CARDIOMETABOLIC SUPPORT

CARDIOMETABOLIC HEALTH AND NORMAL BLOOD GLUCOSE

Clinical Summary

Metabolic syndrome (MetS), is defined as a constellation of cardiovascular and metabolic risk factors, characterised by visceral (abdominal) obesity, insulin resistance, hypertension, and dyslipidaemia. MetS is a widespread problem with up to 25% of adults and 19% of children meeting the criteria for MetS.[1,2]

A combination of nutrients such as chromium, alpha lipoic acid (ALA), green coffee extract and resveratrol has been shown to support healthy glucose metabolism, weight loss and may help to optimise lipid profile and antioxidant status when combined with a healthy diet and exercise. Therefore, incorporating these nutrients into diet and lifestyle recommendations may be an effective adjunctive therapy in the management of MetS.

Clinical Guide to Supplementation

Step 1: Assess 'Clinical presentations of Metabolic Syndrome'

Step 2: Establish nutritional and lifestyle risk factors – See 'Key Nutrient Considerations' and 'Additional Diet and Lifestyle Considerations'

Step 3: Consider evidence-based applications and mechanisms – See 'Clinical uses' and 'Mechanisms of action'

Step 4: Review side effects and drug-nutrient interactions – See 'Safety'

Clinical Presentations and Risk Factors

Clinical presentations of metabolic syndrome[3,4]

- Increased body weight and body mass index (BMI)
- Visceral Obesity
- High blood pressure
- High fasting glucose and insulin resistance (IR)
- Dyslipidaemia
- Elevated inflammatory markers such as C-reactive protein (CRP)
- Disease Associations: Cardiovascular disease, Stroke, Type 2 diabetes mellitus (T2DM), Polycystic ovarian syndrome, Cognitive impartment, Non-alcoholic fatty liver disease, Depression, Acne, skin tags, acanthosis nigricans, Hypothyroidism.[5,6]

Key Nutrient Considerations

- Green coffee extract
- Chromium
- Alpha lipoic acid
- Resveratrol

Additional Diet and Lifestyle Considerations

Healthy diet: Following a Mediterranean-style diet has been shown to have a protective role on every component of MetS and may also decrease the risk of developing MetS.[7,8] The antioxidant and anti-inflammatory properties of the different Mediterranean diet components, including olive oil, fish, cereals, vegetables, and fruits, likely contribute to these benefits.[9]

Nutrient deficiencies: Suboptimal intake of several nutrients such as B vitamins[10] (B1,[11] B6,[12] and B12,[13,14]), magnesium,[15,16] vitamin D,[17] have been linked to MetS. Obese individuals are more likely to have either lower blood concentrations or lower bioavailability of several minerals and vitamins.[18,19]

Genetic predisposition: Single nucleotide polymorphisms (SNPs) of various genes such as APOA2, FTO and ADOPOQ may increase predisposition to weight gain and poor blood glucose metabolism.[20] Consider personalised dietary advice.

Sleep: Adequate sleep has been associated with healthy weight, satiety and dietary choices.[21] Consider sleep hygiene.

Lack of exercise and decreased muscle mass: Skeletal muscle loss and accumulation of intramuscular fat are closely linked to IR and MetS and are associated with a variety of pathologies including oxidative stress, inflammation and mitochondrial dysfunction. Endurance exercise can reduce hyperglycemia and improve IR in patients with T2DM.[22,23,24]

Clinical Uses and Mechanisms of Action

Clinical Uses

Blood glucose: Green coffee extract has been shown to improve fasting blood glucose and serum insulin levels in a number of clinical trials.[25,26] Resveratrol improves insulin resistance and fasting glucose.[27] Chromium has a long history of significantly improving glycaemic control.[28] ALA offers a protective role in diabetes and its complications due to its anti-inflammatory and antioxidant properties.[29]

Dyslipidaemia: Green coffee extract,[26] resveratrol,[27] and ALA[30] have been shown to reduce total and LDL-cholesterol. Furthermore, green coffee[26,31] and chromium[28] may also improve triglycerides, total cholesterol, LDL and HDL-cholesterol levels.

Hypertension: Consumption of green coffee extract[32,33] and resveratrol[34] may reduce elevated systolic and diastolic blood pressure, particularly in individuals at high cardiovascular risk such as those with diabetes and obesity.

Overweight and obesity: Green coffee extract[35,36] and resveratrol[37] reduce body weight, BMI, waist circumference. ALA also has a modest effect on weight loss.[38]

Improvement in body composition: Chromium supplementation has been reported to decrease body fat and improve lean body mass in overweight and obese individuals.[39,40]

Mechanisms of Action

Improved blood glucose metabolism: Green coffee extract is a rich source of chlorogenic acids (CGA) which have been shown to affect signalling pathways related to glucose metabolism.[26] Chromium has been shown to increase the number of insulin receptors and insulin binding at its site of action and may also increase receptor signalling.[41] ALA prevents beta cell destruction, enhances glucose uptake and has an antioxidant effect relevant to reducing diabetic complications.[42]

Anti-hypertensive: CGA, found in green coffee extract, has been shown to decrease blood pressure, by the stimulation of nitric oxide production through the endothelial-dependent pathway; the reduction of free radicals through inhibiting NAD(P)H oxidase expression; and activity, and inhibition of angiotensin-converting enzyme.[43,44] Resveratrol has also been shown to have antihypertensive effect through a multitude of mechanisms including its antioxidant and anti-inflammatory properties; the stimulation of endothelial nitric oxide production; the inhibition of vascular inflammation; and the prevention of platelet aggregation.[45,46,47]

Hypocholesterolemic: Resveratrol has been shown to reduce LDL oxidation and downregulate inflammatory cytokines.[48,49] Chromium may suppress oxidative stress and lipid peroxidation, therefore indirectly initiating the metabolism and decrease of lipids.[50,51,52] Chlorogenic Acid, from green coffee extract, is involved in modifying hepatic metabolism of cholesterol and fatty acids by inhibiting pancreatic lipase and HMGCR 3-hydroxy-3-methylglutaryl-CoA reductase (HMG-CoA reductase) that is involved in cholesterol biosynthesis and the enhancement of lipoprotein lipase activity that performs triglyceride turnover. It has also been shown to increase the activity of fatty acid beta-oxidation and the expression of peroxisome proliferator-activated receptor-alpha in the liver.[53,54]

ALA can change lipid profile by reducing the activity of HMG-CoA reductase.[55,56]

Improvement of antioxidant status: ALA[57,58] and resveratrol[59] are potent antioxidants and have been shown to exert beneficial actions against oxidative stress related to hyperglycaemia.

Optimisation of inflammatory response: Resveratrol[62] and chromium[60] have been shown to reduce C-Reactive Protein (CRP) and tumour necrosis factor-alpha (TNF-Alpha) among patients with MetS, PCOS and Type2 diabetes. ALA may reduce inflammation in diabetics through the inhibition of the transcription factor responsible for inflammatory cytokines; NF-kB.[61,62]

Energy metabolism: Chromium,[63] resveratrol[64] and ALA[57,65] have been shown to support cellular metabolism and glucose homeostasis by promoting healthy 5' adenosine monophosphate-activated protein kinase (AMPK) and mimicking calorie restriction effects through SIRT-1 activation. Additionally, ALA may also regulate appetite controlling adipokines, increasing adiponectin and decreasing leptin.[66] Optimal levels of chromium promote healthy carbohydrate and fat utilisation.[67]

Modulation of the gut microbiome: Resveratrol may mediate cardiometabolic effects via modulation of gut microbiota composition and gut barrier function.[68,69]

Safety

Possible Side Effects

Current evidence suggests that the combination of these nutrients is safe and well tolerated at the recommended dosage:

Green coffee extract is well tolerated when taken in doses up to 1000 mg daily, (providing up to 500 mg chlorogenic acids). Green coffee extract (including specific green coffee extracts such as Svetol) has been used with good safety for up to 12 weeks in clinical research.[31,33,34,70,71] It contains very low levels of caffeine (approx. 10mg per daily dosage) and is unlikely to cause adverse reaction, even in individuals with caffeine sensitivity.[72,73,74]

Chromium has been safely used in a small number of studies at doses of 200-1000 mcg daily for up to 2 years. Side effects are very rare, but may include gastrointestinal discomfort, headaches, insomnia, irritability and mood changes.[75,76,77,78,79,80,81]

Alpha-lipoic acid is generally well tolerated when used orally. ALA appears to be safe in doses of up to 2g/day for 3 months to 2 years. Side effects, if any, are mild and include headache, heartburn, nausea, and in rare instances vomiting.[82,83,84,85,86,87] Concerns have been raised over high intakes of ALA and insulin autoimmune syndrome (IAS). IAS is extremely rare globally.[88]

Resveratrol is well tolerated and safe when taken orally in doses of up to 1,500 mg daily for up to 3 months. Higher doses may lead to mild gastrointestinal discomfort and diarrhoea.[89,90,91,92]

Interactions

Hypolipidemic agents: Chromium[93] and ALA[94] may reduce total cholesterol levels, providing additive effects. Monitor drug requirements (interaction may be beneficial). Separate doses by 2-4 hours.

Hypoglycaemic agents: Chromium[95,96] and green coffee extract[97] may reduce the requirement for the use of hypoglycaemic agents. While beneficial interaction is possible, caution is advised whilst using this combination. Observe the use of these combinations and monitor drug requirement.

Thyroid hormones and antithyroid medications: Chromium might bind to levothyroxine in the intestinal tract and decrease levothyroxine absorption.[98] Observe this combination and separate doses by 2-4 hours.

Antihypertensive drugs: Theoretically, taking green coffee extract with antihypertensive drugs might increase the risk of hypotension.[99,100] However, this has never been observed in clinical trials of patients taking both green coffee extract and anti-hypertensive drugs.[101] Monitor drug requirements (interaction may be beneficial).

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