- <sup>12</sup> Stanko RT, Reynolds HR, Hoysen R, et al. Pyruvate supplementation of a low-cholesterol, low-fat diet: Effects on plasma lipid concentration and body composition in hyperlipidemic patients. *Am J Clin Nutr* 1994; 59:423–27.
- <sup>13</sup> Nageswara RR, Sakariah KK.) Lipid-lowering and antiobesity effect of (-) hydroxycitric acid. *Nutr* 1988. Res. 8:209-212.
- <sup>14</sup> Sullivan AC, Hamilton JG, Miller ON, Wheatley VR. Inhibition of lipogenesis in rat liver by (-)-hydroxycitrate. *Arch Biochem Biophys* 1972;150:183–90.
- <sup>15</sup> McCune SA, Foe LG, Kemp RG, Jurin RR. Aurintricarboxylic acid is a potent inhibitor of phosphofructokinase. *Biochem J* 1989; 259(3):925-27.
- <sup>16</sup> Hellerstein MK, Xie Y. The indirect pathway of hepatic glycogen synthesis and reduction of food intake by metabolic inhibitors. *Life Sciences* 1993; 53(24):1833-45.
- <sup>17</sup> Westerterp-Plantenga MS, Kovacs EM. The effect of (-)-hydroxycitrate on energy intake and satiety in overweight humans. *Int J Obes Relat Metab Disord* 2002; 26(6):870-2.
- <sup>18</sup> Leonhardt M, Langhans W. Hydroxycitrate has long-term effects on feeding behavior, body weight regain and metabolism after body weight loss in male rats. *J Nutr* 2002; 132(7):1977-82.
- <sup>19</sup> Oyanagi E, Yano H, Kato Y, Fujita H, Utsumi K, Sasaki J. L-Carnitine suppresses oleic acid-induced membrane permeability transition of mitochondria. *Cell Biochem Funct.* 2008 Oct;26(7):778-86.
- <sup>20</sup> Koves TR, Ussher JR, Noland RC, Slentz D, Mosedale M, Ilkayeva O, Bain J, Stevens R, Dyck JR, Newgard CB, Lopaschuk GD, Muoio DM. Mitochondrial overload and incomplete fatty acid oxidation contribute to skeletal muscle insulin resistance. *Cell Metab.* 2008 Jan;7(1):45-56.
- <sup>21</sup> Noland RC, Koves TR, Seiler SE, Lum H, Lust RM, Ilkayeva O, Stevens RD, Hegardt FG, Muoio DM. Carnitine insufficiency caused by aging and overnutrition compromises mitochondrial performance and metabolic control. *J Biol Chem.* 2009 Aug 21;284(34):22840-52.
- <sup>22</sup> Stephens FB, Marimuthu K, Cheng Y, Patel N, Constantin D, Simpson EJ, Greenhaff PL. Vegetarians have a reduced skeletal muscle carnitine transport capacity. *Am J Clin Nutr.* 2011 Sep;94(3):938-44.
- <sup>23</sup> Ringseis R, Keller J, Eder K. Role of carnitine in the regulation of glucose homeostasis and insulin sensitivity: evidence from in vivo and in vitro studies with carnitine supplementation and carnitine deficiency. *Eur J Nutr.* 2012 Feb;51(1):1-18.
- <sup>24</sup> Molfini A, Cascino A, Conte C, Ramaccini C, Rossi Fanelli F, Laviano A. Caloric restriction and L-carnitine administration improves insulin sensitivity in patients with impaired glucose metabolism. *JPEN J Parenter Enteral Nutr.* 2010 May-Jun;34(3):295-9.
- <sup>25</sup> Jang A, Kim D, Sung KS, Jung S, Kim HJ, Jo C. The effect of dietary a-lipoic acid, betaine, l-carnitine, and swimming on the obesity of mice induced by a high-fat diet. *Food Funct.* 2014 Jun 27. [Epub ahead of print]
- <sup>26</sup> Neumann, G. Effects of L-carnitine on athletic performance. Seim, H. Loster, H. eds. *Carnitine: Pathophysiological Basics and Clinical Applications* 1996:61-71 Ponte Press Bochum, Germany.
- <sup>27</sup> Manoli I, De Martino MU, Kino T, Alesci S. Modulatory effects of L-carnitine on glucocorticoid receptor activity. *Ann N Y Acad Sci.* 2004 Nov;1033:147-57.
- <sup>28</sup> Famularo G, De Simone C, Trinchieri V, Mosca L. Carnitines and its congeners: a metabolic pathway to the regulation of immune response and inflammation. *Ann N Y Acad Sci.* 2004 Nov;1033:132-8.
- <sup>29</sup> Pertosa G, Grandaliano G, Simone S, Soccio M, Schena FP. Inflammation and carnitine in hemodialysis patients. *J Ren Nutr.* 2005 Jan;15(1):8-12.
- <sup>30</sup> McCarty MF, Gustin JC. Pyruvate and hydroxycitrate/carnitine may synergize to promote reverse electron transport in hepatocyte mitochondria, effectively 'uncoupling' the oxidation of fatty acids. *Med Hypotheses* 1999; 52(5):407-16.
- <sup>31</sup> Timbrell JA, Seabra V, Waterfield CJ. The in vivo and in vitro protective properties of taurine. *Gen Pharmacol.* 1995 May;26(3):453-62.

- <sup>32</sup> Thirupathi A, Freitas S, Sorato HR, Pedroso GS, Effting PS, Damiani AP, Andrade VM, Nesi RT, Gupta RC, Muller AP, Pinho RA. Modulatory effects of taurine on metabolic and oxidative stress parameters in a mice model of muscle overuse. *Nutrition*. 2018 Oct;54:158-164.
- <sup>33</sup> Scicchitano BM, Sica G. The Beneficial Effects of Taurine to Counteract Sarcopenia. *Curr Protein Pept Sci.* 2018;19(7):673-680.
- <sup>34</sup> Cozzi R, Ricordy R, Bartolini F, Ramadori L, Perticone P and de Salvia R (1995). Taurine and ellagic acid: two differently-acting natural antioxidants. *Environmental and Molecular Mutagenesis* 26, 248-254.
- <sup>35</sup> Lourenco R, Camilo ME. Taurine: a conditionally essential amino acid in humans? An overview in health and disease. *Nutr Hosp.* 2002 Nov-Dec;17(6):262-70.
- <sup>36</sup> Schaffer S, Azuma J, Takahashi K, Mozaffari M. Why is taurine cytoprotective? *Adv Exp Med Biol.* 2003;526:307-21.
- <sup>37</sup> Bidri M, Choay P. Taurine: a particular amino acid with multiple functions. *Ann Pharm Fr.* 2003 Nov;61(6):385-91.
- <sup>38</sup> Schaffer SW, Jong CJ, Ramila KC, Azuma J. Physiological roles of taurine in heart and muscle. *J Biomed Sci.* 2010 Aug 24;17 Suppl 1:S2.
- <sup>39</sup> Weiss GB. Metabolism and actions of CDP-choline as an endogenous compound and administered exogenously as citicoline. *Life Sci* 1995;56(9):637-60.
- <sup>40</sup> McCarron DA, Reusser ME. Finding consensus in the dietary calcium-blood pressure debate. *J Am Coll Nutr* 1999; 18: 398S-405S.
- <sup>41</sup> Bowen J, Noakes M, Clifton PM. A high dairy protein, high-calcium diet minimizes bone turnover in overweight adults during weight loss. *J Nutr* 2004; 134: 568-573.
- <sup>42</sup> Denke MA, Fox MM, Schulte MC. Short-term dietary calcium fortification increases fecal saturated fat content and reduces serum lipids in men. *J Nutr* 1993; 123: 1047-1053.
- <sup>43</sup> Hartman TJ, Albert PS, Snyder K, et al. The association of calcium and vitamin d with risk of colorectal adenomas. *J Nutr.* 2005 Feb;135(2):252-9.
- <sup>44</sup> Febbraio MA. Signaling pathways for IL-6 within skeletal muscle. *Exerc Immunol Rev.* 2003;9:34-9.
- <sup>45</sup> Jacobsen R, Lorenzen JK, Toustrup S, Krog-Mikkelsen I, Astrup A. Effect of short-term high dietary calcium intake on 24-h energy expenditure, fat oxidation, and fecal fat excretion. *Int J Obes Relat Metab Disord.* 2005 Jan 18; [Epub ahead of print]
- <sup>46</sup> Davies KM, Heaney RP, Recker RR, Lappe JM, Barger-Lux MJ, Rafferty K, Hinders S. Calcium intake and body weight. *J Clin Endocrinol Metab* 2000; 85: 4635-4638.
- <sup>47</sup> Zemel MB, Shi H, Greer B, Dirienzo D, Zemel PC. Regulation of adiposity by dietary calcium. *FASEB J* 2000; 14: 1132-1138.
- <sup>48</sup> Zemel MB. Effects of calcium-fortified breakfast cereal on adiposity in a transgenic mouse model of obesity. *FASEB J* 2001; 15: A598.
- <sup>49</sup> Shi H, Dirienzo D, Zemel MB. Effects of dietary calcium on adipocyte lipid metabolism and body weight regulation in energy-restricted aP2-agouti transgenic mice. *FASEB J* 2001; 15:291–293.
- <sup>50</sup> Zemel MB, Thompson W, Zemel P, Nocton AM, Morris K, Campbell P. Dietary calcium and dairy products accelerate weight and fat loss during energy restriction in obese adults. *Am J Clin Nutr* 2002; 75:342S
- <sup>51</sup> Heaney RP. Normalizing calcium intake: projected population effects for body weight. *J Nutr* 2003; 133: 268S-270S.
- <sup>52</sup> Melanson EL, Sharp TA, Schneider J, Donahoo WT, Grunwald GK, Hill JO. Relation between calcium intake and fat oxidation in adult humans. *Int J Obes Relat Metab Disord* 2003; 27:196-203
- <sup>53</sup> Papakonstantinou E, Flatt WP, Huth PJ, Harris RBS. High dietary calcium reduces body fat content, digestibility of fat, and serum vitamin D in rats. *Obes Res* 2003; 11: 387-394.
- <sup>54</sup> Shapses SA, Heshka S, Heymsfield SB. Effect of calcium supplementation on weight and fat loss in women. *J Clin Endocrinol Metab.* 2004 Feb;89(2):632-7.

- <sup>55</sup> Zemel MB, Thompson W, Milstead A, Morris K, Campbell P. Calcium and dairy acceleration of weight and fat loss during energy restriction in obese adults. *Obes Res.* 2004 Apr;12(4):582-90.
- <sup>56</sup> Sun X, Zemel MB. Calcium and dairy products inhibit weight and fat regain during ad libitum consumption following energy restriction in Ap2-agouti transgenic mice. *J Nutr.* 2004 Nov;134(11):3054-60.
- <sup>57</sup> Lelovics Z. Relation between calcium and magnesium intake and obesity. *Asia Pac J Clin Nutr.* 2004;13(Suppl):S144.
- <sup>58</sup> Rayssiguier Y, Mazur A. R [Magnesium and inflammation:lessons from animal models.] *Clin Calcium.* 2005;15(2):245-248.
- <sup>59</sup> Maier JA, Malpuech-Brugere C, Zimowska W, Rayssiguier Y, Mazur A. Low magnesium promotes endothelial cell dysfunction: implications for atherosclerosis, inflammation and thrombosis. *Biochim Biophys Acta.* 2004 May 24;1689(1):13-21.
- <sup>60</sup> Consequences of magnesium deficiency on the enhancement of stress reactions; preventive and therapeutic implications (a review). *J Am Coll Nutr.* 1994 Oct;13(5):429-46.
- <sup>61</sup> Nagpal S, Na S, Rathnachalam R. Non-Calcemic Actions of Vitamin D Receptor Ligands. *Endocr Rev.* 2005 Mar 29;
- <sup>62</sup> Chiu KC, Chu A, Go VL, Saad MF. Hypovitaminosis D is associated with insulin resistance and β cell dysfunction. *Am J Clin Nutr.* 2004;79:820-5.
- <sup>63</sup> Rutter MK, Meigs JB, Sullivan LM, D'Agostino RB Sr, Wilson PW. C-reactive protein, the metabolic syndrome, and prediction of cardiovascular events in the Framingham Offspring Study. *Circulation.* 2004;110:380-5.
- <sup>64</sup> Rutter MK, Meigs JB, Sullivan LM, D'Agostino RB Sr, Wilson PW. C-reactive protein, the metabolic syndrome, and prediction of cardiovascular events in the Framingham Offspring Study. *Circulation.* 2004;110:380-5.
- <sup>65</sup> Parikh SJ, Edelman M, Uwaifo GI, Freedman RJ, Semega-Janneh M, Reynolds J, Yanovski J 2004 The relationship between obesity and serum 1,25-dihydroxy vitamin D concentrations in healthy adults. *J Clin Endocrinol Metab.* 89:1196-1199.
- <sup>66</sup> Arunabh S, Pollack S, Yeh J, Aloia JF 2003 Body fat content and 25-hydroxyvitamin D levels in healthy women. *J Clin Endocrinol Metab.* 88:157-161.
- <sup>67</sup> Pludowski P, Holick MF, Pilz S, Wagner CL, Hollis BW, Grant WB, Shoenfeld Y, Lerchbaum E, Llewellyn DJ, Kienreich K, Soni M. Vitamin D effects on musculoskeletal health, immunity, autoimmunity, cardiovascular disease, cancer, fertility, pregnancy, dementia and mortality-a review of recent evidence. *Autoimmun Rev.* 2013 Aug;12(10):976-89.
- <sup>68</sup> Barnard K, Colón-Emeric C. Extraskeletal effects of vitamin D in older adults: cardiovascular disease, mortality, mood, and cognition. *Am J Geriatr Pharmacother.* 2010 Feb;8(1):4-33.
- <sup>69</sup> Motiwala SR, Wang TJ. Vitamin D and cardiovascular risk. *Curr Hypertens Rep.* 2012 Jun;14(3):209-18.
- <sup>70</sup> Nettore IC, Albano L, Ungaro P, Colao A, Macchia PE. Sunshine vitamin and thyroid. *Rev Endocr Metab Disord.* 2017 Jan 14.
- <sup>71</sup> Adams JS, Hewison M. Unexpected actions of vitamin D: new perspectives on the regulation of innate and adaptive immunity. *Nat Clin Pract Endocrinol Metab.* 2008 Feb;4(2):80-90.
- <sup>72</sup> Ceglia L. Vitamin D and skeletal muscle tissue and function. *Mol Aspects Med.* 2008 Dec;29(6):407-14.
- <sup>73</sup> Wang TJ. Vitamin D and Cardiovascular Disease. *Annu Rev Med.* 2016;67:261-72.
- <sup>74</sup> Cannell JJ, Hollis BW, Sorenson MB, Taft TN, Anderson JJ. Athletic performance and vitamin D. *Med Sci Sports Exerc.* 2009 May;41(5):1102-10.
- <sup>75</sup> Buell JS, Scott TM, Dawson-Hughes B, Dallal GE, Rosenberg IH, Folstein MF, Tucker KL. Vitamin D is associated with cognitive function in elders receiving home health services. *J Gerontol A Biol Sci Med Sci.* 2009 Aug;64(8):888-95.

- <sup>76</sup> Kamycheva E, Joakimsen RM, Jorde R. Intakes of calcium and vitamin D predict body mass index in the population of Northern Norway. *J Nutr* 2003;133:102–6.
- <sup>77</sup> Wilson LR, Tripkovic L, Hart KH, Lanham-New SA. Vitamin D deficiency as a public health issue: using vitamin D<sub>2</sub> or vitamin D<sub>3</sub> in future fortification strategies. *Proc Nutr Soc*. 2017 Mar 28;1-8.
- <sup>78</sup> Bjelakovic G, Gluud LL, Nikolova D, Whitfield K, Wetterslev J, Simonetti RG, Bjelakovic M, Gluud C. Vitamin D supplementation for prevention of mortality in adults. *Cochrane Database Syst Rev*. 2014 Jan 10;(1):CD007470.
- <sup>79</sup> Mason RS. Vitamin D: a hormone for all seasons. *Climacteric*. 2011 Apr;14(2):197-203.
- <sup>80</sup> Wolff AE, Jones AN, Hansen KE. Vitamin D and musculoskeletal health. *Nat Clin Pract Rheumatol*. 2008 Nov;4(11):580-8.
- <sup>81</sup> Shantavasinkul PC, Phanachet P, Puchaiwattananon O, Chailurkit LO, Lepananon T, Chanprasertyotin S, Ongphiphadhanakul B, Warodomwichit D. Vitamin D status is a determinant of skeletal muscle mass in obesity according to body fat percentage. *Nutrition*. 2015 Jun;31(6):801-6. doi: 10.1016/j.nut.2014.
- <sup>82</sup> Heller JE, Thomas JJ, Hollis BW, Larson-Meyer DE. Relation between vitamin D status and body composition in collegiate athletes. *Int J Sport Nutr Exerc Metab*. 2015 Apr;25(2):128-35.
- <sup>83</sup> Diamond T, Wong YK, Golombick T. Effect of oral cholecalciferol 2,000 versus 5,000 IU on serum vitamin D, PTH, bone and muscle strength in patients with vitamin D deficiency. *Osteoporos Int*. 2013 Mar;24(3):1101-5.
- <sup>84</sup> Tomlinson PB, Joseph C, Angioi M. Effects of vitamin D supplementation on upper and lower body muscle strength levels in healthy individuals. A systematic review with meta-analysis. *J Sci Med Sport*. 2015 Sep;18(5):575-80.
- <sup>85</sup> Cangussu LM, Nahas-Neto J, Orsatti CL, Bueloni-Dias FN, Nahas EA. Effect of vitamin D supplementation alone on muscle function in postmenopausal women: a randomized, double-blind, placebo-controlled clinical trial. *Osteoporos Int*. 2015 Oct;26(10):2413-21.
- <sup>86</sup> Wyon MA, Koutedakis Y, Wolman R, Nevill AM, Allen N. The influence of winter vitamin D supplementation on muscle function and injury occurrence in elite ballet dancers: a controlled study. *J Sci Med Sport*. 2014 Jan;17(1):8-12.
- <sup>87</sup> Chiang CM, Ismaeel A, Griffis RB, Weems S. Effects of Vitamin D Supplementation on Muscle Strength in Athletes: A Systematic Review. *J Strength Cond Res*. 2017 Feb;31(2):566-574.
- <sup>88</sup> Wyon MA, Wolman R, Nevill AM, Cloak R, Metsios GS, Gould D, Ingham A, Koutedakis Y. Acute Effects of Vitamin D<sub>3</sub> Supplementation on Muscle Strength in Judoka Athletes: A Randomized Placebo-Controlled, Double-Blind Trial. *Clin J Sport Med*. 2016 Jul;26(4):279-84.
- <sup>89</sup> Barcal JN, Thomas JT, Hollis BW, Austin KJ, Alexander BM, Larson-Meyer DE. Vitamin D and Weight Cycling: Impact on Injury, Illness, and Inflammation in Collegiate Wrestlers. *Nutrients*. 2016 Nov 30;8(12).
- <sup>90</sup> Willis, K.S.; Smith, D.T.; Broughton, K.S.; Larson-Meyer, D.E. Vitamin D status and biomarkers of inflammation in runners. *Open Access J. Sports Med*. 2012, 3, 35–42.
- <sup>91</sup> Bartoszewska M, Kamboj M, Patel DR. Vitamin D, muscle function, and exercise performance. *Pediatr Clin North Am*. 2010 Jun;57(3):849-61.
- <sup>92</sup> Hamilton B. Vitamin D and human skeletal muscle. *Scand J Med Sci Sports*. 2010 Apr;20(2):182-90.
- <sup>93</sup> Domingues-Faria C, Boirie Y, Walrand S. Vitamin D and muscle trophicity. *Curr Opin Clin Nutr Metab Care*. 2017 May;20(3):169-174.
- <sup>94</sup> Cannell JJ, Hollis BW, Sorenson MB, Taft TN, Anderson JJ. Athletic performance and vitamin D. *Med Sci Sports Exerc*. 2009 May;41(5):1102-10.
- <sup>95</sup> Agergaard J, Trøstrup J, Uth J, Iversen JV, Boesen A, Andersen JL, Schjerling P, Langberg H. Does vitamin-D intake during resistance training improve the skeletal muscle hypertrophic and strength response in young and elderly men? - a randomized controlled trial. *Nutr Metab (Lond)*. 2015 Sep 30;12:32.

- <sup>96</sup> Koundourakis NE, Avgoustinaki PD, Malliaraki N, Margioris AN. Muscular effects of vitamin D in young athletes and non-athletes and in the elderly. *Hormones (Athens)*. 2016 Oct;15(4):471-488.
- <sup>97</sup> Ksiazek A, Zagrodna A, Slowinska-Lisowska M. Vitamin D, Skeletal Muscle Function and Athletic Performance in Athletes-A Narrative Review. *Nutrients*. 2019 Aug 4;11(8). pii: E1800. doi: 10.3390/nu11081800.
- <sup>98</sup> de la Puente Yagüe M, Collado Yurrita L, Ciudad Cabañas MJ, Cuadrado Cenzual MA. Role of Vitamin D in Athletes and Their Performance: Current Concepts and New Trends. *Nutrients*. 2020 Feb 23;12(2). pii: E579. doi: 10.3390/nu12020579.
- <sup>99</sup> Knechtle B, Nikolaidis PT. Vitamin D and Sport Performance. *Nutrients*. 2020 Mar 21;12(3). pii: E841. doi: 10.3390/nu12030841.
- <sup>100</sup> Glerup H, Mikkelsen K, Poulsen L, et al. Commonly recommended daily intake of vitamin D is not sufficient if sunlight exposure is limited. *J Intern Med* 2000;247:260–8.
- <sup>101</sup> Thomas MK, Lloyd-Jones DM, Thadhani RI, et al. Hypovitaminosis D in medical inpatients. *N Engl J Med* 1998;338:777–83.
- <sup>102</sup> Weaver CM, Fleet JC. Vitamin D requirements: current and future. *Am J Clin Nutr*. 2004 Dec;80(6 Suppl):1735S-9S.
- <sup>103</sup> Park S, Karunakaran U, Jeoung NH, Jeon JH, Lee IK. Physiological Effect and Therapeutic Application of Alpha Lipoic Acid. *Curr Med Chem*. 2014 Jul 6. [Epub ahead of print]
- <sup>104</sup> Chun JN, Cho M, So I, Jeon JH. The protective effects of Schisandra chinensis fruit extract and its lignans against cardiovascular disease: A review of the molecular mechanisms. *Fitoterapia*. 2014 Sep;97C:224-233.
- <sup>105</sup> Panossian AG. Adaptogens in mental and behavioral disorders. *Psychiatr Clin North Am*. 2013 Mar;36(1):49-64.
- <sup>106</sup> Rai D, Bhatia G, Sen T, Palit G. Anti-stress effects of Ginkgo biloba and Panax ginseng: a comparative study. *J Pharmacol Sci*. 2003 Dec;93(4):458-64.
- <sup>107</sup> Hernández-Santana A, Pérez-López V, Zubeldia JM, Jiménez-del-Rio M. A Rhodiola rosea root extract protects skeletal muscle cells against chemically induced oxidative stress by modulating heat shock protein 70 (HSP70) expression. *Phytother Res*. 2014 Apr;28(4):623-8. doi: 10.1002/ptr.5046.
- <sup>108</sup> Block KI, Mead MN. Immune system effects of echinacea, ginseng, and astragalus: a review. *Integr Cancer Ther*. 2003 Sep;2(3):247-67.
- <sup>109</sup> Pereira CPM, Souza ACR, Vasconcelos AR, Prado PS, Name JJ. Antioxidant and anti-inflammatory mechanisms of action of astaxanthin in cardiovascular diseases (Review). *Int J Mol Med*. 2021 Jan;47(1):37-48. doi: 10.3892/ijmm.2020.4783. Epub 2020 Nov 4. PMID: 33155666; PMCID: PMC7723678.
- <sup>110</sup> Franceschelli S, Pesce M, Ferrone A, De Lutiis MA, Patruno A, Grilli A, Felaco M, Speranza L. Astaxanthin treatment confers protection against oxidative stress in U937 cells stimulated with lipopolysaccharide reducing O<sub>2</sub>- production. *PLoS One*. 2014 Feb 10;9(2):e88359. eCollection 2014.
- <sup>111</sup> Santos MS, Duarte AI, Moreira PI, Oliveira CR. Synaptosomal response to oxidative stress: effect of vincocetine. *Free Radic Res*. 2000 Jan;32(1):57-66.
- <sup>112</sup> Parisi A, Tranchita E, Duranti G, Ciminelli E, Quaranta F, Ceci R, Cerulli C, Borrione P, Sabatini S. Effects of chronic Rhodiola Rosea supplementation on sport performance and antioxidant capacity in trained male: preliminary results. *J Sports Med Phys Fitness*. 2010 Mar;50(1):57-63.
- <sup>113</sup> Panossian A, Wikman G. Evidence-based efficacy of adaptogens in fatigue, and molecular mechanisms related to their stress-protective activity. *Curr Clin Pharmacol*. 2009 Sep;4(3):198-219.
- <sup>114</sup> Panossian A, Hambardzumyan M, Hovhanissyan A, Wikman G. The adaptogens rhodiola and schizandra modify the response to immobilization stress in rabbits by suppressing the increase of phosphorylated stress-activated protein kinase, nitric oxide and cortisol. *Drug Target Insights*. 2007;2:39-54.
- <sup>115</sup> Bhargava KP, Singh N. Anti-stress activity of Ocimum sanctum Linn. *Indian J Med Res*. 1981 Mar;73:443-51.

- <sup>116</sup> Jothie Richard E, Illuri R, Bethapudi B, Anandhakumar S, Bhaskar A, Chinampudur Velusami C, Mundkinajeddu D, Agarwal A. Anti-stress Activity of Ocimum sanctum: Possible Effects on Hypothalamic-Pituitary-Adrenal Axis. *Phytother Res.* 2016 May;30(5):805-14. doi: 10.1002/ptr.5584. Epub 2016 Feb 22. PMID: 26899341.
- <sup>117</sup> Li Y, Ma QG, Zhao LH, Guo YQ, Duan GX, Zhang JY, Ji C. Protective Efficacy of Alpha-lipoic Acid against AflatoxinB1-induced Oxidative Damage in the Liver. *Asian-Australas J Anim Sci.* 2014 Jun;27(6):907-15. doi: 10.5713/ajas.2013.13588.
- <sup>118</sup> Amico AP, Terlizzi A, Damiani S, Ranieri M, Megna M, Fiore P1. Endocr Metab Immune Disord Drug Immunopharmacology of the main herbal supplements: a review. *Targets.* 2013 Dec;13(4):283-8.
- <sup>119</sup> Cui H, Liu X, Zhang J, Zhang K, Yao D, Dong S, Feng S, Yang L, Li Y, Wang H, Huang J, Wang J. Rhodiola rosea L. Attenuates Cigarette Smoke and Lipopolysaccharide-Induced COPD in Rats via Inflammation Inhibition and Antioxidant and Antifibrosis Pathways. *Evid Based Complement Alternat Med.* 2021 Mar 2;2021:6103158. doi: 10.1155/2021/6103158. PMID: 33747104; PMCID: PMC7943302.
- <sup>120</sup> Chattopadhyay RR. Hypoglycemic effect of Ocimum sanctum leaf extract in normal and streptozotocin diabetic rats. *Indian J Exp Biol* 1993 Nov;31(11):891-3.
- <sup>121</sup> Panda S, Kar A. Ocimum sanctum leaf extract in the regulation of thyroid function in the male mouse. *Pharmacol Res* 1998 Aug;38(2):107-10.
- <sup>122</sup> Secades JJ, Frontera G. CDP-choline: pharmacological and clinical review. *Methods Find Exp Clin Pharmacol* 1995 Oct;17 Suppl B:1-54.
- <sup>123</sup> Maninger N, Wolkowitz OM, Reus VI, Epel ES, Mellon SH. Neurobiological and neuropsychiatric effects of dehydroepiandrosterone (DHEA) and DHEA sulfate (DHEAS). *Front Neuroendocrinol.* 2009 Jan;30(1):65-91.
- <sup>124</sup> Nerozzi D, Magnani A, Sforza V, et al. Early cortisol escape phenomenon reversed by phosphatidylserine in elderly normal subjects. *Clinical Trials J* 1989;26:33-38.
- <sup>125</sup> Henson PM, Bratton DL, Fadok VA. The phosphatidylserine receptor: a crucial molecular switch? *Nat Rev Mol Cell Biol.* 2001 Aug;2(8):627-33.
- <sup>126</sup> Hellhammer J, Fries E, Buss C, Engert V, Tuch A, Rutenberg D, Hellhammer D. Effects of soy lecithin phosphatidic acid and phosphatidylserine complex (PAS) on the endocrine and psychological responses to mental stress. *Stress.* 2004 Jun;7(2):119-26.
- <sup>127</sup> Rai D, Bhatia G, Palit G, Pal R, Singh S, Singh HK. Adaptogenic effect of Bacopa monniera (Brahmi). *Pharmacol Biochem Behav.* 2003 Jul;75(4):823-30.
- <sup>128</sup> Rohini G, Sabitha KE, Devi CS. Bacopa monniera Linn. extract modulates antioxidant and marker enzyme status in fibrosarcoma bearing rats. *Indian J Exp Biol.* 2004 Aug;42(8):776-80.
- <sup>129</sup> Tagliaferro AR, Davis JR, Truchon S, Van Hamont N. Effects of dehydroepiandrosterone acetate on metabolism, body weight and composition of male and female rats. *J Nutr.* 1986;116:1977-1983.
- <sup>130</sup> Kurzman ID, MacEwen EG, Haffa AL. Reduction in body weight and cholesterol in spontaneously obese dogs by dehydroepiandrosterone. *Int J Obes.* 1990;14:95-104.
- <sup>131</sup> Morales AJ, Haubrich RH, Hwang JY, Asakura H, Yen SS. The effect of six months treatment with a 100 mg daily dose of dehydroepiandrosterone (DHEA) on circulating sex steroids, body composition and muscle strength in age-advanced men and women. *Clin Endocrinol (Oxf).* 1998;49:421-432.
- <sup>132</sup> Herranz L, Megia A, Grande C, Gonzalez-Gancedo P, Pallardo F. Dehydroepiandrosterone sulphate, body fat distribution and insulin in obese men. *Int J Obes Relat Metab Disord.* 1995;19:57-60.
- <sup>133</sup> Maccario M, Mazza E, Ramunni J, et al. Relationships between dehydroepiandrosterone-sulphate and anthropometric, metabolic and hormonal variables in a large cohort of obese women. *Clin Endocrinol (Oxf).* 1999;50:595-600.
- <sup>134</sup> Schneider EL, Reed JD Jr. Life extension. *N Engl J Med.* 1985;312:1159-1168.
- <sup>135</sup> Barrett-Connor E, Khaw KT, Yen SS. A prospective study of dehydroepiandrosterone sulfate, mortality, and cardiovascular disease. *N Engl J Med.* 1986;315:1519-1524.

- <sup>136</sup> Thoman ML, Weigle WO. The cellular and subcellular bases of immunosenescence. *Adv Immunol.* 1989;46:221-261.
- <sup>137</sup> Bloch M, Schmidt PJ, Danaceau MA, Adams LF, Rubinow DR. Dehydroepiandrosterone treatment of midlife dysthymia. *Biol Psychiatry.* 1999;45:1533-1541.
- <sup>138</sup> Bastianetto S, Ramassamy C, Poirier J, Quirion R. Dehydroepiandrosterone (DHEA) protects hippocampal cells from oxidative stress-induced damage. *Brain Res Mol Brain Res.* 1999;66:35-41.
- <sup>139</sup> ED, Buffington CK, Hubert GD, et al. Divergent correlations of circulating dehydroepiandrosterone sulfate and testosterone with insulin levels and insulin receptor binding. *J Clin Endocrinol Metab.* 1988;66:1329-1331.
- <sup>140</sup> Diamond P, Cusan L, Gomez JL, Belanger A, Labrie F. Metabolic effects of 12-month percutaneous dehydroepiandrosterone replacement therapy in postmenopausal women. *J Endocrinol.* 1996;150(suppl):S43-S50.
- <sup>141</sup> Jakubowicz D, Beer N, Rengifo R. Effect of dehydroepiandrosterone on cyclic-guanosine monophosphate in men of advancing age. *Ann N Y Acad Sci.* 1995;774:312-315.
- <sup>142</sup> Genazzani AD, Stomati M, Bernardi F, Pieri M, Rovati L, Genazzani AR. Long-term low-dose dehydroepiandrosterone oral supplementation in early and late postmenopausal women modulates endocrine parameters and synthesis of neuroactive steroids.
- <sup>143</sup> Genazzani AR, Inglese S, Lombardi I, Pieri M, Bernardi F, Genazzani AD, Rovati L, Luisi M. Long-term low-dose dehydroepiandrosterone replacement therapy in aging males with partial androgen deficiency. *Aging Male.* 2004 Jun;7(2):133-43.
- <sup>144</sup> P. Fonlupt, M. Martinet and H. Pacheco, Effect of CDP-choline on dopamine metabolism in central nervous system. In: V. Zappia, E.P. Kennedy, B.I. Nilsson and P. Galetti, Editors, *Novel biochemical, pharmacological, and clinical aspects of CDP-choline*, Elsevier Science, New York (1985), p. 169.
- <sup>145</sup> Matsuoka T, Kawanaka M, Nagai K. Effect of cytidine diphosphate choline on growth hormone and prolactin secretion in man. *Endocrinol Jpn* 1978 Feb;25(1):55-7.
- <sup>146</sup> Salvadorini F, Saba P, Forli C, Tusini G, Galeone F. Effect of cytidine diphosphate choline on growth hormone secretion in patients with brain or pituitary lesions. *Endocrinol Jpn* 1980 Jun;27(3):265-71.
- <sup>147</sup> Imamoglu S, Bereket A, Turan S, Taga Y, Haklar G. Effect of zinc supplementation on growth hormone secretion, IGF-I, IGFBP-3, somatomedin generation, alkaline phosphatase, osteocalcin and growth in prepubertal children with idiopathic short stature. *J Pediatr Endocrinol Metab.* 2005 Jan;18(1):69-74.
- <sup>148</sup> Baltaci AK, Mogulkoc R, Baltaci SB. Review: The role of zinc in the endocrine system. *Pak J Pharm Sci.* 2019 Jan;32(1):231-239.
- <sup>149</sup> Vincent JB. The potential value and toxicity of chromium picolinate as a nutritional supplement, weight loss agent and muscle development agent. *Sports Med.* 2003;33(3):213-30.
- <sup>150</sup> Persaud SJ, Al-Majed H, Raman A, Jones PM. Gymnema sylvestre stimulates insulin release in vitro by increased membrane permeability. *J Endocrinol* 1999;163(2):207-12.
- <sup>151</sup> Shanmugasundaram ER, Gopinath KL, Radha Shanmugasundaram K, Rajendran VM. Possible regeneration of the islets of Langerhans in streptozotocin-diabetic rats given Gymnema sylvestre leaf extracts. *J Ethnopharmacol.* 1990; 30(3):265-79.
- <sup>152</sup> Sugihara Y, Nojima H, Matsuda H, Murakami T, Yoshikawa M, Kimura I. Antihyperglycemic effects of gymnemic acid IV, a compound derived from Gymnema sylvestre leaves in streptozotocin-diabetic mice. *J Asian Nat Prod Res.* 2000;2(4):321-7.
- <sup>153</sup> Basakaran, K.; Ahmath, B. K.; Shanmugasundaram, K. R.; Shanmugasundaram, E. R. B. Antidiabetic effect of a leaf extract from Gymnema sylvestre in non-insulin-dependent diabetes mellitus patients. *J. Ethnopharm.* 1990, 30, 295-305.
- <sup>154</sup> Kakuda T, Sakane I, Takihara T, Ozaki Y, Takeuchi H, Kuroyanagi M. Hypoglycemic effect of extracts from Lagerstroemia speciosa L. leaves in genetically diabetic KK-AY mice. *Biosci Biotechnol Biochem.* 1996 Feb;60(2):204-8.

- 
- <sup>155</sup> Suzuki Y, Unno T, Ushitani M, Hayashi K, Kakuda T. Antiobesity activity of extracts from Lagerstroemia speciosa L. leaves on female KK-Ay mice. *J Nutr Sci Vitaminol (Tokyo)*. 1999 Dec;45(6):791-5.
- <sup>156</sup> Marreiro DN, Geloneze B, Tambascia MA, Lerario AC, Halpern A, Cozzolino SM. [Participation of zinc in insulin resistance] *Arq Bras Endocrinol Metabol*. 2004;48(2):234-9.
- <sup>157</sup> Larson-Meyer DE, Gostas DE. Thyroid Function and Nutrient Status in the Athlete. *Curr Sports Med Rep*. 2020 Feb;19(2):84-94. doi: 10.1249/JSR.0000000000000689. PMID: 32028353.
- <sup>158</sup> Tripathi YB, Malhotra OP, Tripathi SN. Thyroid stimulating action of Z-guggulsterone obtained from Commiphora mukul. *Planta Med* 1984; 1:78-80.
- <sup>159</sup> Tripathi YB, Tripathi P, Malhotra OP, Tripathi SN. Thyroid stimulatory action of (Z)-guggulsterone: mechanism of action. *Planta Med* 1988 Aug;54(4):271-7.
- <sup>160</sup> Tripathi YB, Tripathi P, Malhotra OP, Tripathi SN. Thyroid stimulatory action of (Z)-guggulsterone: mechanism of action. *Planta Med*. 1988 Aug;54(4):271-7.
- <sup>161</sup> Urizar NL, Moore DD. Gugulipid: A Natural Cholesterol-Lowering Agent. *Annu Rev Nutr* 2003; 26; 303-313.
- <sup>162</sup> Antonio J, Colker CM, Torina GC, et al. Effects of a Standardized Guggulsterone Phosphate Supplement on Body Composition in Overweight Adults: A Pilot Study. *Current Therapeutic Research* 1999; 60(4):220-227.
- <sup>163</sup> Ventura M., Melo M., Carrilho F. Selenium and thyroid disease: From pathophysiology to treatment. *Int. J. Endocrinol.* 2017;2017:1297658.
- <sup>163</sup> Andrade GRG, Gorgulho B, Lotufo PA, Bensenor IM, Marchioni DM. Dietary Selenium Intake and Subclinical Hypothyroidism: A Cross-Sectional Analysis of the ELSA-Brasil Study. *Nutrients*. 2018 May 30;10(6).

