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Review

Functional foods against metabolic syndrome (obesity, diabetes, hypertension and dyslipidemia) and cardiovasular disease

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Metabolic syndrome is a condition of at least three of the cardiovascular risk factors: obesity, excessive visceral fat storage, dyslipidemia, hypertension and hyperglycaemia or Type 2 diabetes. It is a state of insulin resistance, oxidative stress and chronic inflammation. Cardiovascular disease is the highest cause of death globally. Certain dietary components and over 800 plants help prevent or moderate metabolic syndrome by assisting the body homeostasis mechanisms. This review compiles the most current studies on foods that help fight metabolic syndrome and the scientific evidences to support their use. This includes functional fats, digestive enzymes inhibitors, various beverages, different fruits, specific vegetables, grains, legumes, herbs and spices that can reduce cardiovascular disease risk, through several cellular mechanisms.

Introduction

Cardiovascular disease is the highest cause of death globally. Metabolic syndrome is a combination of least three of the cardiovascular risk factors: obesity, dyslipidemia, hypertension and hyperglycaemia or Type 2 diabetes. It covers insulin resistance, oxidative stress and an inflammatory state. Functional food and over 800 plants help prevent or reduce metabolic syndrome by assisting the body homeostasis mechanisms. Type II diabetes expresses the decreased disposal of glucose in the peripheral tissues due to insulin resistance, overproduction of glucose by the liver, defects in pancreatic B-cell function and decreased B-cell mass. Obesity, insufficient physical activity and excess calorie intake are factors contributing to its development. Excess energy consumption subsequently causes hypoxia (oxygen deficiency) in the adipose tissues. This induces the adipocytes (fat cells) to secrete pro-inflammatory chemokines (e.g. COX-2, iNOS) that attracts immune cells, macrophages and inflammatory responses.

Besides secreting pro-inflammatory cytokines, the white adipose tissues have endocrine function to produce hormones, lipid metabolism regulators, vascular hemostasis controllers; or comparable system (e.g. leptin, angiotensinogen, adipsin, acylation-stimulating protein, adiponectin, retinol-binding protein, TNF-alpha, interleukin 6, plasminogen activator inhibitor-1 and tissue factor). Fasting induces adipocyte secretory proteins production, a fibrinogen–angiopoietin–related protein, metallothionein and resistin. Resistin induces insulin resistance, that links diabetes to obesity, while metallothionein is an antioxidant metal-binding and stress-response protein.

Culinary plants, herbs and spices are a good source of peroxisome proliferators-activated receptor (PPAR)γ ligands. PPARγ is a therapeutic drug target for metabolic syndrome. Pomegranate, apple, clove, cinnamon, thyme, green coffee, bilberry, bay leaves and many other edible plant components bind to PPARγ in a competitive ligand binding assay. Others like nutmeg, licorice, black pepper, holy basil and sage transactivated PPARγ in chimeric GAL4-PPARγ-LBD (part of the nuclear receptor structure) system and may function as selective PPARγ modulators. Selective PPARγ modulators improve insulin resistance without weight gain and PPARγ antagonists exert antiobesity effects. PPARγ activators can inhibit the NF-KB activation and down-regulate the pro-inflammatory cytokines (Mueller & Jungbauer, 2009).

Omega 3 and 6 fats

The type and amount of fats consumed affect obesity, insulin resistance and atherosclerosis in animal models.

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Chronic soybean, coconut and lard consumption (but not fish oil), reduced serum adiponectin that regulate glucose and fatty acid oxidation (Bueno *et al*., 2008). High saturated fat diets increase calories consumption, retroperitoneal fat, liver glycogen, plasma/liver cholesterol and triacylglycerol levels more than other high calorie fat diets and reduced the anti-atherogenic Paraoxonase 1 activity and glucose tolerance test in rats (Hoefel *et al*., 2011). Conjugated linoleic acid but not conjugated linolenic acid consumption reduced rats' adipose tissues. Although both conjugated linoleic acid and conjugated linolenic acid reduced non-HDL-cholesterol, conjugated linolenic acid impaired the insulin function (Miranda *et al*., 2009). Bovine milk contains conjugated linoleic acid, short and medium-chain fatty acids that may have anti-inflammatory, immune enhancing, antibacterial, anti-ulcerative colitis, anti-cancer, anti-atherosclerosis and anti-hypertension effects (Micinski *et al*., 2012).

Free fatty acids mediate adipose tissue signaling through toll-like receptor 4. The pro-inflammatory mediator expressions are via NF-KB or JNK. JNK bind and phosphorylate c-Jun on Ser-63 and Ser-73 within its transcriptional activation domain and belong to the mitogen-activated protein kinase family, responsive to stress stimuli, e.g. cytokines, ultraviolet irradiation, heat and osmotic shock.

The dietary recommendations to prevent coronary heart disease is to (1) replace trans and saturated fats with nonhydrogenated unsaturated fats; (2) increase omega-3 fatty acids from fish, fish oil supplements, or plant sources to balance omega-6 polyunsaturated oil intake; (3) consume lots of fruits, vegetables, nuts and whole grains and (4) reduce refined grain products.

Human studies showed that monounsaturated fatty acids consumption (MUFA or oleic acid) help inhibit metabolic syndrome, age-related cognitive decline and certain cancers (breast, colorectal and prostate). Oleic acid contents are high in olive oil (70%) and palm olein (50%). MUFA and phenol-rich plant oils improve cardiovascular risk factors (dyslipidemia, hypertension, endothelial dysfunction, oxidative stress and antithrombotic profiles) and have antioxidant and anti-inflammatory properties (Lopez-Miranda *et al*., 2010). Consuming repeatedly heated oils causes postprandial inflammation. Natural or added polyphenols-rich oils reduce postprandial inflammation in twenty obese humans in a randomized, crossover study (Perez-Herrera *et al*., 2012). Acute supplementation did not affect triacylglycerols or oxidative stress biomarkers of overweight and obese hypertriglyceridemic men (Hanwell, Kay, Lampe, Holub, & Duncan, 2009). Daily consumption of 2 g phytosterol by hypercholesterolaemic subjects lowered LDL-C, cholesterol synthesis and increased cholesterol absorption (Casas-Agustench *et al*., 2012).

Obesity, hypercholesterol and type 2 diabetes

Obesity is associated with systemic oxidative stress, adipokine imbalance and reduced antioxidant defences, leading to dyslipidemia, vascular disease and hepatic steatosis. Anti-obesity strategies include: (1) increasing physical activity (2) consuming non-starch polysaccharides/fiber and micronutrient-rich plant products, (3) breastfeeding; and (4) reducing energy-dense, micronutrient-poor diets (Swinburn, Caterson, Seidell, & James, 2004). High protein diets produce greater satiety and weight loss, lower plasma triglyceride, blood pressure and spare lean mass than high carbohydrate diets; with no harmful effects on bone density or renal function (Clifton, 2012). Some over-the-counter weight loss carbohydrate blocker produced larger testes in animals, while fat-blockers increased soluble pancreatic proteins in growing male rats (Erlwanger *et al*., 2007).

Digestive enzymes inhibitors

Alpha-glucosidase and alpha-amylase inhibitors help retard post-prandial blood glucose increase. Food compounds with such properties include tannins (ellagitannins and proanthocyanidins), anthocyanins, chlorogenic acid in coffee and many other polyphenols (Boath, Grussu, Stewart, & McDougall, 2012). Phlomis armeniaca, Salvia limbata and Plantago lanceolata teas exhibited weak alpha-amylase inhibitory activities and pronounced a-glucosidase inhibitory activities (Dalar & Konczak, 2013).

Gastrointestinal lipase inhibitors hinder fat digestion and absorption. Phenolic lipase inhibitors such as epigallocatechin-3-gallate, grape seed, kaempferol, quercetin (Sergent, Vanderstraeten, Winand, Beguin, & Schneider, 2012), ellagitannin, tannins and proanthocyanidins are present in green and black tea, berries (lingonberry, bearberry, arctic bramble, cloudberry, strawberry, raspberry and blueberry); garden pea (Pisum sativum), Norway spruce (Picea abies), large-leaved lime (Tilia platyphyllos) (Slanc *et al*., 2009) and Plantago lanceolata (Dalar & Konczak, 2013).

Beverages

Black Tea (*Camellia sinensis*) polyphenols (theaflavins, theaflavin 3-O-gallate, theaflavin 3′-O-gallate, theaflavin 3,3′-O-gallate, epigallocatechin gallate, epicatechin gallate, catechins, 2 quercetin glycosides, quinic acid, gallic acid and caffeine) inhibits pancreatic lipase (Yuda *et al*., 2012).

Cocoa powder supplementation reduced body weight gain, obesity-related inflammation, insulin resistance, fatty liver disease and down-regulated the pro-inflammatory gene expression in the white adipose tissues (WAT) of high-fat diet mice (Gu, Yu, & Lambert, 2013). Cocoa extract reduced postprandial glucose, plasma free fatty acid and oxidative stress biomarker (8-isoprostane), but did not affect the fasting plasma glucose and insulin level in obese-diabetic rats (Jalil, Ismail, Pei, Hamid, & Kamaruddin, 2008). The antioxidative cocoa polyphenols can modify glycemic response, lipid profile, decrease platelet aggregation, inflammation and blood pressure. They modulate intestinal inflammation by reducing neutrophil infiltration, proinflammatory enzymes and cytokines production. Cocoa has antiproliferative, antimutagenic,