Nutrition Research Reviews (2020), 33, 1–18
doi:10.1017/S0954422419000155

Dietary Approaches to Stop Hypertension (DASH): potential mechanisms of action against risk factors of the metabolic syndrome

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Abstract

The metabolic syndrome is a cluster of disorders dominated by abdominal obesity, hypertriacylglycerolaemia, low HDL-cholesterol, high blood pressure and high fasting glucose. Diet modification is a safe and effective way to treat the metabolic syndrome. Dietary Approaches to Stop Hypertension (DASH) is a dietary pattern rich in fruits, vegetables and low-fat dairy products, and low in meats and sweets. DASH provides good amounts of fibre, K, Ca and Mg, and limited quantities of total fat, saturated fat, cholesterol and Na. Although DASH was initially designed for the prevention or control of hypertension, using a DASH diet has other metabolic benefits. In the present review, the effect of each dietary component of DASH on the risk factors of the metabolic syndrome is discussed. Due to limited fat and high fibre and Ca content, individuals on the DASH diet are less prone to overweight and obesity and possess lower concentrations of total and LDL-cholesterol although changes in TAG and HDL-cholesterol have been less significant and available evidence in this regard is still inconclusive. Moreover, high amounts of fruit and vegetables in DASH provide great quantities of K, Mg and fibre, all of which have been shown to reduce blood pressure. K, Mg, fibre and antioxidants have also been effective in correcting glucose and insulin abnormalities. Evidence is provided from cross-sectional investigations, cohort studies and randomised controlled trials, and, where available, from published meta-analyses. Mechanisms are described according to human studies and, in the case of a lack of evidence, from animal and cell culture investigations.

Key words: **Dietary Approaches to Stop Hypertension: Metabolic syndrome: Blood pressure: Obesity: Diabetes: TAG: Cholesterol**

Introduction

The metabolic syndrome is a global public health problem[1]. Approximately 25 % of the world's population has the metabolic syndrome[2] although the prevalence varies from < 10 to 84 % depending on the region, urban or rural environment, population demographics such as sex, age, race and ethnicity, and the definition of the syndrome used[3]. Reduced HDL-cholesterol was the most prevalent component of the metabolic syndrome, followed by elevated blood pressure, abdominal obesity, high TAG and high fasting glucose[1].

CVD are chief consequences of the metabolic syndrome[4]. Each component of the metabolic syndrome is an independent risk factor for CVD and the combination of these risk factors elevates the incidence and severity of CVD[4]. However, a wide spectrum of other morbidities occurs concurrent with or consequent on the metabolic syndrome. These include, but not limited to, type 2 diabetes, non-alcoholic fatty liver disease[5], polycystic ovary syndrome[6], several types of cancer[7], inflammatory bowel syndrome[8] and chronic kidney disease[9]. Accordingly, the metabolic syndrome is an important risk factor for all-cause mortality[10]. A meta-analysis of prospective cohort studies showed that individuals with the metabolic syndrome have a 46 % increased risk of mortality compared with individuals without the syndrome[10].

Dietary modification and physical activity are suggested as the safest and most effective strategy for the prevention of the incidence or fundamental correction of the components of the metabolic syndrome[11]. The best dietary modifications focus on correction of all items of the diet, what is called a dietary pattern. Instead of correcting individual nutrients or foods, dietary patterns suggest overall diet change which provides a firmer effect on the prevention of diseases. By definition, dietary patterns are the quantities, proportions, variety, or combination of different foods and drinks in diets, and the frequency with which they are habitually consumed[12].

Dietary Approaches to Stop Hypertension (DASH), a dietary pattern which was initially proposed for the treatment of hypertension, is rich in fruits, vegetables and low-fat dairy products, and low in total and saturated fat and cholesterol[13]. DASH has similarities with the Mediterranean diet, which is a dietary pattern with proved benefits against CVD[14,15]. The cardioprotective effect of DASH has been examined less than the Mediterranean diet in epidemiological studies and randomised controlled trials (RCT). Due to emphasis on the consumption of whole grains and low-fat dairy products and caution in consuming red meats and salt, DASH may provide a better diet composition than the Mediterranean dietary pattern against metabolic diseases[16].

Abbreviations: DASH, Dietary Approaches to Stop Hypertension; GLP-1, glucagon-like peptide 1; RCT, randomised controlled trial; RR, relative risk.

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In the present review, we discuss evidence on the effect of each dietary component of the DASH diet on risk factors of the metabolic syndrome. It is worth noting that consuming DASH has other profitable consequences relative to the metabolic syndrome and CVD that are not mentioned in this article. For instance, antioxidant vitamins and phytochemicals present in fruit and vegetables may reduce oxidative stress, improve antioxidant capacity and impede inflammatory responses, all of which are important in instigation or development of the atherosclerosis process[17,18]. Also, fruit and vegetables provide great quantities of folic acid, which is essential for optimising levels of homocysteine[19], a known risk factor associated with CVD and the metabolic syndrome[20].

Definition

The metabolic syndrome is a cluster of abnormalities including abdominal obesity, hypertriacylglycerolaemia, low HDL-cholesterol, high blood pressure and high fasting glucose[21]. During the years between 1998 and 2009, a number of definitions were proposed by different organisations based on various criteria and cut-off points[22]. For instance, in earlier definitions proposed by the WHO, European Group for Study of Insulin Resistance, and American Association of Clinical Endocrinologists, insulin resistance or impaired glucose tolerance was suggested to be the fixed item in the diagnosis of the metabolic syndrome[22]. In 2009, however, when the latest definition currently being used was proposed, the International Diabetes Federation, National Heart, Lung, and Blood Institute, American Heart Association, World Heart Federation, International Atherosclerosis Society and International Association for the Study of Obesity agreed on a definition, in which there is no compulsory component, but waist circumference may be considered as a useful screening tool[23]. The harmonised criteria for clinical diagnosis of the metabolic syndrome are as follows: elevated waist girth according to population- and country-specific definitions, serum. The last four components will also be considered positive in the case of pharmacological treatment[23].

Pathophysiology

Abdominal obesity is supposed to play a pivotal role in the development of abnormalities associated with the metabolic syndrome[24]. Abdominal fat comprises fat depots accumulated in subcutaneous and visceral areas. Compared with subcutaneous fat, visceral adipose tissue is more metabolically active, more insulin resistant and more prone to lipolysis, the latter mainly through stimulation by catecholamines[25]. The critical impact of visceral adipose tissue on metabolism is due to its proximity to the liver which allows direct drainage of visceral tissues, including NEFA and adipokines, into the portal vein.

In slim individuals, small adipocytes function as a sink for absorbed NEFA and TAG. In obese individuals, however, adipocytes become large and disordered. Large adipocytes are insulin-resistant and hyperlipolytic. This type of adipocytes is found more in visceral adipose tissue while subcutaneous fat contains rather insulin-sensitive small adipocytes[25].

Excessive release of NEFA from adipose tissue induces insulin resistance in the peripheries and the liver[26,27]. Hence, there may be a vicious cycle between the level of NEFA and the extent of insulin resistance[28]. Insulin resistance in turn prevents uptake of glucose and fatty acids by cells, thus increasing their half-life in the circulation[25]. Hepatic insulin resistance as well as high levels of NEFA stimulate gluconeogenesis which consequently causes hyperglycaemia, one of the features of the metabolic syndrome[29]. High concentrations of unused glucose and fatty acids in the blood expedite oxidative reactions and consequently instigate release of inflammatory cytokines from adipose tissue[30,31]. Inflammatory cytokines are also involved in insulin resistance[32].

One the other hand, excessive influx of NEFA into the liver results in fat deposition in hepatic cells, leading to fatty liver[33]. Also, hepatic overload of NEFA can result in overproduction of VLDL and subsequently hypertriacylglycerolaemia, another component of the metabolic syndrome[34]. Hypertriacylglycerolaemia activates cholesteryl ester transfer protein, the enzyme involved in the transfer of TAG from VLDL to HDL and LDL in exchange for cholesteryl esters[35]. This results in increased TAG content of HDL and LDL particles. TAG-enriched HDL is cleared from blood more rapidly, leading to decreased concentration of HDL particles in blood. Likewise, TAG-enriched LDL particles are more susceptible to lipolytic activity of lipoprotein lipase and hepatic lipase, thus decreasing the size of LDL particles, which have a higher atherogenic activity.

Compared with other components, the mechanisms of metabolic syndrome-related hypertension are less recognized, but a role for the renin–angiotensin–aldosterone system has been suggested. Although the liver is the major source of angiotensinogen under normal conditions, in obese individuals adipocytes may also produce angiotensinogen[36]. Also, hyperglycaemia stimulates renin release and increases the expression of renin receptor, angiotensin and angiotensin-converting enzyme in animal kidneys. Hyperinsulinaemia may additionally increase blood pressure through stimulation of the sympathetic nervous system[29]. Hypertension may also occur as a result of endothelium malfunction due to destroying NO by reactive oxygen species produced following hyperglycaemia and high plasma NEFA[29]. Adipose tissue-derived cytokines may contribute to high blood pressure, as well[37]. Fig. 1 depicts the sequence and interconnections between events that lead to the development of the metabolic syndrome.

Dietary Approaches to Stop Hypertension (DASH) diet

The DASH diet was proposed for the first time in 1997 for the control of blood pressure[13]. The diet was rich in fruits (5·2 servings/d), vegetables (4·4 servings/d) and low-fat dairy foods (2 servings/d) and with reduced total (25·6 % of energy) and saturated (7 % of energy) fat. The diet also had higher quantities of nuts, seeds and legumes (0·7 servings/d), whole grains (3·8 servings/d) and fish (0·5 servings/d), and lower amounts of red meats (0·5 servings/d), sweets and sugar-sweetened beverages (0·7 servings/d). There was primarily no restriction on Na. Na content of the original DASH diet was approximately 3 g/d

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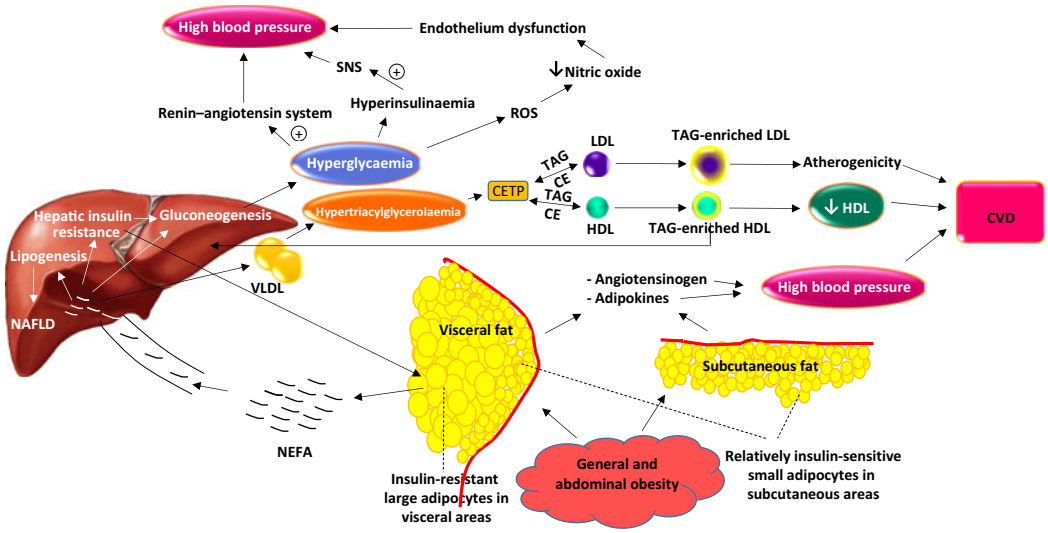

Fig. 1. Overview of pathological events which successively occur and lead to components of the metabolic syndrome. SNS, sympathetic nervous system; CETP, cholesteryl ester transfer protein; CE, cholesteryl esters; NAFLD, non-alcoholic fatty liver disease. For a colour figure, see the online version of the paper.

(equal to 8 g salt/d). However, complementary investigations revealed that dietary Na restriction to less than 6 g/d enhances DASH benefits on blood pressure[38].

Due to possessing specific food items, the DASH diet provides good amounts of fibre, K, Ca, Mg and antioxidants, and limited quantities of total fat, saturated fat, cholesterol and Na (Fig. 2)[39]. Consumption of each of the beneficial dietary components and limiting ingestion of each of the unfavourable elements have proved to be advantageous for the prevention of hypertension[40]. However, the combination of these dietary components in the form of a dietary pattern provides more substantial benefits[41].

Although the DASH diet was initially designed for the prevention or control of hypertension, using a DASH diet has other metabolic rewards. For instance, epidemiological studies have shown benefits of DASH on the metabolic syndrome. In a large-scale cross-sectional study in Korea, the number of individuals with the metabolic syndrome was greatest in the DASH first quartile, which had the lowest consumption of protein, fibre, Ca and K, and the highest consumption of fat and Na[42]. Also, in a 3·6-year cohort study on children and adolescents, OR of developing the metabolic syndrome in the highest, compared with the lowest, quartile of DASH score was 0·36[43]. The incidence of hypertension, high fasting glucose and abdominal obesity decreased along with strengthening adherence to the DASH diet[43]. Also, a 24-year prospective cohort study showed that adherence to the DASH diet was associated with a lower risk of CHD and stroke[44].

RCT have confirmed the findings of observational studies. For instance, 8-week consumption of DASH by overweight and obese individuals decreased body weight, serum TAG, VLDL-cholesterol, total to HDL-cholesterol ratio, insulin levels and insulin resistance, and increased the insulin sensitivity index[45]. Likewise, in type 2 diabetes patients, DASH reduced body weight, waist circumference, fasting blood glucose levels, HbA1c, LDL-cholesterol, systolic and diastolic blood pressure, and inversely increased HDL-cholesterol[46]. Also, in a large-scale 8-week trial, the DASH diet reduced estimated 10-year CHD risk by 18 and 11 %, in comparison with regular and fruit and vegetable-rich diets, respectively[41]. In agreement, a meta-analysis predicted a 13 % reduction in the 10-year Framingham CVD risk score following consumption of DASH[47]. DASH decreased systolic and diastolic blood pressure, total and LDL-cholesterol, but no change in HDL-cholesterol and TAG was observed[47].

Effect of Dietary Approaches to Stop Hypertension (DASH) on components of the metabolic syndrome

Waist circumference

Although reducing energy intake is not among the guidelines of the DASH diet, weight loss strategies are always recommended with DASH to improve its effectiveness[48]. In a clinical trial on hypertensive overweight patients, addition of energy restriction and aerobic exercise to the DASH diet led to lower glucose levels after an oral glucose load, improved insulin sensitivity, and lower total cholesterol and TAG compared with the DASH diet alone[48]. However, a meta-analysis of RCT showed that compared with non-DASH diets with equal energy, individuals on a DASH diet lose more weight, BMI and waist circumference[49]. Like any other nutritional intervention, long treatments may not function as effectively as short interventions. A 1-year home-delivered DASH meal did not affect BMI in a group of mostly overweight or obese older adults with hypertension and/or hyperlipidaemia[50].

Subcutaneous fat responds more rapidly than visceral fat to weight loss programmes. A meta-analysis using different strategies for weight loss (diet/physical activity, hypoenergetic diets, promoting drugs, testosterone and bariatric surgery) showed that the decrease of subcutaneous fat was greater than visceral fat with no difference between different strategies[51]. No intervention preferentially targets visceral fat. Visceral adipose

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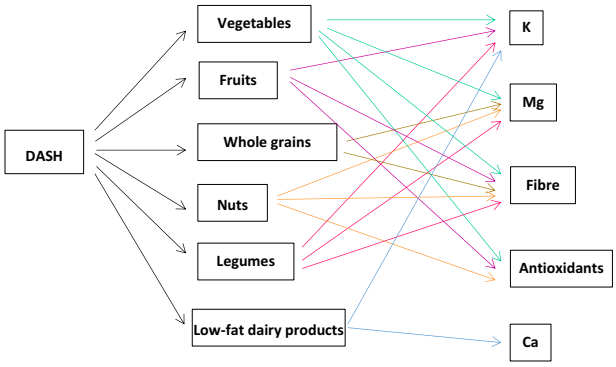

Fig. 2. Major nutrients provided by Dietary Approaches to Stop Hypertension (DASH) components. For a colour figure, see the online version of the paper.

tissue is lost with moderate weight loss, but the effect is attenuated with greater weight losses[52]. The decrease in weight, visceral adipose tissue, and less significantly subcutaneous fat, is associated with improved metabolic conditions, in particular decreased insulin levels[51].

Fasting glucose and insulin

The DASH diet has also been effective on glucose and insulin levels. In an interventional study, the DASH diet plus weight loss and physical activity improved fasting insulin and glucose[53]. Similarly, in pregnant women with gestational diabetes, the DASH diet for 4 weeks resulted in decreased fasting plasma glucose, serum insulin levels and insulin resistance index[18]. However, meta-analyses have not shown the effect of DASH on fasting blood glucose and insulin resistance[54,47], but a decreasing effect on fasting insulin levels was observed[54].

Blood lipids

In the original DASH study, the DASH diet decreased total cholesterol, LDL-cholesterol and, to a lesser extent, HDL-cholesterol but no change in TAG levels was observed[55]. A meta-analysis of RCT similarly demonstrated the beneficial effect of DASH on total and LDL-cholesterol but no change in HDL-cholesterol and TAG[47]. The effect of DASH on total and LDL-cholesterol is probably the result of a decreased intake of saturated fat because DASH contains three times less red meat than a control diet[13]. The Ca content of DASH may also contribute to the cholesterol-lowering effect of DASH considering that the amount of dairy products (low-fat + regular fat) in DASH is five times more than a control diet[13]. The reduction in HDL-cholesterol is an unfavourable consequence of DASH which could be due to decreasing total dietary fat[55].

Blood pressure

Na restriction is one of the components of DASH for reducing blood pressure. In fact, Na restriction was added to the initially designed DASH diet in order to augment its blood pressure-lowering effect. Decreased consumption of saturated fats may also control blood pressure[56] at least partially through enhancement of serum concentrations of angiotensin-converting enzyme[57]. In addition, high amounts of fruit and vegetables in DASH provide great quantities of K, Mg and fibre, all of which have been shown to reduce blood pressure. These dietary components were associated with lower blood pressure in observational and interventional studies[58,59]. However, K, Mg and fibre supplements were less effective in lowering blood pressure of obese hypertensive patients than DASH, indicating that there are other components in the DASH diet which help in blood pressure control[60].

Possible mechanisms of Dietary Approaches to Stop Hypertension (DASH) protection against the metabolic syndrome

Potassium

Blood pressure. Fruits and vegetables of DASH provide ample quantities of K. Epidemiological, observational and interventional studies have proposed a protective effect of K on blood pressure and the prevention of hypertension[61]. Epidemiological studies show that blood pressure is lower in populations with higher fruit and vegetable consumption[62]. In the INTERSALT study[63], a worldwide epidemiological study of large sample size from thirty-two countries, K intake (as measured by 24 h urinary K excretion) was an important determinant of population blood pressure, independent of Na[63]. A meta-analysis of RCT showed that K supplementation lowered blood pressure in hypertensive patients and those who did not use antihypertensive medications[64]. The American Heart Association[65] and American Society of Hypertension[66] suggest 4·7 g dietary K per d. This amount is equal to the amount of K provided in the DASH diet[13].

In addition to K intake, the ratio of dietary Na to K is also important for blood pressure control. In high K consumptions, elevated dietary Na may not lead to increased blood pressure[67]. A large cross-sectional study estimated adjusted OR for hypertension as 1·40 (95 % CI 1·07, 1·83), 0·72 (95 % CI 0·53, 0·97) and 1·30 (95 % CI 1·05, 1·61), respectively, for the highest *v.* the lowest quartiles of intake of Na, K or Na:K ratio[68]. A high dietary Na:K ratio was also positively associated with cardiovascular risk and mortality[69]. Genetics may also affect blood pressure response to dietary Na and K. A family-based study in China showed that a genetic polymorphism in the adiponectin gene may play a role in blood pressure change in response to dietary Na and K although mechanisms of this contribution have not been discovered[70].

K causes vasodilation through hyperpolarisation of vascular smooth muscle cells through stimulation of Na^+/K^+ ATPase pumps, increased activity of the Na–Ca exchanger, and subsequently decreased cytosolic Ca (Fig. 3)[71]. Other possible mechanisms by which K affects blood pressure include increased Na excretion, reduced sensitivity to vasoconstrictive activity of noradrenaline and angiotensin II, modulation of baroreceptor sensitivity, and improved insulin sensitivity[61,72]. However, K also benefits the cardiovascular system and prevents mortality independent of its effect on blood pressure through mechanisms such as inhibition of vascular smooth muscle cell proliferation, thrombosis and macrophage adhesion to the vascular wall[73].

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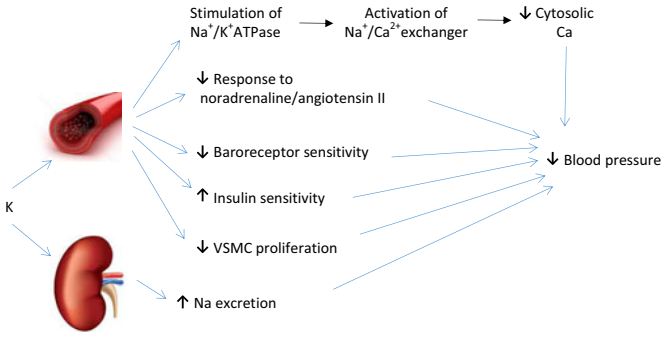

Fig. 3. Mechanisms by which potassium prevents hypertension. VSMC, vascular smooth muscle cells. For a colour figure, see the online version of the paper.

Glucose tolerance. K has beneficial effects other than blood pressure reduction. A large cohort study with 9 years of in-person follow-up and 17 years of telephone follow-up indicated that serum K level is an independent predictor of type 2 diabetes mellitus incidence[74]. Compared with individuals with normal to high serum K levels (5·0–5·5 mEq/l), those with serum K levels < 4·0 mEq/l, 4·0 to < 4·5 mEq/l, and 4·5 to < 5·0 mEq/l had an adjusted hazard ratio of incident diabetes mellitus of 1·64, 1·64 and 1·39, respectively. This type of association was also observed for dietary and urinary K in African Americans but not whites[75]. A meta-analysis of prospective cohort studies confirmed the inverse association between serum K level and diabetes risk but no association between dietary or urinary K and the risk of diabetes was observed[76]. K may be involved in glucose-dependent insulin secretion from pancreatic β-cells. In the resting state, β-cell membranes are polarised by K efflux from ATP-sensitive K channels. Upon a glucose load, uptake of glucose by β-cells leads to production of ATP and inactivation of ATP-sensitive K channels. Subsequently, depolarisation of β-cell membranes leads to opening voltage-gated Ca^{2+} channels, Ca influx, a rise in intracellular Ca concentrations and insulin secretion[77]. Besides the proposed insulin secretagogic effect of K, a protective effect of K against salt-induced insulin resistance has been reported through suppression of IL-17A, an inflammatory cytokine involved in the metabolic syndrome, especially in salt loading states[78]. In addition to the direct effect of K on insulin secretion, an inverse association between serum K and fasting insulin levels was observed[74]. This inverse association is proposed to be due to stimulation of K entry to cells by insulin, leading to reduced serum K levels[79].

Magnesium

Blood pressure. Due to containing green leafy vegetables, nuts, legumes, seeds and whole grains, the DASH diet has a high Mg content. A large cross-sectional study showed that a higher DASH score is associated with higher urine concentrations of K and Mg[80]. Many health benefits have been attributed to Mg, but Mg is famous for its beneficial effects on the cardiovascular system, particularly hypertension. Atherosclerosis, hypertension, arrhythmias, dyslipidaemia, impaired glucose tolerance, insulin resistance and increased risk of the metabolic syndrome are reported in Mg deficiency[81]. A meta-analysis of prospective cohort studies supported the inverse dose–response relationship between dietary Mg intake and the risk of hypertension[82]. Meta-analyses of RCT have also reported benefits of Mg supplementation on blood pressure[83,84].

Various mechanisms have been suggested for the antihypertensive effect of Mg. Mg inhibits the renin–angiotensin–aldosterone system, by counteracting angiotensin II and inhibiting aldosterone production. This inhibition may be exerted through activation of Na^+/K^+ ATPase and decreasing intracellular Na and Ca levels[85]. Mg also acts as a Ca antagonist by raising the excitation threshold of voltage-gated Ca^{2+} channels, thus decreasing vascular smooth muscle cell contractility[86,87]. Moreover, the production of vasoactive agents, such as endothelin-1, in vascular cell membranes is decreased in the presence of Mg. Furthermore, along with ATP, Mg mitigates catecholamine release from the adrenal gland in response to Ca. Mg may also reduce vascular stiffness[88], probably through regulating the synthesis of structural molecules in the vascular extracellular matrix[86]. A part of the vasodilatory potential of Mg may be exerted through inhibiting systemic inflammation[89]. Interestingly, in salt-induced hypertension a decrease in intracellular Mg along with accumulation of intracellular Ca is observed[90].

Glucose tolerance. Prospective cohort studies and meta-analyses have also shown Mg to be advantageous in other metabolic disorders. For instance, in a prospective cohort study with 15 years follow-up, individuals in the highest quartile of Mg had lower risk (hazard ratio 0·69) for the development of the metabolic syndrome compared with those in the lowest quartile[91]. Also, a longitudinal study with 15·6 years of follow-up on a non-diabetic Japanese population showed decreased incidence of type 2 diabetes with a hazard ratio of 0·63 in the highest quartile of Mg intake compared with the lowest[92]. Moreover, a meta-analysis of cohort studies indicated a significant inverse association between Mg intake and diabetes risk[93]. In another meta-analysis of prospective cohort studies an inverse correlation between plasma Mg levels and incidence of hypertension, CHD and type 2 diabetes was observed[94].

Mg is also involved in insulin function. Mg is necessary for all reactions in which high-energy phosphate bonds are transferred. It functions as a cofactor for phosphorylation of tyrosine kinase at the insulin receptor[86]. Therefore, decreased Mg may impair insulin signalling. Mg may also improve insulin secretion as reported by cross-sectional[95] and interventional[96] studies. Individuals with the metabolic syndrome generally have inadequate dietary Mg intake, and thus Mg supplementation may help in correction of their metabolic disturbances[97,98]. Meta-analyses of controlled trials have supported the effectiveness of Mg supplementation in reducing fasting glucose[99,100] and raising HDL-cholesterol levels in patients with type 2 diabetes[99]. Another meta-analysis revealed that Mg supplementation for more than 4 months improved insulin resistance and fasting glucose in both diabetic and non-diabetic individuals[101].

It is worth noting that it is not only Mg which affects glucose tolerance but hyperglycaemia, even in transient form as occurs in non-diabetic subjects following consumption of meals, also decreases intracellular Mg and increases

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intracellular Ca, indicating that Mg depletion can be both a cause and consequence of hyperglycaemia[90]. In addition, insulin resistance may impair Mg reabsorption in the kidney resulting in urinary Mg excretion[102].

Calcium and dairy products

Weight. One of the important ingredients of DASH is Ca. In the DASH diet, Ca is mainly supplied by dairy products and to a less extent by green leafy vegetables, soya, nuts, particularly almonds, and fish when the bones are eaten. Ca and dairy products protect against the metabolic syndrome through a variety of mechanisms. Reduced adiposity is one of the mechanisms of Ca against the metabolic syndrome. A meta-analysis of cross-sectional studies showed the inverse association between dairy product consumption and decreased risk of obesity[103]. However, meta-analyses of randomised clinical trials did not show a beneficial effect of dairy products on the weight of overweight/obese adults but advantages were reported when dairy products were consumed in combination with energy-restricted diets[104–106]. The evidence suggests that individuals with a low Ca intake may benefit from dairy products for decreasing waist circumference and sagittal abdominal diameter[107]. The reductions in weight and waist circumference may eventually lead to lower blood pressure and control of hypertension[108].

There are mechanisms by which Ca may engage in weight control. Dietary Ca may decrease fat absorption through formation of insoluble fatty acid soaps in the intestine[109]. On the other hand, stimulation of parathyroid hormone in response to low serum Ca concentrations results in the elevation of intracellular Ca concentration and the triggering of adiposity through stimulation of enzymes involved in lipogenesis and inhibition of lipolysis[110]. Sufficient ingestion of dietary Ca can hinder this process through optimising serum Ca levels and inhibiting stimulation of parathormone, leading to reduced adipogenesis and body fat mobilisation and oxidation.

Compared with supplemental Ca, dairy Ca has a greater effect on weight, suggesting that dairy components other than Ca may be effective[111,112]. For instance, dairy proteins may help in the suppression of appetite. Whey is supposed to have a stronger effect than casein on appetite control but each of whey and casein executes distinct mechanisms. While the casein fraction postpones gastric emptying following coagulation in the stomach, whey induces satiety due to rapid digestion, absorption and elevation of amino acids in the blood[113]. Bioactive compounds, low-glycaemic index carbohydrates and Ca content of dairy foods may also be implicated in appetite control[114]. It is worthwhile to note that the beneficial effect of dairy products on weight occurs when low-fat dairy products are consumed, but whole-fat dairy products may promote weight gain[115].

Glucose tolerance. Decreased weight has positive metabolic consequences such as improved insulin sensitivity. A meta-analysis of observational studies indicates a relatively consistent association between low Ca or dairy product intake and prevalent type 2 diabetes or the metabolic syndrome[116]. Similarly, a meta-analysis of cohort studies suggested an inverse association between the intake of dairy products, low-fat dairy products and cheese and the risk of type 2 diabetes[117]. A prospective cohort study showed an association of higher consumption of dairy products and Ca with lower 9-year incidence of the metabolic syndrome and impaired fasting glucose or type 2 diabetes[118]. Also, a prospective cohort study with 20 years of follow-up revealed the inverse association of milk and dairy product consumption and prevalence of the metabolic syndrome[119]. A possible mechanism for dairy product protection against type 2 diabetes is the low-glycaemic index of milk and other dairy foods which suppresses postprandial hyperglycaemia[120]. The beneficial effect of dairy products on weight may also contribute to the prevention of type 2 diabetes by dairy foods. Moreover, milk proteins, in particular whey, have insulinotropic activity when consumed with meals[121]. Ca is also essential for insulin secretion by pancreatic β-cells (Fig. 4)[116].

Blood pressure. Blood pressure is also affected by Ca and dairy product intake. Meta-analyses of prospective cohort studies support the inverse association between low-fat dairy products and risk of elevated blood pressure[122,123]. The pooled relative risk (RR) per 200 g/d was 0·97 (95 % CI 0·95, 0·99) for total dairy products, 0·96 (95 % CI 0·93, 0·99) for low-fat dairy products and 0·96 (95 % CI 0·94, 0·98) for milk[122]. The protective effect may be greater in an at-risk population[124]. On the other hand, high-fat dairy products may have an adverse effect on blood pressure due to the increasing effect on weight[115]. Both casein and whey constituents of milk protein have been effective in reducing blood pressure and arterial stiffness[125–127]. The effect is supposed to be exerted mainly by bioactive tripeptides which are produced in the gut following digestion of milk proteins. A part of the beneficial effect of milk on blood pressure may result from its K. Dairy products have a relatively high K content which contributes largely to daily K intake[120]. Furthermore, through prevention of transient postprandial hyperglycaemia, dairy products as a low-glycaemic index food prevent hyperglycaemia-induced oxidative stress, thus improving NO bioavailability and vascular function[120].

Sodium

Blood pressure. Although reducing Na intake was not initially among the principles of the DASH diet[13], Na restriction is recommended along with DASH in order to augment its blood pressure-lowering effect[38]. However, reduced blood pressure following consumption of DASH does not occur due to Na restriction only, but other DASH components are also effective in the regulation of blood pressure. In fact, in the absence of salt restriction, a reduction in blood pressure is still observed following DASH consumption[13]. Reducing Na intake from a high-Na ordinary diet (about 3·5 g/d Na) to a low-Na DASH diet (1·8 g/d Na) resulted in mean systolic blood pressure decreases of 7·1 and 11·5 mmHg in normotensive and hypertensive individuals, respectively[38]. The American Heart Association and American College of Cardiology recommend no more than 2·4 g Na per d (equal to 6 g salt per d)[128]. A further decrease to 1·5 g/d may be required for high-risk patients, for instance, for those at risk of stroke[129]. On the other hand, very intensive Na restriction is also not recommended because a low Na intake is associated with

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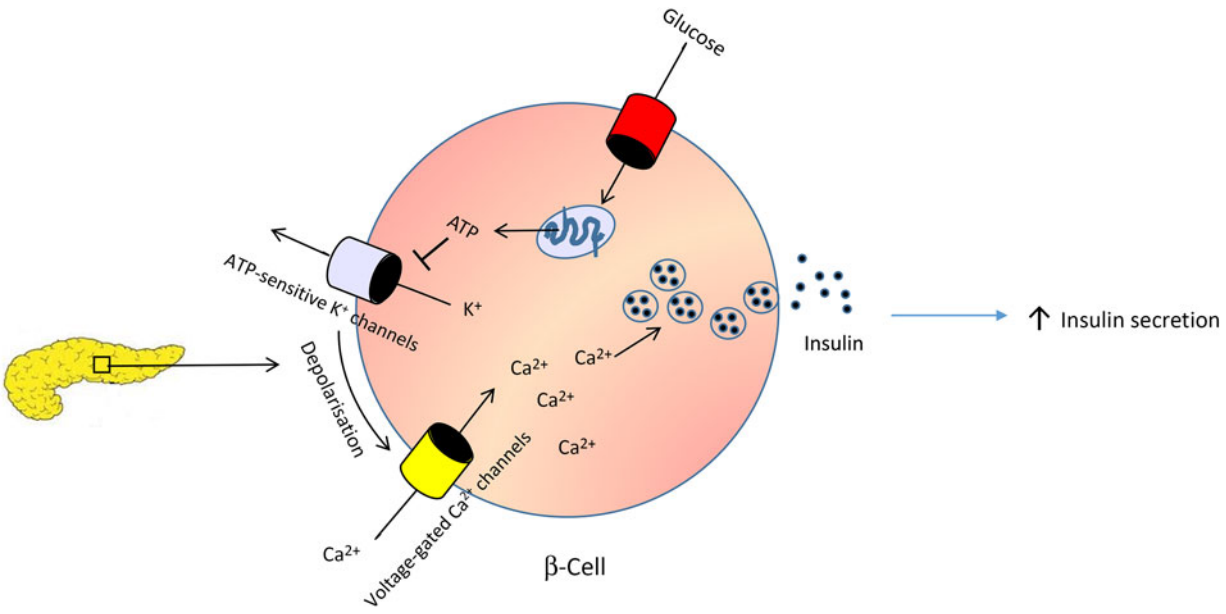

Fig. 4. The role of calcium in secretion of insulin by pancreatic β-cells. For a colour figure, see the online version of the paper.

increased cardiovascular mortality, indicating that a U-shaped relationship may exist between Na intake and health outcomes[130].

Mechanisms by which Na increases blood pressure include expansion of extracellular fluid volume and increased cardiac output[131], impaired renin–angiotensin–aldosterone system[132], activation of the sympathetic nervous system[133], augmented vascular smooth muscle cell proliferation[134] and reduced NO bioavailability, which decreases endothelium-dependent vasodilation[135]. Kidneys and the vascular system play pivotal roles in modifying the haemodynamic changes caused by Na, but their function is impaired in salt sensitivity[131].

Glucose tolerance. There are other benefits with Na restriction which may help against the metabolic syndrome. For instance, low dietary Na reduces insulin secretion without effecting insulin sensitivity, probably through interruption of the renin–angiotensin–aldosterone system[136]. High aldosterone concentrations may impair β-cell function[137]. Also, a direct relationship between aldosterone, insulin resistance and hyperinsulinaemia[138] has been suggested.

Fibre

Weight. Prospective studies on cereal fibre and whole grains reported small but significant reductions in weight gain[139]. A meta-analysis of RCT also showed reductions in weight, BMI and body fat in overweight and obese adults consuming soluble fibre supplements[140]. Due to resistance to gastrointestinal enzymes, dietary fibre is devoid of energy, and fibre-containing foods such as whole grains, vegetables and fruit have low energy density. In addition, because of their bulking properties, fibre-containing foods stimulate satiety signals without adding much into daily energy intake[141]. As a result of their viscosity and formation of gel in the stomach, soluble fibres delay gastric emptying, thus slowing down food transition through the small intestine which results in decelerating glucose absorption[142]. Slow glucose absorption suppresses the insulin response and prevents episodes of hypoglycaemia, thus minimising hunger sensations. Moreover, SCFA produced as a result of colonic fermentation of soluble fibres have shown potential in regulating appetite through suppressing hunger hormones and stimulating satiety hormones although large doses of fibre are required to exhibit such effects[143]. SCFA may also increase energy expenditure through increased thermogenesis and fat oxidation although this effect has not been investigated in human studies[144].

Glucose tolerance. A meta-analysis of prospective cohort studies indicated that a two servings/d increase in whole grain consumption was associated with a 21 % decrease in the risk of type 2 diabetes[145]. Another meta-analysis of cohort studies showed a reduced risk of diabetes with higher intake of cereal fibre (RR for extreme categories 0·67), but no significant association for fruit was observed[93]. Later meta-analyses showed the inverse association between intake of total dietary fibre and cereal fibre as well as insoluble fibre and fruit and risk of type 2 diabetes[146]. In a large case–control study, lower risk of diabetes was associated with the intake of cereal and vegetable fibre, but not fruit fibre[147]. Meta-analyses of RCT have also shown benefits of low-glycaemic index foods in the prevention of diabetes[148] or improvement of glycaemic control[140,149–153].

The anti-diabetic effect of fibre may be partly due to its beneficial effect on weight. In a meta-analysis of cohort studies, the inverse association of fibre intake with diabetes risk diminished after adjustment for BMI[147]. Fibre also has a direct impact on gastric emptying which increases intestinal transit time. SCFA that are produced in the colon as a result of colonic bacteria fermentation can also delay gastric emptying and decelerate glucose absorption through stimulating secretion of anorectic hormones, peptide YY and glucagon-like peptide-1 (GLP-1)[154,155]. There are also additional mechanisms by which

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SCFA may contribute to the prevention of diabetes. These include anti-inflammatory effect of SCFA, balancing composition and activity of gut microbiota, and reducing hepatic glucose production by suppressing gene expression of the gluconeogenic enzymes glucose 6-phosphatase and phosphoenolpyruvate carboxykinase[156–158]. The above-mentioned mechanisms are suggested for soluble fibre. Nevertheless, benefits of fibre on diabetes are related to both types of soluble and insoluble fibre. In fact, data for the anti-diabetic potential of insoluble fibre are stronger and more consistent than soluble fibre although the mechanisms of the protection are less recognised[159]. Insoluble fibre may exert its effect through accelerating secretion of glucose-dependent insulinotropic polypeptide (GIP) and insulin response following meals, thus reducing the postprandial glucose rise[160]. In addition, the consumption of high-cereal fibre diets may prevent high-protein diet-induced insulin resistance by interfering with protein absorption[161]. High-protein diets are generally applied in weight loss programmes and impair insulin signalling through phosphorylation of serine kinase-6-1[161].

Lipids. In an umbrella review, thirty-one meta-analyses reported reductions in the RR of CVD mortality (RR 0·77–0·83), the incidence of CVD (RR 0·72–0·91), CHD (RR 0·76–0·93) and stroke (RR 0·83–0·93) in the highest *v.* the lowest dietary fibre intake[162]. The evidence also suggests effectiveness of fibre on risk factors of CVD. Meta-analyses on supplementation studies using viscous soluble fibres, β-glucan, psyllium or konjac glucomannan also reported statistically significant reductions in both total and LDL-cholesterol concentrations[162–164]. Similarly, a systematic review revealed that a breakfast based on oats, barley or psyllium may lower cholesterol concentrations[165]. In another meta-analysis, TAG levels did not change but HDL-cholesterol concentrations were increased slightly by fibre[166]. The mechanisms involved include: (1) interfering with enterohepatic circulation through prevention re-absorption of bile acids in the ileum, thus enhancing utilisation of blood cholesterol for *de novo* synthesis of bile acids; (2) slowing glucose absorption and subsequently suppressing insulin response, thereby reducing stimulation of hepatic cholesterol synthesis by insulin; (3) increasing hepatic LDL receptors; and (4) diminution of intestinal cholesterol absorption and its hepatic synthesis by SCFA[141,167,168]. Compared with soluble fibres, insoluble fibres exhibit a smaller reduction on blood cholesterol, but binding bile acids has been mentioned as their mechanism of action against blood cholesterol[169].

Blood pressure. A meta-analysis of RCT showed a lowering effect of viscous soluble fibre on systolic and diastolic blood pressure[170]. Psyllium had a stronger effect than β-glucan, guar gum, konjac and pectin. Another meta-analysis indicated the effectiveness of dietary fibre in trials conducted on hypertensive patients and in trials with an intervention duration of ≥ 8 weeks but reduction in normotensive subjects was less conclusive[171]. However, compared with other components of the metabolic syndrome, the mechanisms of the effect of fibre on blood pressure are less recognised. The beneficial effect of fibre on blood pressure may have resulted from of its impact on weight. Also, some of the antihypertensive effect of fibre may be exerted through amelioration of insulin resistance and reducing insulin concentrations[59,172]. Insulin has an antinatriuretic potential by which it stimulates renal Na reabsorption[172]. Therefore, reduction of insulin concentrations could be beneficial for blood pressure. Furthermore, fermentation of soluble fibre in the distal intestine and colon produces acidic metabolites which may improve the absorption of minerals that are advantageous for blood pressure[173]. Since hypercholesterolaemia and hypertension are closely related, fibre may hinder hypertension by preventing hypercholesterolaemia[174].

Antioxidants

Oxidative stress is a common feature of the metabolic syndrome[175]. Reactive oxygen species are produced during normal metabolism by mitochondria and extra-mitochondrial systems. However, the production of reactive oxygen species is increased in pathological conditions including obesity and the metabolic syndrome[176]. In oxidative stress conditions, antioxidants are depleted in cellular and extracellular compartments. A case–control study showed that plasma levels of vitamins A, C and E are significantly lower in patients with the metabolic syndrome than in healthy subjects[177]. Therefore, consumption of antioxidants such as polyphenols, vitamin C, vitamin E and carotenoids may correct metabolic syndrome-associated oxidative stress[178]. Fruit, vegetables and nuts of DASH provide good quantities of antioxidant vitamins and polyphenols.

Weight. A systematic review of observational studies showed that obese individuals in any age group possess lower concentrations of antioxidants[179]. Plasma levels of carotenoids, vitamins E and C, as well as Zn, Mg and Se were inversely correlated with obesity and body fat mass[179]. In addition to antioxidant vitamins and minerals, polyphenols present in fruits and vegetables can prevent obesity. For instance, meta-analyses of RCT have shown the anti-obesity effect of flavanols[180] and isoflavones[181]. The anti-obesity effect of polyphenols may be exerted through increasing β-oxidation of fatty acids, induction of satiety, stimulating thermogenesis in brown adipose tissue, increasing lipolysis, control of adipocyte differentiation, down-regulation of fatty acid synthase gene expression, and functioning as a prebiotic for gut microbiota (Fig. 5)[182–186]. Similarly, carotenoids may deter adiposity by enhancing fat oxidation and increasing energy waste in brown and white adipocytes[187]. Likewise, vitamin C may inhibit adipocyte differentiation, increase lipolysis and prevent glucose uptake by adipocytes[188].

Glucose tolerance. The association between antioxidants and risk of diabetes has also been reported. A large retrospective cohort study with 5 years of follow-up on twenty-five communities across Japan showed an inverse association between consumption of green tea, coffee and total caffeine and the risk for type 2 diabetes[189]. Also, in a prospective cohort study with 10 years of follow-up in Japan, the hazard ratio for development of type 2 diabetes in the highest *v.* the lowest tertiles of serum α-carotene, β-cryptoxanthin and total carotenoids was 0·35, 0·43 and 0·41, respectively[190]. Various mechanisms have been

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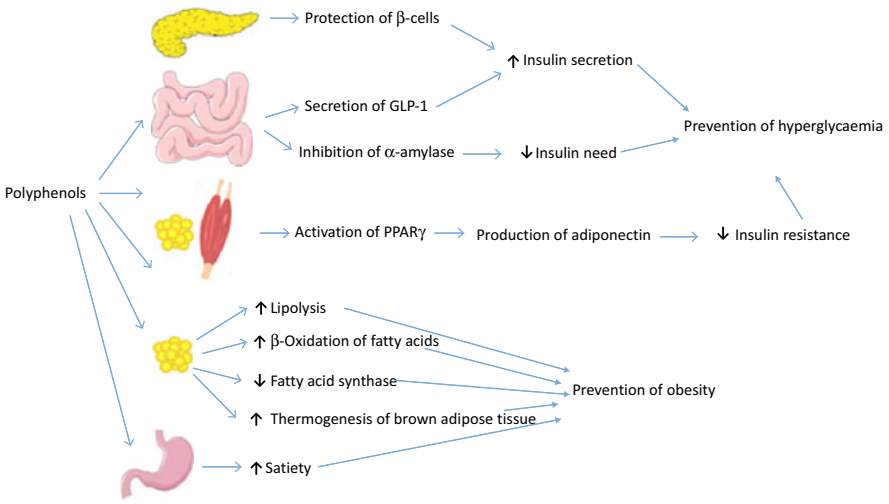

Fig. 5. Mechanisms of polyphenols against hyperglycaemia and obesity. GLP-1, glucagon-like peptide 1. For a colour figure, see the online version of the paper.

suggested for the effect of polyphenols on glucose tolerance and insulin sensitivity (Fig. 5). Polyphenols may increase insulin secretion through protection of β-cell integrity[191]. They may also stimulate secretion of GLP-1, a hormone involved in quick postprandial insulin response, increase GLP-1 half-life, stimulate β-cells to secrete insulin, and increase insulin sensitivity in peripheral tissues[192]. In peripheral tissues, polyphenols may activate PPARγ, thus inducing adiponectin production and improving insulin resistance[193]. In addition, cell culture studies indicate that green tea polyphenols inhibit gluconeogenesis in hepatocytes and stimulate glucose uptake in rat skeletal muscle cells by using a phosphatidylinositol 3-kinase-dependent mechanism that mimics metabolic actions of insulin[194]. Polyphenols have also potential to decrease starch digestion by inhibiting α-amylase activity[195].

No meta-analysis has ever examined the effect of vitamin C or vitamin E on the risk of type 2 diabetes but meta-analyses on the effect of these antioxidants on patients with type 2 diabetes have produced conflicting results. Two meta-analyses showed no beneficial effect of vitamin E supplementation on glycaemic control of patients with type 2 diabetes but results were more promising for individuals with poor glycaemic control or low serum vitamin E levels[196,197]. Another meta-analysis indicated that supplementation with vitamin C, vitamin E or their combination did not improve insulin resistance of type 2 diabetes patients[198], but a limited number of RCT showed that a single dose of vitamin C may be beneficial in reducing fasting blood glucose of these patients[199]. Another meta-analysis revealed that vitamin C did not modify glucose, HbA1c and insulin concentrations in a population containing both diabetic and non-diabetic participants but subgroup analyses indicated that vitamin C significantly reduced glucose concentrations in patients with type 2 diabetes and in interventions longer than 30 d; also vitamin C administration had a greater effect on fasting compared with postprandial insulin concentration[200].

Mechanisms of the possible effect of vitamin C and vitamin E in the management of diabetes are largely unknown but the beneficial effect of these antioxidants in establishing glycaemic control may be exerted through a direct effect on pancreatic β-cells by protecting them from oxidative stress-induced cell damage[196]. Hyperglycaemia-associated oxidative stress is also suggested to be involved in the development of insulin resistance[201,202]. Thus, a part of antioxidants' protection against type 2 diabetes may be delivered by suppression of oxidative stress. Carotenoids may reduce insulin resistance by induction of PPARγ as well as inhibiting c-Jun NH_2-terminal kinase (JNK) and inhibitor κB kinase β (IKKβ) which induce insulin resistance through phosphorylation of insulin receptor substrate-1 (IRS-1)[203].

Lipids. There is limited evidence for the effect of antioxidants on blood lipids. A meta-analysis of RCT showed that vitamin C supplements may decrease TAG and LDL-cholesterol but the increase in HDL-cholesterol was not significant[204]. Similarly, meta-analyses of RCT showed that consumption of green tea catechins was associated with a significant reduction in total and LDL-cholesterol levels without causing significant changes in HDL-cholesterol or TAG levels[205,206]. Another meta-analysis revealed beneficial effects of dark chocolate and cocoa products on total and LDL-cholesterol with no major effect on HDL-cholesterol and TAG[207]. The cholesterol-lowering effect of polyphenols may be due to interfering with cholesterol absorption[208], inhibiting cholesterol synthesis[209], and inducing expression and activity of LDL receptors[210]. Moreover, by preventing LDL oxidation, antioxidants such as vitamin C improve recognition of LDL particles by hepatic LDL receptors and thus expedite their removal from blood[204]. In addition, by preventing oxidation of HDL, antioxidants may improve reverse cholesterol transport which is a process that exchanges cholesterol from peripheral tissues and circulating lipoproteins with TAG of HDL, thereby facilitating elimination of cholesterol from blood[211].

Blood pressure. Meta-analyses of RCT have shown benefits of polyphenols[212–215] and vitamin C on blood pressure[216]. Dietary polyphenols have shown a vasoprotective effect by augmentation of endothelial synthesis of NO and endothelium-derived hyperpolarising factor, inhibition of angiotensin-converting enzyme, suppression of endothelin-1 synthesis and increased bioavailability

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of NO by scavenging free radicals[217,218]. There is also evidence that polyphenols promote vasodilation through an endothelium-independent mechanism by a direct effect on vascular smooth muscle cells via blocking Ca channels[219].

Low total fat

Weight. Although less important than total energy content, the macronutrient composition of the diet is also believed to affect weight. Low-fat diets may have potential in weight control attempts[220]; however, meta-analyses of controlled trials suggest that the effect of low-fat diets on weight depends on the diet of the control group[221]. As an example, a meta-analysis of RCT indicated that low-fat diets lead to weight reduction only when compared with usual diet, but not in comparison with other dietary compositions such as low-carbohydrate or high-fat interventions[221].

Glucose tolerance. Large-scale cohort studies on healthy populations have shown a positive association between total and saturated fat intake and the development of type 2 diabetes; however, the association disappeared after adjustment for BMI[222]. Nonetheless, individuals in the prediabetic state or those who are genetically vulnerable to metabolic disorders may develop type 2 diabetes following the consumption of high-fat diets[223]. In fact, the susceptibility of individuals to insulin resistance is affected by genes, and dietary factors can alter this susceptibility[224]. High-fat diets increase concentration of TAG constituents such as diacylglycerols and ceramides in muscle and adipose tissue. Such compounds phosphorylate serine residues of insulin receptor substrate through activation of serine kinases, leading to an impaired insulin function, decreased translocation of insulin-dependent GLUT-4, and eventually decreased glucose uptake[225]. On the other hand, as high-fat diets have low carbohydrate content, they may benefit patients with type 2 diabetes. In this regard, a meta-analysis of RCT suggested that high-fat diets reduce fasting blood glucose in type 2 diabetes patients, but not prediabetic individuals[226].

Blood pressure. The quantity of dietary fat has less impact on blood pressure than fatty acid composition of the diet[227]. However, an increased concentration of NEFA in blood as occurs following consumption of high-fat meals can impair endothelial function. This postprandial acute effect may potentiate stronger chronic impacts on endothelium if high-fat meals are consumed persistently[227]. An increased serum concentration of angiotensin-converting enzyme is proposed as a mechanism of a high-fat diet (45 %) on blood pressure[57].

Low saturated fats

Weight. The ratio of saturated:unsaturated fats also affects weight. Saturated fats are probably more obesogenic than unsaturated fats[228]. Compared with saturated fats, unsaturated fatty acids induce greater energy expenditure, diet-induced thermogenesis and fat oxidation[228]. Gene studies revealed that polyunsaturated fats up-regulate expression of PPARα, a transcription factor involved in lipid oxidation, and down-regulate expression of PPARγ, a transcription factor involved in lipogenesis[229]. Saturated fats have the opposite effect on these genes[230].

Glucose tolerance. The quality of consumed fats is more important than their quantity for the incidence of diabetes and insulin sensitivity. Saturated fats are associated with an increased risk of type 2 diabetes while unsaturated fats are associated with insulin sensitivity[225]. In a multinational study, newly diagnosed diabetes was observed more frequently in patients with higher consumption of total and animal fat and lower plant to animal fat ratio[231]. It is worthwhile to note that high quantities of saturated fat (for instance > 15 %) probably increase the risk of insulin resistance and type 2 diabetes, but moderate quantities may not have such an effect[232].

In diabetes patients, serum cholesteryl esters are mainly composed of SFA. In contrast, a number of studies reported the association of high concentration of unsaturated fatty acids in serum and muscle of healthy individuals and insulin sensitivity[233]. Fatty acids which are received through the diet incorporate into the cell membrane and affect its activity. The ratio of unsaturated fatty acids to SFA present in membrane phospholipids affects membrane fluidity and has a direct relevance to insulin function and glucose transport efficiency[234,235]. Apart from the direct effect on insulin sensitivity of peripheral tissues, PUFA also improve hepatic insulin sensitivity through the suppression of lipogenesis and stimulation of fat oxidation[235,229].

Lipids. Despite the general notion for the atherogenicity of saturated fats, cohort studies do not consistently support the link between saturated fats and CVD. A meta-analysis of prospective studies with follow-up periods of 5 to 23 years showed no significant relationship between dietary saturated fat and risk of CHD or CVD[236]. Another meta-analysis of prospective cohort studies supported a causal relationship between CHD and intake of high-glycaemic index foods and *trans*-fatty acids and an inverse association between CHD and consumption of vegetables, nuts and MUFA, and healthy dietary patterns, but no association was observed between saturated fats and CHD[237]. The lack of the association of saturated fats with CHD in cohort studies is probably due to substitution of dietary carbohydrates for saturated fats which reduces concentrations of total, LDL- and HDL-cholesterol in a way that total to HDL-cholesterol ratio, an indicator of CVD risk, does not change[238]. In contrast, replacement of saturated fats with unsaturated fats lowers total and LDL-cholesterol, resulting in a decreased total:HDL-cholesterol ratio[238,239]. Such substitution has reduced the incidence of cardiovascular events when embedded in an eating pattern for a period of more than 2 years[240]. In this regard, a prospective cohort study with 14 years of follow-up indicated that replacement of 5 % energy from saturated fats with unsaturated fats would reduce the risk of CHD by 42 %[241]. Also, a meta-analysis of RCT suggested that each 5 % energy increase from polyunsaturated fats in place of saturated fats led to a 10 % reduction in CHD[242]. Nevertheless, evidence on the effect of substitution of polyunsaturated fats for saturated fats on risk factors of CVD is still lacking. For instance, insufficient available data did not allow a meta-analysis of RCT to find significant reductions in total cholesterol, LDL-cholesterol and TAG following replacement of unsaturated fats for saturated fats[243].

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Blood pressure. Studies on the relationship between blood pressure and dietary fats are rather scarce and no meta-analysis has been performed based on the current evidence. The available evidence suggests that saturated fats have unfavourable and unsaturated fats have beneficial impact on blood pressure and vascular function[227]. A cross-sectional study revealed that saturated fat intake was independently and strongly associated with hypertension[244]. Also, in a RCT, substitution of 10 % saturated fats with either mono- or polyunsaturated fats decreased blood pressure and E-selectin without affecting flow-mediated dilation and other measures of vascular function[56]. *n*-3 Fatty acids are the most advantageous fatty acids for blood pressure control. These fatty acids inhibit angiotensin-converting enzyme activity and increase NO bioavailability through augmentation of endothelial NO synthase activity, suppression of pro-inflammatory cytokines and inhibition of cyclo-oxygenase activity[245].

Clinical relevance

Based on original reports and meta-analyses, the magnitude of alterations by DASH in risk factors of CVD and the metabolic syndrome is rather small. A meta-analysis by Siervo *et al.*[47] indicates that DASH causes small reductions in systolic (–5·2 mmHg) and diastolic (–2·6 mmHg) blood pressure, total cholesterol (–7·73 mg/dl; –0·20 mmol/l) and LDL-cholesterol (–3·87 mg/dl; –0·10 mmol/l)[47]. Evidence is also promising for fasting insulin levels (–0·16 mU/l) and fasting blood glucose (–3·42 mg/dl; –0·19 mmol/l), although the effect on glucose has been marginally significant (P=0·07)[47,54]. The magnitude of the change in any single risk factor is small and far to be clinically important *per se*. But the cumulative alterations in these risk factors can produce noticeable effects. For instance, Siervo *et al.*[47] predicted that the above-mentioned changes lead to approximately 13 % decrease in the 10-year Framingham risk score for CVD[47]. Also, a meta-analysis of cohort studies showed that a DASH-like diet reduces the risk of CVD, CHD, stroke and heart failure by 20, 21, 19 and 29 %, respectively[246]. On the other hand, the risk reduction in a single individual may be negligible but small risk reductions in individuals in a population become clinically important[247]. Interventions that promote healthy dietary patterns like DASH or the Mediterranean diet can effectively improve health status and reduce the risk of metabolic diseases[248].

Conclusions

As a healthy diet, DASH contains food items and nutrient composition that help in the prevention of metabolic diseases and control of their risk factors. Epidemiological, observational and interventional studies as well as meta-analyses performed have shown benefits of DASH dietary constituents including K, Mg, Ca, fibre and antioxidants and limited content of total fat, saturated fats and Na on components of the metabolic syndrome. Although implementation of each of the DASH dietary guidelines into the diet can help in the prevention of the metabolic syndrome, combination of these instructions augments the benefits. Nonetheless, randomised clinical trials have not examined the effect of DASH on the metabolic syndrome, in some parts the available data for the effect of DASH dietary items on components of the metabolic syndrome are insufficient to allow performing valuable meta-analyses, and mechanisms of the effects are largely unknown. These areas of research call for further investigations in the future.

Acknowledgements

There are no acknowledgements or funding to declare.

There are no conflicts of interest.

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