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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,

chemoprotective and anticariogenic effects, beneficial for preventing cardiovascular and inflammatory diseases, metabolic disorders and cancer (Andujar, Recio, Giner, & Rios, 2012).

Coffee polyphenols (mono- or di-caffeoyl quinic acids CQA) enhanced energy metabolism and reduced abdominal and liver fat accumulation. They inhibited lipogenesis (fat synthesis) by downregulating sterol regulatory element-binding protein (SREBP-1c), acetyl-CoA carboxylase-1 and -2, stearoyl-CoA desaturase-1 and pyruvate dehydrogenase kinase-4 in the liver and reduced infiltration of macrophages into the fat tissues (Murase *et al*., 2011). Coffee mitigated glucose intolerance, hypertension, cardiovascular remodeling and fatty liver without affecting abdominal obesity and dyslipidemia in diet-induced obese rat model (Panchal, Poudyal, Waanders, & Brown, 2012). The chlorogenic acid (5-caffeoyl quinic acid, 5-CQA) inhibits pancreas a-amylase (Narita & Inouye, 2009) and help reduce hepatic TG level (Shimoda, Seki, & Aitani, 2006). Other coffee polyphenols (di-caffeoyl quinic acids, caffeoyl quinic acids and feruloyl quinic acids) inhibit maltase, sucrose and pancreatic lipase, to help reduce postprandial hyperglycaemia, hyperinsulinaemia, obesity and cardiovascular disease development (Murase *et al*., 2012). Caffeine suppresses fat absorption, while neochlorogenic acid and feruloyl quinic acid mixture in green coffee enhanced hepatic carnitine palmitoyltransferase activity to suppress visceral fat accumulation and body weight gain in mice model (Shimoda *et al*., 2006).

Green tea consumption helps to reduce metabolic syndrome and some cancer risk, while benefitting oral health, infections, bone mineral density, fibrosis and neuronal degeneration (Cabrera, Artacho, & Gimenez, 2006). Green tea catechins (~1 g/day) decreased the body weight of overweight/obese men, without affecting blood pressure or metabolic function biomarkers (Brown *et al*., 2011). Green tea polyphenols and caffeine apparently interacted synergistically to prolong brown adipose tissue thermogenesis, by sympathetically released noradrenaline. The catechin-polyphenols inhibit the release of noradrenaline degrading enzyme (catechol-O-methyl-transferase) and caffeine inhibits noradrenaline-induced the cAMP (tissues regulator) degrading enzymes (trancellular phosphodiesterases) (Dulloo *et al*., 2000). Green tea increase the lipolytic pathway, reduces adipose tissue and low-grade inflammation in high fat diet animal model, to produce anti-obesity, anti-oxidant, hypolipidemic and hepatoprotective effects (Cunha *et al*., 2013). Epigallocatechin-3-gallate (EGCG) is the most active catechin in green tea. The green tea catechin gallate was the strongest inhibitor of fatty acid synthase, better than EGCG (epigallocatechin gallate) or epicatechin gallate (Zhang, Xiao, Wang, Wu, & Tian, 2006). Green tea polyphenols affected the glucose uptake and insulin signaling genes in a high-fructose-diet animal model (Cao, Hininger-Favier, *et al*., 2007). Tea and tea polyphenols suppress fatty acid synthase gene by down-regulating EGFR/PI3K/Akt/Sp-1 (a human protein transcription factor) signal transduction pathways (Lin & Lin-Shiau, 2006). Akt or Protein Kinase B (PKB) is a serine/threonine-specific protein kinase for various cellular processes e.g. glucose metabolism, apoptosis, cell proliferation, transcription and cell migration.

White tea, made from the unfermented young shoots of Camellia sinensis protected from sunlight to avoid polyphenol degradation, has higher catechins levels than green tea. White tea does not reduce food intake, body weight, visceral adiposity, cholesterol lipoprotein profile, but reduces blood triacylglycerols by increasing cecal lipids and oxidative stress in the liver and adipose tissue (Teixeira *et al*., 2012).

Herbal teas may have comparable or superior phenolic and antioxidant levels to black tea and many suppressed the activity of enzymes involved in metabolic syndrome, namely alpha-amylase, alpha-glucosidase, pancreatic lipase and angiotensin I-converting enzyme (ACE). Ilex paraguariensis (mate) tea, contains caffeine and antioxidants to produce (i) vasodilating and lipid reduction properties, (ii) antimutagenic effects, (iii) anti-glycation effects (iv) weight reduction properties, (v) lowers LDL-cholesterol levels in humans, synergistic with statins, (vi) pancreatic lipase inhibition, (vii) activation of adenosine-monophosphate-activated protein kinase (AMPK) and uncoupling of electron transport, (viii) anti-inflammatory effects, acting on macrophage migration and inactivating matrix-metalloproteinase (Bracesco, Sanchez, Contreras, Menini, & Gugliucci, 2011).

Fruits

Acai (*Euterpe oleracea* Mart.) berry: a small, black-purple palm fruit reduced fasting glucose, insulin levels, total cholesterol and LDL-cholesterol, but not blood pressure, hs-CRP or eNO (endothelial nitric oxide) in healthy overweight adults (Udani, Singh, Singh, & Barrett, 2011).

Anthocyanin (cyanidin 3-glucoside) reduced blood glucose and enhanced insulin sensitivity by downregulating retinol binding protein 4 expression in type 2 diabetic mice. The anthocyanins caused upregulation of the glucose transporter 4 and downregulation of both RBP4 and the inflammatory adipocytokines (MCP-1; TNF-alpha) in white adipose tissues (Sasaki *et al*., 2007). Pure blueberries and strawberry anthocyanins (but not whole berries, purple corn anthocyanins or black raspberry anthocyanins) prevented dyslipidemia and obesity development in mammals on high fat diet (Prior, Wilkes, Rogers, Khanal, Wu, & Hager, 2010).

Apples consumption improved the lipid and oxidative status of the tissues and organs by producing larger intestinal pool and greater fecal excretion of bile acids in obese rats (Aprikian *et al*., 2002). Dietary apples also reduced the retroperitoneal and epididymal adipose tissue weights in rats (Nakazato, Song, & Waga, 2006).

Bilberries and to a lesser extent seabuckthorn decreased waist circumference, weight, vascular cell adhesion molecule and intercellular adhesion molecule of overweight and obese women (Lehtonen *et al*., 2011). Bilberry anthocyanidins-enriched extracts inhibited adipocyte differentiation by affecting the genes expressions of the insulin pathway; decreased peroxisome proliferator-activated receptor (PPAR) and sterol regulatory element-binding protein 1c (SREBP1c) and tyrosine residues of IRS1 phosphorylation (Suzuki *et al*., 2011).

Blueberries (*Vaccinium*) help prevent degenerative diseases like diabetes, hyperlipidemia, hypertension, obesity, cancer, neurodegeneration and osteoporosis, through its apoptosis, antioxidant, antiinflammation and antiangiogenesis effects. Blueberries also improve visual function by increasing rhodopsin regeneration and have antimicrobial actions to prevent urinary tract infections. Blueberries bioactives include anthocyanins (anthocyanidins, or phenolic aglycone, conjugated with sugar), chlorogenic acid, flavonids, a-linolenic acid, pterostilbene, resveratrol and vitamins, that passes through the blood-brain barrier (Chen, Li, & Xu, 2010). Blueberries improved insulin sensitivity in obese, insulin-resistant men and women, without changing adiposity, energy intake and inflammatory biomarkers (Stull, Cash, Johnson, Champagne, & Cefalu, 2010). Blueberry attenuated insulin resistance in mammals by reducing adipocyte death, inflammation and insulin resistance (DeFuria *et al*., 2009). Blueberry reduced insulin resistance, triglycerides, fasting insulin, abdominal fat mass, liver weight, body weight and total fat mass, but increased adipose and skeletal muscle PPAR activity and affected PPAR transcripts involved in fat oxidation and glucose uptake/oxidation in obese rats (Seymour *et al*., 2011). Blueberry juice and especially purified blueberry anthocyanins retarded obesity, serum leptin elevation and diabetes development in mice on obesogenic diet (Prior, Wilkes, Rogers, Khanal, Wu, & Howard, 2010). Blueberry polyphenols suppressed adipocyte differentiation, adipogenesis and cell proliferation (Moghe, Juma, Imrhan, & Vijayagopal, 2012). Blueberry anthocyanins reduced glucose production in hepatocytes, but did not increase glucose uptake (Roopchand, Kuhn, Rojo, Lila, & Raskin, 2013).

Chokeberry reduced weight gain and modulates insulin, adipogenic and inflammatory signaling pathways in epididymal adipose tissue of rats on a fructose-rich diet (Qin & Anderson, 2012).

Citrus polyphenols (from red orange, grapefruit, orange) produced lipolytic effect (via cAMP-phosphodiesterase inhibition) in overweight human adipocytes, more potently than cyanidin-3 glycoside, narangin or caffeine (Dallas, Gerbi, Tenca, Juchaux, & Bernard, 2008).

Cranberry flavonoids ameliorated (i) insulin resistance (ii) plasma lipid profile, (iii) visceral fat mass, via the adiponectin-AMPK pathway, and (iv) plasma atherogenic cholesterol by downregulating the hepatic cholesterol synthesis pathway (Shabrova *et al*., 2011).

Grapes or grape products contain numerous polyphenols, including the stilbene resveratrol, the flavanol quercetin, catechins and anthocyanins that help mitigate diabetes, by improving B-cell function and protecting against B-cell loss (Zunino, 2009). Grape-seed procyanidins modulated inflammation on human differentiated adipocytes by inhibiting NF-KB translocation to the nucleus; and reduces IL-6 and MCP-1 expression and enhances the anti-inflammatory adipokine adiponectin production (Chacon *et al*., 2009). Resveratrol formed by injured grapes, produced these benefits: (i) calorie restriction effects, (ii) improved human adipocyte secretion profile in obesity-induced metabolic disorders, (iii) elevated basal glycerol release, (iv) reduced intracellular TG content, (v) increased intracellular lipolysis (vi) down-regulated extracellular matrix proteins, (vii) up-regulated processing proteins, (viii) induced protective proteins secretion against cellular stress and apoptosis regulating proteins, (ix) up-regulated adiponectin and ApoE, (x) down-regulated PAI-1 and PEDF secretion which may improve anti-inflammatory processes, (xi) increased insulin sensitivity, (xii) inhibited cyclic adenosine monophosphate-specific phosphodiesterases, and (xiii) activated 5'-adenosine monophosphate-activated kinase (Rosenow *et al*., 2012; Xu & Si, 2012). Vitisin a resveratrol tetramer, strongly and dose dependently reduced (i) adipocyte differentiation and fat accumulation by cell cycle arrest through p21, (ii) PPARγ expression (iii) Rb phosphorylation level and (iv) cell cycle at the G1-S phase transition, causing cells to remain in the preadipocyte state (Kim *et al*., 2008).

Hibiscus sabdariffa Linnaeus (Malvaceae), is traditionally used against hypertension, diabetes metabolic syndrome and liver disorders (Perez-Torres, Ruiz-Ramirez, Banos, & El-Hafidi, 2013).

Mango peel extracts from Irwin and especially Nam Doc Mai (but not the flesh or Kensington Pride mango peel) inhibited adipogenesis, similar to resveratrol (Taing *et al*., 2012).

Maqui Berry (*Aristotelia chilensis*) anthocyanins (delphinidin 3-sambubioside-5-glucoside) produced anti-diabetic effects by decreasing glucose production, enhancing insulin and down-regulating glucose-6-phosphatase (the gluconeogenic enzyme) in liver cells (Rojo *et al*., 2012).

Mulberry polyphenols (gallic acid, chlorogenic acid, rutin and anthocyanins) help prevent obesity by reducing (i) hepatic lipogenesis (fatty acid synthase and 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) reductase); (ii) body weight gain and visceral fat accumulation, (iii) dyslipidemia (iv) hepatic lipids thus prevents liver injury; while elevating (v) hepatic PPAR a (vi) lipolysis and (vii) carnitine palmitoyltransferase-1 (Peng *et al*., 2011).

Plums reduced blood glucose during an insulin tolerance test and increased insulin sensitivity, plasma adiponectin and adipose tissues PPARγ mRNA expression (Utsunomiya, Yamakawa, Kamei, Kadonosono, & Tanaka, 2005).

Pomegranates exert (i) hypoglycaemic effects, (ii) increase insulin sensitivity, (iii) inhibit a-glucosidase, (iv) impact glucose transporter type 4 function, (v) reduce total cholesterol, (vi) improve blood lipid profiles, and (vii) retard inflammation by modulating PPAR pathways. Pomegranate contains polyphenols such as ellagitannins, anthocyanins, phenolic acids, fatty acids and a variety of volatile compounds (Medjakovic & Jungbauer, 2013).

Rose hips, strawberry and raspberry contain the antioxidative glycosidic flavonoid tiliroside, that inhibits (i) inflammation, (ii), obesity-induced hepatic and muscular triglyceride accumulation (iii) carcinogen (iv) liver damage (v) hyperinsulinemia (vi) hyperlipidemia; while enhancing (i) adiponectin signaling (ii) liver and skeletal muscle fatty acid oxidation (iii) liver and skeletal muscle protein kinase adenosine-monophosphate and (iv) liver PPARα. Tiliroside does not suppress body weight gain and visceral fat accumulation in obese-diabetic mice model (Goto *et al*., 2012).

Strawberry anthocyanin, pelargonidin sulfate and pelargonidin-3-O-glucoside reduced postprandial inflammation and increased insulin sensitivity in overweight adults (Edirisinghe *et al*., 2011). Strawberry phenolics mitigated postprandial LDL oxidation and lipid metabolism after a high-fat meal in overweight hyperlipidemic men and women (Burton-Freeman, Linares, Hyson, & Kappagoda, 2010).

Watermelon (*Citrullus vulgaris*) helps fight diabetes, dyslipidemia, thyroid dysfunction and oxidation (Khan, Najmi, & Pillai, 2012).

Wild Alaskan berries (Vaccinium ovalifolium, Vaccinium uliginosum, Rubus chamaemorus, Rubus spectabilis and Empetrum nigrum) anthocyanins and proanthocyanidins-enriched fractions reduced lipid accumulation in adipocytes and serum glucose levels (Kellogg *et al*., 2010).

Vegetables

Onions and garlic family (Allium)

Onion (*Allium cepa* L.) and garlic (*Allium sativum* L.), contain pungent thiosulfinates, phenolics, steroidal and volatile sulfur compounds, that hinder cancer, coronary heart disease, obesity, hypercholesterol, type 2 diabetes, hypertension, cataract and gastrointestinal tract ailments (e.g. colic pain, flatulent colic and dyspepsia) (Lanzotti, 2006). Both Allium species contains N-acetylcysteine, which improved the antioxidant defences (superoxide dismutase, catalase, glutathione peroxidase, reduced glutathione) and mitigated glucose intolerance, dyslipidemia, LDL-oxidation and serum oxidative stress (Souza *et al*., 2011). Onion dose-dependently reduced (i) diabetes related liver damage, (ii) blood glucose levels and (iii) lipid peroxidation product malondialdehyde (MDA), in diabetes animal models (Ogunmodede, Saalu, Ogunlade, Akunna, & Oyewopo, 2012). Onion has hypoglycemic, cardioprotective, hypolipidemic and bone strengthening properties. Onion is rich in flavonoids, polyphenols, organic sulfur and saponins. Onion is more potent in its raw form (Sohail, Karim, Sarwar, & Alhasin, 2011).

Garlic works synergistically with type 2 antidiabetic agents (Ashraf, Khan, & Ashraf, 2011). Garlic and propranolol are potent antihypertensive and cardioprotective agents and when combined, garlic doubled or tripled the bioavailability and half life of propranolol. Garlic effectively reduced fluid intake, body weight, blood pressure, cholesterol, triglycerides and blood glucose (Asdaq & Inamdar, 2011). Garlic acts synergistically with turmeric against hyperglycemia, HbA1C and dyslipidemia in type-2 diabetes-dyslipidemia patients (Sukandar *et al*., 2010).

Cabbage family (Brassica)

Brassicas (cabbage, cauliflower, broccoli, broccolini, brussels sprouts, chinese cabbage, swedes and turnips, broccoli raab, collards, cress, kale, kohlrabi, mustard, kailan and bok choi) contain glucosinolates, carotenoids, chlorophylls, ascorbic acid, sinigrin; gluconapin, glucobrassicanapin and progoitrin, phenolics like hydroxycinnamic acids (sinapic, ferulic, p-coumaric and caffeic acids), glycosides of quercetin and kaempferol and derivatives of p-coumaric, ferulic, sinapic and caffeic acid (Krumbein, Schonhof, & Schreiner, 2005; Olsen, Aaby, & Borge, 2009).

Randomized double-blind placebo-controlled trial showed that 10 weeks Brassica rapa turnip extract supplementation increased the high-density lipoprotein cholesterol and reduced the total-C/HDL-C ratio, free fatty acid and adipsin levels (Jeon *et al*., 2013). Red cabbage that is rich in anthocyanin increased faecal lipid excretion to prevent atherogenic diet-induced serum /tissue lipids elevation, cardiac and hepatic peroxidation and injuries (Sankhari, Thounaojam, Jadeja, Devkar, & Ramachandran, 2012). Kale leaves extracts inhibited lipid peroxidation in both isolated VLDL and LDL (Kural, Kucuk, Yucesan, & Orem, 2011), while Yamato-mana (Brassica rapa L. Oleifera) gluconapin (3-butenyl glucosinolate) and sinigrin (2-Propenyl glucosinolale) suppressed postprandial hypertriglyceridemia in mice (Washida, Miyata, Koyama, Yazawa, & Nomoto, 2010). Brassica oleraceae L. combined with hydrosoluble chitosan synergistically decreased serum total cholesterol, LDL-cholesterol, VLDL-cholesterol and triglycerides (Geremias *et al*., 2006).

Solanum (potato, tomato, eggplant)

Potato (*Solanum tuberosum*) proteins (patatin) and other potato by-products has antioxidant and ACE-inhibitory (potential anti-hypertensive agent) properties (Pihlanto, Akkanen, & Korhonen, 2008). Potato tubers are a source of B-carotene, α-tocopherol, chlorogenic acid, petanin, carotenoids, lutein zeaxanthin and anthocyanins (dark purple-fleshed cultivars) (Andre *et al*., 2007). Potato extract supplements suppressed human autoimmune rheumatoid arthritis, rheumatoid factor, anti-type II collagen antibody,

interleukin (IL)-1, IL-6, LDL-cholesterol and serum malondialdehyde levels, and increased the glutathione peroxidase and glutathione reductase activities in mice spleens (Choi, 2007).

Tomato (*Solanum lycopersicum*) consumption reduced cardiovascular disease, age-related macular degeneration and certain cancers risk. It is rich in vitamins C and E, lycopene, B-carotene, lutein and flavonoids such as quercetin. Green tomato extract (but not the red tomato extract) prevented obesity in high-fat-diet mice by activating AMPK and acetyl-CoA carboxylase phosphorylation in the liver. The green tomato decreased epididymal adipose tissue, liver weights, liver cholesterol and serum low-density lipoprotein cholesterol. The green tomato extract decreased the liver HMG-CoA reductase expression, PPARγ (PPAR gamma), CCAAT/enhancer-binding protein alpha and perilipin in the adipose tissue (Choi *et al*., 2013). Nucleotides with GGCCAATCT consensus sequence are 75-80 bases upstream to the initial transcription site and signal the binding site for the RNA transcription factor. Red tomatoes had higher lycopene, total phenolic and antioxidant content than yellow tomatoes (Walia, Singh, Kaur, Kumar, & Joshi, 2010).

Eggplants (*Solanum melongena*) are cardioprotective, improve left ventricular function, reduce myocardial infarct size and cardiomyocyte apoptosis (Das *et al*., 2011). Unfortunately, eggplants have high histamine and other amine levels that may enhance LDL oxidation and its endocytosis. Eggplant did not decrease plasma cholesterol nor prevent the development of atherosclerosis in mice, but increased their oxidative stress atherosclerosis risk (Botelho *et al*., 2004). Eggplant phenolics inhibit α-glucosidase inhibitory and ACE, indicating its potential beneficits for type 2 diabetes and hypertension (Kwon, Apostolidis, & Shetty, 2008).

Other vegetables

Beetroot (*Beta vulgaris* var. rubra) has oxidative, pro-apoptotic and anti-inflammatory effects in obese women neutrophils (Zielinska-Przyjemska, Olejnik, Dobrowolska-Zachwieja, & Grajek, 2009).

Bitter melon (*Momordica charantia*) helps repair damaged B-cells, increase insulin levels and sensitivity, and inhibit intestinal glucosidase and disaccharidases to produce hypoglycemic and hypolipidemic effects. Bitter melon increases thyroid hormones, adiponectin and AMPK release, to improve glucose and fatty acid transport in the cells and mitochondria, modulation of insulin secretion, and uncoupling proteins elevation in the adipose and skeletal tissues (Chaturvedi, 2012).

Garcinia cambogia which is a common Asian food acidulant contains hydroxyl citric acid, which can suppress fat accumulation but was reportedly toxic to the testis of developing male Zucker obese rats (Saito *et al*., 2005).

Korean fermented red pepper paste (Kochujang) reduced body fat gain, adipocytes size, serum lipid levels, leptin secretion, tumor necrosis factor-a mRNA levels, and lipid accumulation by inhibiting adipogenesis through down-regulation of SREBP-1c and PPAR-γ, and by stimulating lipolysis (increased hormone-sensitive lipase activity and glycerol secretion) (Ahn *et al*., 2006).

Mulberry leaves positively affect adipocytokines expression and atherosclerosis by decreasing oxidative stress; blood glucose, serum triglycerides; TNF-alpha, MCP-1, macrophage markers and NADPH oxidase subunits expression in white adipose tissue (WAT); and increasing adiponectin expression in mice (Sugimoto *et al*., 2009).

Mushroom help increase nitric oxide production and are potentially good for diabetes, obesity, atherosclerosis, high blood pressure, and metabolic disorders. They have low fat content and are a good source of carbohydrate, protein, free amino acids, dietary fiber, antioxidants, calcium, magnesium, potassium, phosphorous and iron (Rai & Acharya, 2012). Edible mushrooms have immunomodulatory properties that protect against mutagens, tumor, virus, thrombosis, hypercholesterol, dyslipidemia and oxidative stress. Fungal polysaccharides especially B-glucans and other bioactive compounds show anti-inflammatory properties (Garcia-Lafuente *et al*., 2011).

Piper sarmentosum reduces visceral fat comparable to glycyrrhizic acid and inhibits 11B-hydroxysteroid dehydrogenase type 1 that regulates cortisol metabolism in adipose tissue, to hinder visceral obesity and metabolic disorders (Fairus *et al*., 2013).

Plaintain (*Musa Sapientum*) stem juice is traditionally used for obesity, kidney stones, diabetes and metabolic disorders. The plantain flower and stem core showed good metal chelating, and antioxidant properties but the flower possessed greater antioxidant potential than the stem (Jayamurthy, Aparna, Gayathri, & Nisha, 2013).

Seaweeds are especially rich in soluble fiber to help slow digestion, gastric emptying, food absorption and moderating appetite. Seaweeds antioxidant properties help reduce lipid oxidation and increase the animals' endogenous antioxidant response elements. Brown seaweeds contain the anti-obesity carotenoid fucoxanthin that upregulate mitochondrial uncoupling protein 1 (UCP1) gene expression and increase basal metabolic rates, reduce blood glucose and plasma insulin and increase insulin sensitivity. Seaweeds also contain omega-3 fatty acids that lower triglyceride and inflammation indices (Mohamed, Hashim, & Abdul-Rahman, 2012). Seaweeds antioxidative fucoidans deter inflammation, allergy, tumor, obesity, coagulation, virus, hepatopathy, uropathy and renalpathy (Vo & Kim, 2013). Fucoidan suppresses lipid accumulation and adipocyte differentiation by suppressing inflammation-related cytokines, PPARγ, CCAAR/enhancer-binding protein a, and adipocyte protein 2 (Kim & Lee, 2012).

Soybeans that are sprouted or bioprocessed by *Rhizopus oligosporus* or *Lentinus edodes* have amylase and ACE inhibition properties that are beneficial for diabetes and hypertension (McCue, Kwon, & Shetty, 2005).

Grains and legumes

Whole grain consumption was inversely associated with body mass index in school children even after adjustment for body weight potential dietary effectors (fruit, vegetable and dairy intakes) (Choumenkovitch *et al*., 2013). Whole grains consumption is protective against stroke and metabolic syndrome. They contain antioxidants, dietary fiber (inulin, beta-glucan, resistant starch), phenolics, phytate, phyto-estrogens, phytostanols, phytosterols, vitamins (carotenoids, tocotrienols, tocopherols) and minerals. Fiber-rich cereals consumption help reduce cholesterol, hypertension, constipation and obesity. Rice protein improves mammals' body weight and lipids level because they have lower digestibility, which help upregulate lipolysis and downregulate lipogenesis (Yang *et al*., 2012).

Nuts (tree nuts and peanuts) are nutrient dense (rich in unsaturated fats, protein, fiber, minerals, tocopherols, phytosterols, phenolics and other bioactive compounds) but epidemiologic and intervention studies showed they do not contribute to weight gain. Nut consumption showed reduced coronary heart disease and gallstones incidences in both genders and diabetes in women (Ros, 2010). Nuts have antioxidant, hypocholesterolemic, cardioprotective, anticancer, anti-inflammatory, anti-obesity and antidiabetic properties (Vadivel, Kunyanga, & Biesalski, 2012).

Sesame contains sesamol, the powerful antioxidant that alleviates diet-induced inflammation and cardiometabolic syndrome in mammals by up-regulating PPARγ, PPAR a and e-NOS. Sesamol dose-dependently decreased TBARS, nitrotyrosine, insulin resistance, hyperinsulinemia, hyperglycemia, dyslipidemia, TNF-alpha, IL-6, leptin, resistin, highly sensitive C-reactive protein (hs-CRP), hepatic transaminases and alkaline phosphatase. Sesamol normalizes adiponectin, nitric oxide, arterial pressures, antioxidant enzyme activities, hepatic steatosis and hepatocytes deterioration. Sesamol decreases LXRa (a nuclear receptor protein), SERBP-1c, P-JNK and NF-KB expression (Sharma *et al*., 2012).

Early-life soya intake produced higher leptin and MCP-1 levels but soya intervention did not affect inflammation markers in men (Maskarinec, Oum, Chaptman, & Ognjanovic, 2009). In animals, Isoflavones (e.g Genistein) lowered plasma glucose, liver damage markers (aspartate amino transferase, alanine amino transferase). Isoflavones had significant effect on plasma insulin, leptin, blood sugar, triglycerides and glucagon in lean rats but not in obese rats (Ali, Velasquez, Hansen, Mohamed, & Bhathena, 2005).

The polyphenol-rich black soybean seed coat extract containing cyanidin 3-glucoside, catechins, and procyanidins amongst others, suppressed abdominal fat accumulation, plasma glucose level, major inflammatory cytokines, tumor necrosis factor-a and monocyte chemoattractant protein-1. The extract enhanced insulin sensitivity, UCP-1 and UCP-2 expression in the high-fat diet mice, to deter obesity and diabetes by enhancing energy expenditure and suppressing inflammation (Kanamoto *et al*., 2011).

Many legumes (e.g *Phaseolus vulgaris*) inhibit alpha-amylase (Obiro, Zhang, & Jiang, 2009). Pigeon pea (*Cajanus cajan* L.) has linoleic acid and phytosterol (B-sitosterol, campesterol, stigmasterol) that synergistically produce antioxidant and antidyslipidemic effects by promoting cholesterol conversion to bile acid and increasing hepatic carnitine palmitoyltransferase-1 (CPT-1), LDL receptor, and cholesterol 7 a-hydroxylase (or cytochrome P450 7A1, CYP7A1) expression in high fat diet-fed hamsters (Dai *et al*., 2013). Chia seed in contrast does not promote weight loss or alter disease risk factors in overweight adults (Nieman *et al*., 2009).

Herbs and spices

The pungent compounds in herbs and spices help enhance metabolism and deter against obesity, diabetes, and chronic inflammation. Many herbs and spices have good positive effects on blood sugar, insulin sensitivity, dyslipidaemia, weight gain and the cardiovascular system. They activate PPARa and PPARγ, inhibit NF-KB activation, and enhance anti-inflammatory cytokines expression (Jungbauer & Medjakovic, 2012).

Black cumin (*Nigella sativa*) reduced blood total cholesterol and weight gain in animal models (Tauseef, Butt, & Anjum, 2009).

C*atharanthus roseus, Thymus vulgaris, Hypericum perforatum,* and *Artemisia annua* are also potently antioxidative. Rosmarinic acid was the main phenolic in Salvia officinalis, Thymus vulgaris, Origanum majoricum, and P. longiflora (Patel, Prasad, Kumar, & Hemalatha, 2011).

Cinnamon extract helped safeguard against tissue changes by minimizing protein aggregation, preventing glycation and oxidative stress in fructose-fed rodents. Cumin, cinnamon, and black pepper, inhibited in vitro advanced glycation end-products (AGE) formation at 1.0 mg/ml (Saraswat *et al*., 2010). Piperine from black pepper (Piper nigrum) inhibited lipid peroxidation (Chonpathompikunlert, Wattanathorn, & Muchimapura, 2010).

Cinnamon water extract or polyphenols with doubly linked procyanidin type-a polymers display insulin-like activity to improve blood glucose and lipid profiles of diabetes patients. Cinnamon increased proteins for insulin signaling, glucose transport and anti-inflammatory/anti-angiogenesis response (Cao, Polansky, & Anderson, 2007). Metabolic syndrome subjects consuming 1-6g cinnamon had improved fasting blood glucose, systolic blood pressure, body fat and lean body mass compared with the placebo group (Anderson, 2008). Cinnamon normalizes fasting blood glucose by decreasing hepatic glucose production and the gene expression of related enzymes (phosphoenolpyruvate carboxykinase and glucose-6-phosphatase) in obese hyperglycemic mice (Cheng *et al*., 2012).

Clove aqueous extracts have insulin-like biological activity (Broadhurst, Polansky, & Anderson, 2000) and

can gradually lower fasting blood glucose levels (Shukri, Mohamed, & Mustapha, 2010). The eugenol and eugenyl acetate in cloves are anti-oxidative.

Fenugreek (*Trigonella foenum-graecum* Linn) seeds alcoholic extract has beneficial effects on body weight, blood glucose and cataract development in aging humans. Fenugreek, garlic, gingers and red pepper are effective as hypocholesterolemics. Capsaicin (from chilli), curcumin, fenugreek and ginger also enhance bile acids secretions (Srinivasan, Sambaiah, & Chandrasekhara, 2004).

Ginger (*Zingiber officinalis*) is thermogenic, antioxidative, stimulating, anti-inflammatory, anti-hyperglycemic and inhibited glycation (Saraswat *et al*., 2010).

Houttuynia cordata decreased body weight, epididymal fat, insulin resistance, plasma and liver lipids, and enhanced hepatic malic enzyme, fatty acid synthase (FAS) and 3-hydroxy-3-methylglutaryl coenzyme a reductase activities in mice. It suppressed the related oxidative and inflammatory stress in the heart and liver via glutathione and glutathione peroxidase activity, decreasing tumor necrosis factor-alpha, interleukin (IL)-1beta and IL-6 production (Lin, Hsu, & Yin, 2013).

Licorice (*Glycyrrhiza glabra*) oil, contain hydrophobic flavonoids that have anti-obesity (decreased abdominal adipose tissue and liver and plasma triglycerides) properties in rats. The oil decreased acetyl-CoA carboxylase and fatty acid synthase and increased fatty acid oxidation through acyl-CoA dehydrogenase (Kamisoyama, Honda, Tominaga, Yokota, & Hasegawa, 2008).

Momordica charantia, Morinda citrifolia fruit, and *Centella asiatica* extract have anti-pancreatic lipase and antioxidant activitis that help prevent obesity (Gooda *et al*., 2012). Processed Aloe vera gel reduced circulating blood glucose, insulin resistance, plasma insulin, liver and plasma triacylglyceride and adipocytes size (Kim *et al*., 2009). Korean red ginseng (Panax ginseng) inhibited angiogenesis (VEGF-a and FGF-2), matrix metalloproteinase (MMP-2 and MMP-9) and prevented obesity in high fat diet-induced obese mice. Ginseng increased angiogenic inhibitors (TSP-1, TIMP-1, and TIMP-2 mRNA levels) in adipose tissues (Lee, Park, & Yoon, 2013).

Oregano (*Origanum majoricum*, O. vulgare) and *Poliomintha longiflora* have higher antioxidant and phenolics content than many other culinary and medicinal herbs (Patel *et al*., 2011). Oregano contains rosmarinic acid, protochatechuic acid, quercetin, p-coumaric acid and protein (McCue, Vattem, & Shetty, 2004). *Murraya koenigii* (curry leaves), and tamarind (*Tamarindus indica*) also inhibit a-amylase (Narkhede, 2012).

Rosemary extracts (REs) has hepatoprotective, anti-obesity and anti-inflammatory properties (Takahashi *et al*., 2009). Carnosic acid and carnosol from rosemary inhibited gastric lipase and adipocyte differentiation in mouse by activating phase2 enzymes (Gsta2, Gclc, Abcc4, and Abcc1), and glutathione metabolism (Vaquero *et al*., 2012).

Saffron (*Crocus sativus* L.) increases blood flow in certain tissues, has antihypertensive, antioxidant, anti-inflammatory, relaxant properties (Srivastava, Ahmed, Dixit, Dharamveer, & Saraf, 2010), cardiovascular, lipids, insulin resistance, tissues oxygenation effects (Kianbakht & Hajiaghaee, 2011).

Turmeric contains the antioxidant curcumin (diferuloylmethane) that affect signaling mediators like NFKB, cyclooxygenase-2 (COX-2), lipooxygenase (LOX), and inducible nitric oxide synthase (iNOS), for modulating inflammation, angiogenesis, transcription, enzymes, protein kinases, protein reductases, carrier proteins, cell survival, resistance, adhesion, growth factors, receptors, cell cycle regulation, chemokines, DNA, RNA and metal ions. Turmeric helps prevent and/or treat arteriosclerosis, oxidation, respiratory, hepatic, pancreatic, and degenerative diseases in humans (Anand, Kunnumakkara, Newman, & Aggarwal, 2007). Turmeric and curcumin are not anti-hyperglycemic but prevented oxidative stress in hyperglycemic rats and induced the glutathione-linked detoxification enzymes in rats (Suryanarayana *et al*., 2005). Curcumin at the 0.002% level inhibited oxidation, glycation, lipid peroxidation, AGE and protein aggregation. Under hyperglycemic conditions, higher levels of dietary curcumin (0.01%) may have the opposite effect of being pro-oxidative, enhancing AGE formation and protein aggregation. However feeding curcumin to normal rats at up to 0.01% level did not cause any changes in morphology or biochemical parameters (Suryanarayana *et al*., 2005) because of its limited bioavailability. Curcumin protective effects against lipid peroxidation or galactose induced oxidative stress are (i) through glutathione S-transferase isozyme induction and (ii) by decreasing cells apoptosis (Pandya *et al*., 2000). Dietary curcumin improved tissue morphology, physiology, and gene expression, tissue structure and function in animal models.

Vitex negundo help normalize blood sugar and decreasing oxidative stress (Rooban *et al*., 2009). Other herbs like Dendrobium moniliforme is antioxidative, and helped normalize serum glucose, total cholesterol, renal lipid and renoprotective in high fat diet mice. The Dendrobium decreased high-fat diet-induced renal damage in mice through the regulation of lipid-induced oxidative stress (Lee *et al*., 2012). Cleistocalyx operculatus flower buds inhibit pancreatic lipase and a-amylase to help prevent or treat obesity (Zhang & Lu, 2012). Bergenia crassifolia leaves extract is an appetite suppressant that helps prevent obesity, and improve glucose tolerance without affecting cholesterol level (Shikov *et al*., 2012).

Table 1 summarises the categories of food for cardiovascular health and representative structures of their bioactive compounds. Other edible plants with antidiabetic properties include, guar gum seeds (*Acacia areca*), sweet flag roots (*Acorus calamus*), Aloe vera leaves, dill leaves (*Anethum graveolens*) sugar apple leaves (*Anona squamosa*), betel nut (*Areca catecu*), yellow leader root (*Astragalus*

Table 1. Bioactive compounds in food for cardiovasular health.

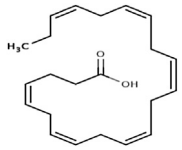
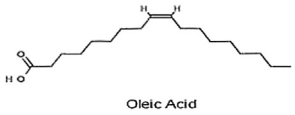
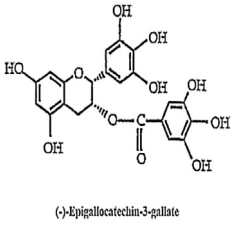
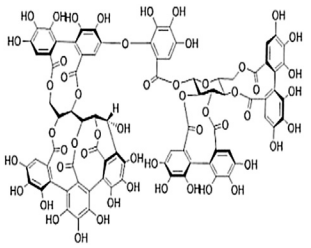
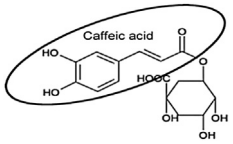
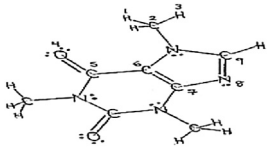
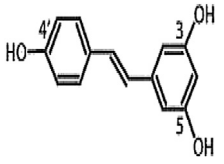
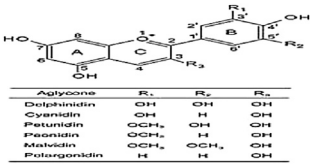
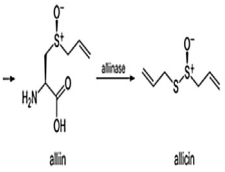
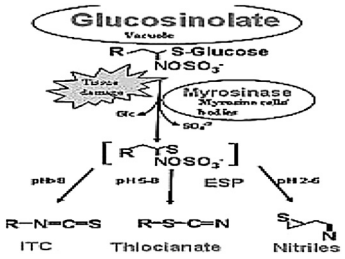
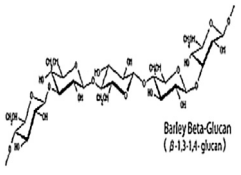
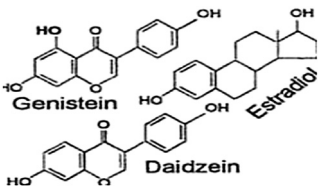
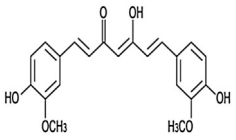
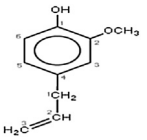
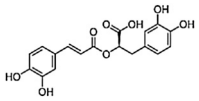
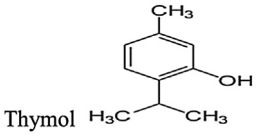
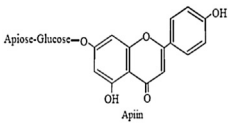
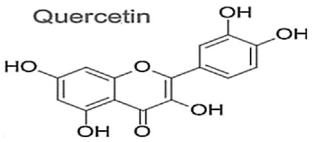
Category	Examples	Structures of bioactive compounds	
Oils and fats	Fish oil, olive oil, flax seed oil, OMEGA 3 fatty acid, Omega 6 fatty acid	Dodecahexaenoic acid 	Oleic acid 
Digestive Enzymes Inhibitors (Alpha-glucosidase, alpha-amylase & Gastrointestinal lipase inhibitors	Green and black tea, berries (lingonberry, bearberry, arctic bramble, cloudberry, strawberry, raspberry, blueberry, garden pea	Epigallocatechin-3-gallate, 	Tannins 
Beverages	Black and green Tea, cocoa, coffee, herbal tea	chlorogenic acid (5-caffeoyl quinic acid 	Caffeine 
Fruits	Berries, apples, citrus, grapes, pomegranates, plums, rose hips, roselle, watermelon, mangoes	Resveratrol 	Anthocyanin 
Vegetables	Onions and garlic, brassica (cabbage family), tomatoes, potatoes, bitter melon, mushrooms, seaweeds	Alliin, all-cin 	
Grains and legumes	Nuts, sesame, whole grain cereals, soya,	beta-glucan 	Isoflavones 

Table 1 (*continued*)

Category	Examples	Structures of bioactive compounds	
Spices	Turmeric, cinnamon, black cumin, clove, fenugreek, pepper, ginger, chilli	Curcumin 	Eugenol 
Herbs	Oregano, thyme, rosmary, vitex negundo, mint,	Rosmarinic acid 	Thymol 
Anti-hypertensive food	Celery, banana, grapes, edible shoots		

membranaceus), bilimbi leaves (*Averrhoa bilimbi*), neem leaves and seeds (*Azadurachta indica*), barberries root (*Berberis aristata*), beetroot (*Beta vulgaris*), achiote leaves (*Bixa orellana*), mustard leaves (*Brassica juncea*), Flame of the forest bark, leaves and flower (*Butea monosperma*), caper bush fruit (*Capparis spinosa*), caraway seeds (*Carum carvi*), Sena leaves and fruit (*Cassia auriculata*), spiral flag leaves (*Costus igneus*), crape ginger root (*Costus speciosus*), golden bow orchid stem (*Dendrobium crysotoxum*), bunyan aerial parts (*Ficus bengalensis*), Fig leaves (*Ficus carica* and *F. racemosa*), flax seeds (*Linum usitatisumum*), *Momordica cymabalaria* fruit, *Morus indica* leaves, *Murraya koenigii* (curry) leaves, *Polygonatum odoratum* roots, *Rhaphanus sativus* (radish), cocos palm seed (*Syagrus romanzoffiana*), and winter cherry root (*Withania somnifera*) (Khan *et al*., 2012).

Food against hypertension

Hypertension is a risk factor for apoplectic stroke. ACE regulates blood pressure and ACE inhibition will help reduce hypertension, cardiovascular disease and other related ailments. Foods with anti-hypertensive effects are listed below.

Banana is rich in potassium and is reportedly beneficial for hypetension (Puri, 1999).

Celery is a well known vegetable that helps reduce blood pressure. Chinese celery reduced the blood pressure of twenty mild essential hypertension patients (B.P. 150/95-179/110 mmHg.) and produced no side-effects (Jaroonvesama & Attatippaholkun, 1991).

Concord grape juice antioxidant polyphenols reduce inflammation, blood pressure and vascular pathology in individuals with CVD (Krikorian *et al*., 2010).

Extra virgin olive oils, olive leaves, pumpkins, corn, and beans phenolics inhibited a-glucosidase, a-amylase and ACE (Kwon, Apostolidis, Kim, & Shetty, 2007; Loizzo, Lecce, Boselli, Menichini, & Frega, 2011).

Green tea polyphenols and epigallocatechin-3-gallate reduced diastolic blood pressure and improved mood but did not affect insulin sensitivity, insulin secretion or glucose tolerance in a randomized control trial in CVD risk humans (Brown *et al*., 2009).

Partial replacement of dietary carbohydrate with protein helps prevent and treat hypertension (Rebholz *et al*., 2012).

Seaweeds (Wakame, Undaria pinnafitida, Ecklonia stolonifera) peptides and phlorotannin produced vasodilation, cholesterol and blood pressure reduction; powerful ACE inhibition and affect the rennin-angiotensin system in a random, case controlled study on hypertensive humans (Mohamed *et al*., 2012).

Solanum tuberosum extract (but not α-solanine, α-chaconine or chlorogenic acid) decreased the blood pressure in a noradrenalin-induced hypertensive rats (Gomez & Guerrero, 2009).

Conclusion

Plant polyphenols have antioxidant, vasodilatory, anti-inflammatory, anti-fibrosis and antiapoptosis properties that activate prosurvival cellular pathways. They mediate by modulating metabolic intermediates, microRNAs,

sirtuins and reperfusion injury salvage kinases and survivor activating factor enhancement pathways (Lecour & Lamont, 2011). The polyphenols effect blood vessels, endothelial cells and increase the vasoprotective factors including nitric oxide (NO) and endothelium-derived hyperpolarizing factor, to reduce vascular oxidative stress and hypertension. Regular dietary polyphenols consumptions are negatively related to cardiovascular and degenerative disease risk in epidemiological studies (Schini-Kerth, Etienne-Selloum, Chataigneau, & Auger, 2011). Nonpharmacologic therapies against metabolic syndrome include good optimal nutrition, ideal body weight maintenance, exercise programs and scientifically proven dietary supplements.

Polyphenols like flavonoids, resveratrol, quercetin, epigallocathechin-3-gallate and curcumin, help retard elevated fat storage, blood pressure, blood glucose, lipid levels, hemoglobin-A1c and insulin resistance in mammals (Cherniack, 2011). Oxidative stress induces mitochondrial increase and arrest preadipocytes proliferation. Preconditioning preadipocytes with some dietary polyphenols totally or partially protects them against mitochondrial changes, obesity-associated diabetes and cardiovascular diseases (Baret *et al.*, 2013). Polyphenols present in green tea, grape seeds, orange and grapefruit combat adipogenesis at the molecular level and also induce lipolysis.

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