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THE ROLE OF NUTRITION IN PREVENTING AND MANAGING METABOLIC SYNDROME: EVIDENCE-BASED APPROACHES

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ABSTRACT

Background: Metabolic Syndrome (MetS) encompasses a cluster of interrelated metabolic disorders, including obesity, hyperglycemia, dyslipidemia, and hypertension. The condition has become increasingly prevalent globally, correlating with lifestyle factors such as poor dietary habits and sedentary behavior. MetS contributes to serious health complications, including cardiovascular diseases and type 2 diabetes. Aim: This review aims to evaluate the role of various dietary patterns and bioactive compounds in preventing and managing MetS, using evidence-based approaches. Methods: We conducted a comprehensive literature review, focusing on the impact of energyrestricted diets, omega-3 fatty acids, low glycemic index/load diets, total antioxidant capacity, moderate-high protein diets, high meal frequency patterns, Mediterranean diet, and specific nutrients such as vitamin C and hydroxytyrosol on MetS. Results: Energy-restricted diets effectively reduce weight and improve metabolic markers, including lowering LDL cholesterol and plasma triglycerides. Omega-3 fatty acids show moderate evidence in reducing cardiovascular risks and inflammation. Low glycemic index/load diets help stabilize blood glucose levels, while diets high in antioxidants improve oxidative stress and inflammatory responses. Moderatehigh protein diets may enhance satiety and metabolic outcomes, though results are mixed. The Mediterranean diet is consistently beneficial, associated with reduced risks of type 2 diabetes and cardiovascular diseases. Bioactive compounds like vitamin C and hydroxytyrosol offer antioxidant and anti-inflammatory benefits. Conclusion: Dietary interventions play a crucial role in managing MetS. While energy-restricted and Mediterranean diets show significant benefits, the effectiveness of other dietary patterns varies. Personalized nutrition strategies incorporating bioactive compounds could enhance MetS management and prevention.

KEYWORDS: Metabolic Syndrome, Dietary Patterns, Bioactive Compounds, Obesity, Hyperglycemia, Dyslipidemia, Hypertension, Mediterranean Diet.

INTRODUCTION

The concept of a cluster of interconnected metabolic disturbances first emerged between 1910 and 1920.^[1] Since that time, various health organizations have proposed numerous definitions of metabolic syndrome (MetS), but a universally accepted definition remains elusive. Despite these variations, it is evident that MetS represents a clinical condition marked by significant heterogeneity, typically characterized by a combination of obesity (particularly abdominal obesity), hyperglycemia, dyslipidemia, and/or hypertension. ^[2,3,4,5,6] Obesity is defined by an abnormal or excessive accumulation of fat, primarily resulting from a chronic imbalance between energy intake and expenditure. ^[7,8] The surplus energy is chiefly stored in adipose tissue as triglycerides (TG). ^[9]

Dyslipidemia is characterized by elevated serum TG levels, increased low-density lipoprotein cholesterol (LDL-c) particles, and decreased high-density lipoprotein cholesterol (HDL-c) levels. [10] It is associated with conditions such as hepatic steatosis [11], pancreatic β-cell dysfunction [12], and an increased risk of atherosclerosis [13], among other issues. Hypertension, another key modifiable feature of MetS, is defined by a resting systolic blood pressure (SBP) \geq 140 mmHg, a diastolic blood pressure (DBP) \geq 90 mmHg, or the use of antihypertensive medication. [14] It often involves narrowed arteries and is recognized as a major risk factor for cardiovascular and renal diseases, including heart disease, stroke, and myocardial infarction. [13,15,16,17] Hyperglycemia, along with insulin resistance and type 2

diabetes mellitus, is marked by impaired glucose uptake by cells, leading to elevated plasma glucose levels, glycosuria, and ketoacidosis. This condition causes various forms of tissue damage that reduce life expectancy, including cardiovascular diseases (CVD), atherosclerosis, hypertension $^{[19]}$, β -cell dysfunction kidney disease $^{[20]}$, and blindness. Diabetes is currently one of the leading causes of death in developed countries.

Additionally. stress and low-grade oxidative inflammation are critical mechanisms in the etiology and development of MetS. [23] Oxidative stress is defined as an imbalance between pro-oxidants and antioxidants in the body. [24] It plays a significant role in atherosclerosis through mechanisms such as the oxidation of LDL-c particles^[25] and the impairment of HDL-c functions.^[26] Inflammation, an immune response to injury, is believed to be a major mechanism in the pathogenesis and progression of obesity-related disorders, linking adiposity, insulin resistance, MetS, and CVD. [27] The prevalence of MetS varies widely globally and depends on the definition used, but there has been a marked increase in cases over the past 40-50 years. [28] The syndrome is more common in developed countries, among sedentary individuals, smokers, those with lower socioeconomic status, and people with poor dietary habits. [29,30] Given these concerns, there is significant interest in identifying effective strategies for detecting, treating, and managing MetS and its associated comorbidities. Due to its heterogeneous nature, addressing the various factors involved in its development is complex. This review examines different dietary patterns and bioactive compounds that have been identified as effective in managing MetS.

Dietary Pattern Energy-Restricted Diets

Energy-restricted diets are among the most prevalent and investigated strategies for addressing excess weight and comorbidities. These diets associated involve personalized plans that provide fewer calories than the total energy expended by an individual. [31] A hypocaloric diet creates a negative energy balance, leading to weight loss as the body mobilizes fat from various compartments through lipolysis to meet energy needs. [32,33] For individuals who are overweight or obese, which is common among those with metabolic syndrome (MetS), weight loss is crucial as it is linked to improvements in conditions such as abdominal obesity (visceral fat), type 2 diabetes, cardiovascular disease (CVD), and inflammation. [32,33,34,35,36] Additionally, lowgrade inflammation, a common feature of MetS and obesity, can be mitigated by hypocaloric diets. For instance, obese individuals on a reduced-calorie diet have shown decreased plasma inflammatory markers, such as interleukin (IL)-6.[34] Thus, caloric restriction may ameliorate the systemic pro-inflammatory state in these individuals.

Weight reduction is also associated with enhancements in cellular insulin signaling, increased peripheral insulin sensitivity, and improved insulin secretory responses. [32,36] Individuals with excess body weight at risk for type 2 diabetes may experience better plasma glucose levels and reduced insulin resistance from a hypocaloric regimen. Furthermore, various intervention trials have linked energy-restricted diets to a decreased risk of developing CVD. Obese participants on hypocaloric diets have demonstrated improvements in lipid profiles, including reductions in LDL cholesterol and plasma TG levels, and decreases in both systolic and diastolic blood pressure. [35,37] Among nutritional interventions, a reduction of 500-600 kcal per day is a well-documented hypocaloric strategy effective for weight loss. [38,39] However, sustaining weight loss presents a challenge, as many individuals can adhere to a diet for a few months but struggle to maintain these habits long-term.[40,41]

Diets Rich in Omega-3 Fatty Acids

Eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) are long-chain omega-3 polyunsaturated fatty acids (n-3 PUFAs) essential for human health. These fatty acids are primarily sourced from fish and algal oils, though they can also be synthesized from α-linolenic acid. [40] Moderate evidence supports the role of n-3 PUFAs, particularly EPA and DHA, in the prevention and management of conditions associated with MetS.[42] These fatty acids are known to lower the risk of developing CVD and cardiometabolic disorders, as well as reducing CVD-related mortality. [42] The beneficial effects are likely due to their ability to lower plasma TG levels. [43] Moreover, studies have indicated that increased dietary n-3 PUFAs can reduce levels of proinflammatory cytokines such as IL-6 and tumor necrosis factor-alpha (TNFα), and plasma C-reactive protein (CRP). [44] These effects are likely mediated by resolvins, maresins, and protectins, which are anti-inflammatory metabolic products of EPA and DHA. [44]

Although some studies have suggested that n-3 PUFA consumption may improve or prevent type 2 diabetes, other studies have reported contrary results. [44] Therefore, definitive conclusions in this area are still uncertain. The European Food Safety Authority advises a daily intake of 250 mg of EPA + DHA for general cardiovascular disease prevention [45], which can be achieved by consuming 1–2 servings of fatty fish per week. [45]

Diets Based on Low Glycemic Index/Load

In recent years, there has been increased focus on the quality of carbohydrate (CHO) intake. [46] The glycemic index (GI) is employed as a measure of CHO quality, ranking carbohydrate-containing foods on a scale from 0 to 100 based on their impact on postprandial glucose levels. [47] Foods with a higher GI cause a more rapid increase in postprandial serum glucose and a swift insulin response. This quick insulin response can lead to rapid hypoglycemia, which may be linked to increased

hunger and subsequent higher caloric consumption. [47] The glycemic load (GL) is calculated by multiplying the GI by the amount of CHO in a serving. [48]

A hypothesis suggests that MetS may result from chronic consumption of high GI foods, among other unhealthy dietary practices. [49] Diets rich in high GI carbohydrates have been associated with hyperglycemia, insulin resistance, type 2 diabetes, hypertriglyceridemia, CVD, and obesity^[47,50,51], all of which are directly related to MetS. Conversely, a low GI diet is associated with slower CHO absorption and more stable blood glucose levels, indicating improved glycemic control. [46] In individuals with type 2 diabetes, low GI diets are linked to reductions in glycated hemoglobin (HbA1c) and fructosamine levels, which are critical biomarkers for management.^[52,53] Consequently, recommendations for MetS management often include limiting high GI carbohydrates, particularly from "readyto-eat processed foods" such as sweetened beverages, soft drinks, cookies, cakes, candy, juice drinks, and other foods high in added sugars.[54]

Diets with High Total Antioxidant Capacity

Total antioxidant capacity (TAC) of a diet is an indicator of diet quality, representing the cumulative antioxidant activities of all antioxidants present in the food. [55] These antioxidants help neutralize free radicals and other reactive species produced within the body. [56] Given that oxidative stress is a significant physiological condition associated with MetS, dietary antioxidants are crucial for the prevention and management of this disorder.^[57] Diets rich in spices, herbs, fruits, vegetables, nuts, and chocolate have been linked to a reduced risk of diseases related to oxidative stress.^[58,59,60] Furthermore, several studies have investigated the impact of dietary TAC on individuals with MetS or related conditions. [61,62] The Tehran Lipid and Glucose Study demonstrated that high TAC has favorable effects on metabolic disorders and helps prevent weight and abdominal fat gain. [61] Similarly, research conducted at our institutions has shown that higher TAC intake correlates with improved body weight, oxidative stress biomarkers, and other MetS characteristics. [63,64,65] In line with these findings, the World Health Organization (WHO) recommends consuming at least 400 grams of fruits and vegetables (high TAC foods) daily for the general population. [66] Additionally, using spices in cooking is advised to boost TAC intake, enhance flavor, and reduce consumption. [67]

Moderate-High Protein Diets

The typical macronutrient distribution for weight loss diets has been established as 50%–55% of total caloric intake from carbohydrates (CHO), 15% from proteins, and 30% from lipids. [57,68] However, given the challenge many individuals face in sustaining weight loss over time [69,70], research has explored increasing protein intake (>20%) at the expense of carbohydrates. [71,72,73,74,75,76,77] Two primary mechanisms have been proposed to explain the potential benefits of moderate-high protein diets:

increased diet-induced thermogenesis and enhanced satiety. Thermogenesis is heightened due to the energy required for processes such as peptide bond synthesis, urea production, and gluconeogenesis, which demand more energy than lipid or CHO metabolism. The satiety effect may be attributed to elevated levels of appetite-regulating hormones such as insulin, cholecystokinin, and glucagon-like peptide 1. [79]

Other reported benefits of moderate-high protein diets include improved glucose homeostasis^[80], potential reductions in blood lipid levels^[81], decreased blood pressure^[82], preservation of lean body mass^[83], and a lower risk of cardiometabolic diseases.^[84,85] However, some studies have failed to find benefits associated with high protein diets.^[76] These discrepancies may be due to variations in protein types, amino acid compositions^[80], and study populations.^[85] Consequently, further research is necessary to standardize these findings. When implementing a hypocaloric diet, a slight increase in protein intake is essential to meet the protein energy requirements, which are set at 0.83 g/kg/day for isocaloric diets and likely need to be at least 1 g/kg/day for energy-restricted diets.^[86]

High Meal Frequency Pattern

Increasing meal frequency in weight loss and weight control interventions has gained popularity among professionals.[87,88] This approach involves distributing total daily energy intake into more frequent, smaller meals. However, strong evidence supporting this practice is lacking. [89] While some studies report an inverse relationship between the number of daily meals and body weight, body mass index (BMI), fat mass percentage, or metabolic diseases like coronary heart disease or type 2 diabetes^[71,88,90,91,92], other studies have found no such associations. [93,94,95]</sup> Several mechanisms have been proposed to explain the potential benefits of higher meal frequency on weight and metabolic management. One hypothesis suggests increased energy expenditure; however, studies have found no significant difference in total energy expenditure across varying meal frequencies. Another hypothesis posits that more frequent meals could enhance fat oxidation, though consensus is lacking. [89,98] Additionally, it is suggested that more frequent meals might stabilize plasma glucose levels and reduce insulin secretion, potentially aiding appetite control. These effects have been observed in individuals with overweight or high glucose levels, but results in normal-weight or normoglycemic individuals remain inconsistent. [93,99,100,101]

The Mediterranean Diet

The Mediterranean Diet (MedDiet) was first characterized by Ancel Keys, who noted that countries around the Mediterranean Sea, with their distinctive dietary patterns, exhibited lower risks of coronary heart disease [102,103]. The traditional MedDiet emphasizes a high intake of extra-virgin olive oil and plant-based foods (such as fruits, vegetables, cereals, whole grains,

legumes, nuts, seeds, and olives), moderate consumption of dairy products, fish, and red wine, and low intake of sweets and red meat. [104]

Extensive literature supports the health benefits of the MedDiet. High adherence to this dietary pattern has been associated with reduced mortality and morbidity from various causes.^[105] The MedDiet is also considered effective in preventing and treating MetS and related comorbidities. [106,107,108] Recent meta-analyses have found that adherence to the MedDiet is linked to a reduced risk of type 2 diabetes and improved glycemic control in individuals with the disorder. [107,109,110] Additionally, the MedDiet is positively correlated with a of developing cardiovascular risk diseases^[111,112,113,114], with studies showing improvements in lipid profiles, including reductions in total cholesterol, LDL-c, and triglycerides, and increases in HDL-c. [111,112,113,114,115] Furthermore, adherence to the MedDiet has been associated with significant reductions in body weight and waist circumference, indicating its potential effectiveness in obesity management. [108,116,117] The high fiber content of the MedDiet, which promotes satiety and aids in weight control, as well as its rich antioxidants and anti-inflammatory nutrients such as n-3 fatty acids, oleic acid, and phenolic compounds, are considered key contributors to its beneficial effects.[118] For these reasons, maintaining the MedDiet in Mediterranean countries and promoting its adoption in countries with less healthy dietary patterns should be prioritized.

Single Nutrients and Bioactive Compounds

Recent research into the molecular actions of nutritional bioactive compounds aims to develop more personalized strategies within the realm of molecular nutrition, particularly for Metabolic Syndrome (MetS). Flavonoids and antioxidant vitamins are among the most extensively studied compounds, noted for their potential benefits including antioxidant, vasodilatory, anti-atherogenic, antithrombotic, and anti-inflammatory effects. [119]

Ascorbate

Vitamin C (ascorbic acid or ascorbate) is an essential water-soluble antioxidant found in fruits (especially citrus) and vegetables (such as peppers and kale). [120] It is renowned for its antioxidant and anti-inflammatory properties, contributing to the prevention and treatment of cardiovascular disease (CVD) and type 2 diabetes.[121,122,123] Ascorbate primarily exerts its antioxidant effect by neutralizing free radicals and other reactive oxygen and nitrogen species, thereby preventing the oxidation of molecules like LDL-c. [122] It can also regenerate other antioxidants, such as tocopherol. [124] Additionally, ascorbate is associated with reduced inflammation, which is significant for individuals with MetS. often who experience low-grade inflammation. [27,125] Vitamin C supplementation has been linked to improved endothelial function, potentially lowering blood pressure. [121,126] These effects are thought to arise from enhanced endothelial nitric oxide synthase (eNOS) activity and reduced HDL-c glycation. [127]

Moreover, ascorbate may improve insulin sensitivity and glucose control in people with type 2 diabetes, likely through optimization of insulin secretion by pancreatic islet cells and increased expression of muscle sodium-dependent vitamin C transporters (SVCTs). [123,128] However, most people obtain sufficient ascorbic acid through their diet (recommended intake: 95–110 mg/day) and do not require supplementation. Excessive vitamin C intake can lead to oxidative damage. [130,131]

Hydroxytyrosol

(3,4-dihydroxyphenylethanol) is a Hvdroxvtvrosol phenolic compound predominantly found in olives. [132] It is recognized as a powerful antioxidant, scavenging free radicals, breaking radical chains, and chelating metals. [133] Hydroxytyrosol inhibits LDL-c oxidation by macrophages and is the only phenol officially recognized by the European Food Safety Authority (EFSA) as a protector of blood lipids from oxidative damage. [135] This compound also exhibits anti-inflammatory effects, possibly by suppressing cyclooxygenase activity and inducing eNOS expression. [136] Hydroxytyrosol's cardiovascular protective effects include anti-atherogenic properties through the reduction of vascular cell adhesion protein 1 (VCAM-1) and intercellular adhesion molecule $(ICAM-1)^{[132,137]}$. potentially bv inactivating transcription factors and enzymes such as NFkB, AP-1, and NAD(P)H oxidase. [138,139] Additionally, it has antidyslipidemic effects, lowering LDL-c, total cholesterol, and triglycerides while increasing HDL-Despite its benefits, most studies hydroxytyrosol have involved olive phenol mixtures, suggesting a potential synergistic effect. [140]

Ouercetin

Ouercetin, a prevalent flavanol found in vegetables, fruits, green tea, and red wine, often appears as glycosides like rutin. [141] It is known for its antioxidant properties, inhibiting lipid peroxidation and enhancing antioxidant enzymes such as superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPX). [142] Quercetin also has anti-inflammatory effects, mediated by attenuating tumor necrosis factor α (TNFα), NFκB, mitogen-activated protein kinases (MAPK), and reducing gene expression of IL-6, IL-1B, IL-8, and MCP-1. [143] In terms of obesity and weight management, quercetin may inhibit adipogenesis by activating AMPactivated protein kinase (AMPK) and decreasing expression of adipogenic factors such as CCAATenhancer-binding protein-α (C/EBPα), peroxisome proliferator-activated receptor gamma (PPARy), and sterol regulatory element-binding protein 1 (SREBP-1). [141,144] It may also act as a PPARγ agonist, improving insulin-stimulated glucose uptake in adipocytes, and ameliorate hyperglycemia by inhibiting glucose transporter 2 (GLUT2) and phosphatidylinositol-3-kinase (PI3K). [142,145] Quercetin's potential to reduce blood pressure is noted, though mechanisms remain unclear. It may increase eNOS activity, contributing to improved

endothelial function and platelet aggregation inhibition^[146,147], but findings are inconsistent. [148]

Resveratrol

Resveratrol (3,5,4'-trihydroxy-stilbene) is a phenolic compound found in red grapes and their derivatives (e.g., red wine, grape juice). [149] It exhibits antioxidant and anti-inflammatory properties and has been linked to cardioprotective, anti-obesity, effects. [150,151,152,153,154,155,156] Res and antidiabetic Resveratrol's antioxidant effects involve scavenging hydroxyl, superoxide, and metal-induced radicals and reducing reactive oxygen species (ROS).[150] Its anti-inflammatory effects are mediated by inhibiting NFkB signaling and reducing proinflammatory cytokines such as IL-6, IL-8, TNF-α, MCP-1, and eNOS, and by inhibiting cyclooxygenase (COX). [152] In diabetes management, resveratrol has shown significant improvements in fasting glucose levels, insulin concentrations, glycated hemoglobin, and Homeostasis Model Assessment Insulin Resistance (HOMA-IR). [153,154] Cardioprotective effects include enhanced endothelial function through increased nitric oxide (NO) production via activation of eNOS, Sirt 1, and AMPK. [155] Resveratrol also stimulates NF-E2related factor 2 (Nrf2) and reduces expression of adhesion proteins like ICAM-1 and VCAM-1. [152] Resveratrol's role in obesity prevention is linked to improved energy metabolism, increased lipolysis, and decreased lipogenesis^[157], although further research is needed to confirm these effects.

Tocopherol

Tocopherols, commonly known as vitamin E, comprise a group of eight fat-soluble phenolic compounds, with primary dietary sources including vegetable oils, nuts, and seeds. Vitamin E has long been associated with potential preventive effects on various metabolic diseases, primarily due to its role as a potent antioxidant. It acts by scavenging lipid peroxyl radicals through hydrogen donation, which helps inhibit the peroxidation of membrane phospholipids and prevents free radical generation in cell membranes. [159,160] Supplementation with α -tocopherol or γ -tocopherol, two of the vitamin E isoforms, has been shown to influence inflammation by levels.[16] protein reducing C-reactive (CRP) Additionally, tocopherols may contribute to antiinflammatory effects through inhibition cyclooxygenase (COX) and protein kinase C (PKC) and by reducing cytokines such as IL-8 and plasminogen activator inhibitor-1 (PAI-1).[162,163] However, recent clinical trials have produced mixed results regarding the benefits of vitamin E. Some studies have not observed the expected benefits and, in some cases, have found potentially harmful effects. [164] These discrepancies may be attributed to the loss of antioxidant capacity when vitamin E is ingested, which could occur due to various mechanisms.[162]

Anthocyanins

Anthocyanins are water-soluble polyphenolic compounds that impart red, blue, and purple colors to a variety of fruits, vegetables, and other foods, including berries, black currants, black grapes, and red cabbage. [165,166,167] They are among the most abundant polyphenols in the diet and are also found in teas, honey, nuts, and cocoa. [168] These compounds are recognized for their high antioxidant capacity, as they can inhibit or reduce free radicals by donating or transferring electrons from hydrogen atoms. [167] Clinical studies suggest that anthocyanins may help prevent type 2 diabetes by enhancing insulin sensitivity, although the exact mechanisms remain unclear. It is proposed that anthocyanins may improve glucose uptake by muscle and adipocyte cells in an insulin-independent manner. [169] Anthocyanins have also shown potential in preventing cardiovascular disease (CVD) by improving endothelial function. They can enhance brachial artery flowmediated dilation and increase HDL-c levels while VCAM-1 LDL-c decreasing serum and concentrations. [170,171,172,173] Furthermore, anthocyanins may exert anti-inflammatory effects by reducing proinflammatory molecules such as IL-8, IL-1B, and CRP.[172,174] Most studies have utilized anthocyanin-rich extracts rather than purified anthocyanins, leaving the possibility of a synergistic effect with other polyphenols.

Catechins

Catechins are polyphenolic compounds found in various foods, including fruits, vegetables, chocolate, wine, and tea. [175] Among them, epigallocatechin 3-gallate (EGCG), found in tea leaves, is the most studied. [176] Catechins are associated with anti-obesity effects through mechanisms such as increasing energy expenditure and fat oxidation while reducing fat absorption. These effects are thought to be mediated by catechol-O-methyltransferase and phosphodiesterase inhibition, which stimulate the sympathetic nervous system and activate brown adipose tissue. [177] Fat oxidation is facilitated by upregulation of acyl-CoA dehydrogenase and peroxisomal β-oxidation enzymes.[178,179] Catechins have also been linked to a lower risk of cardiovascular disease by improving lipid biomarkers, such as increasing HDL-c and decreasing LDL-c and total cholesterol. [180] Additionally, catechins have shown antidiabetic effects by lowering fasting glucose levels and improving insulin sensitivity.

CONCLUSION

Metabolic Syndrome (MetS) represents a significant public health challenge due to its association with obesity, type 2 diabetes, cardiovascular diseases, and other serious health issues. This review underscores the importance of dietary interventions in managing and preventing MetS. Energy-restricted diets are highlighted for their effectiveness in inducing weight loss and improving metabolic parameters. Such diets not only reduce body fat but also lead to improvements in lipid profiles, blood pressure, and insulin sensitivity, thereby addressing several key components of MetS. Diets rich in omega-3 fatty acids, particularly eicosapentaenoic acid

(EPA) and docosahexaenoic acid (DHA), provide moderate evidence for cardiovascular risk reduction and inflammation control, though further research is needed to solidify these benefits for type 2 diabetes prevention. Low glycemic index/load diets improve glycemic control and are beneficial for managing blood glucose levels in individuals with type 2 diabetes, demonstrating a positive effect on metabolic health. The Mediterranean diet consistently emerges as a highly effective dietary pattern for MetS management. It is associated with reduced mortality, lower risk of cardiovascular diseases, and improved metabolic outcomes. The high content of antioxidants, fiber, and healthy fats in the Mediterranean diet contributes to its success in managing obesity and associated metabolic disturbances. Bioactive compounds. such as vitamin C and hydroxytyrosol, also play significant roles. Vitamin C's antioxidant properties support cardiovascular health and glucose control, while hydroxytyrosol's antioxidant and anti-inflammatory effects offer protection against oxidative damage and dyslipidemia. In summary, adopting a comprehensive approach that includes energy restriction, consumption of omega-3 fatty acids, low glycemic index foods, antioxidant-rich diets, and the Mediterranean dietary pattern can significantly impact MetS management. Personalized nutrition strategies that consider individual dietary needs and health conditions are essential for effective MetS prevention and treatment.

REFERENCES

- 1. Sarafidis, P.A.; Nilsson, P.M. The metabolic syndrome: A glance at its history. *J. Hypertens*, 2006; 24: 621–626.
- Alberti, K.G.; Zimmet, P.Z. Definition, diagnosis and classification of diabetes mellitus and its complications. Part 1: Diagnosis and classification of diabetes mellitus provisional report of a WHO consultation. *Diabet. Med.*, 1998; 15: 539–553.
- 3. Balkau, B.; Charles, M.A. Comment on the provisional report from the WHO consultation. European Group for the Study of Insulin Resistance (EGIR). *Diabet. Med.*, 1999; *16*: 442–423.
- Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. Executive Summary of The Third Report of The National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). JAMA., 2001; 285: 2486–2497.
- Grundy, S.M.; Cleeman, J.I.; Daniels, S.R.; Donato, K.A.; Eckel, R.H.; Franklin, B.A.; Gordon, D.J.; Krauss, R.M.; Savage, P.J.; Smith, S.C., Jr.; et al. Diagnosis and management of the metabolic syndrome: An American Heart Association/National Heart, Lung, and Blood Institute Scientific Statement. Circulation, 2005; 112: 2735–2752.
- 6. Alberti, K.G.; Zimmet, P.; Shaw, J. The metabolic syndrome—A new worldwide definition. *Lancet*, 2005; *366*: 1059–1062

- 7. Selassie, M.; Sinha, A.C. The epidemiology and aetiology of obesity: A global challenge. *Best Pract. Res. Clin. Anaesthesiol*, 2011; 25: 1–9.
- 8. WHO, W.H.O. Available online: http://www.who.int/mediacentre/factsheets/fs 311/es/ (accessed on 4 June 2016).
- 9. Shimano, H. Novel qualitative aspects of tissue fatty acids related to metabolic regulation: Lessons from Elovl6 knockout. *Prog. Lipid Res.*, 2012; *51*: 267–271.
- 10. Bosomworth, N.J. Approach to identifying and managing atherogenic dyslipidemia: A metabolic consequence of obesity and diabetes. *Can. Fam. Phys.*, 2013; 59: 1169–1180.
- 11. Vidal-Puig, A. The Metabolic Syndrome and its Complex Pathophysiology. In *A Systems Biology Approach to Study Metabolic Syndrome*; Oresic, M., Ed.; Springer: New York, NY, USA, 2014; 3–16.
- 12. Poitout, V.; Robertson, R.P. Glucolipotoxicity: Fuel excess and beta-cell dysfunction. *Endocr. Rev.*, 2008; 29: 351–366.
- 13. Rizza, W.; Veronese, N.; Fontana, L. What are the roles of calorie restriction and diet quality in promoting healthy longevity? *Ageing Res. Rev.*, 2014; *13*: 38–45.
- Lloyd-Jones, D.M.; Levy, D. Epidemiology of Hypertension. In *Hypertension: A Companion to Braunwald's Heart Disease*; Black, H.R., Elliott, W.J., Eds.; Elsevier: Philadephia, PA, USA, 2013; 1–11.
- 15. Zanchetti, A. Challenges in hypertension: Prevalence, definition, mechanisms and management. *J. Hypertens*, 2014; *32*: 451–453.
- 16. Thomas, G.; Shishehbor, M.; Brill, D.; Nally, J.V., Jr. New hypertension guidelines: One size fits most? *Clevel. Clin. J. Med.*, 2014; *81*: 178–188.
- 17. James, P.A.; Oparil, S.; Carter, B.L.; Cushman, W.C.; Dennison-Himmelfarb, C.; Handler, J.; Lackland, D.T.; LeFevre, M.L.; MacKenzie, T.D.; Ogedegbe, O.; et al. 2014 evidence-based guideline for the management of high blood pressure in adults: Report from the panel members appointed to the Eighth Joint National Committee (JNC 8). *JAMA*., 2014; *311*: 507–520.
- 18. Klandorf, H.; Chirra, A.R.; DeGruccio, A.; Girman, D.J. Dimethyl sulfoxide modulation of diabetes onset in NOD mice. *Diabetes*, 1989; *38*: 194–197.
- 19. Ballard, K.D.; Mah, E.; Guo, Y.; Pei, R.; Volek, J.S.; Bruno, R.S. Low-fat milk ingestion prevents postprandial hyperglycemia-mediated impairments in vascular endothelial function in obese individuals with metabolic syndrome. *J. Nutr.*, 2013; *143*: 1602–1610.
- 20. Pugliese, G.; Solini, A.; Bonora, E.; Orsi, E.; Zerbini, G.; Fondelli, C.; Gruden, G.; Cavalot, F.; Lamacchia, O.; Trevisan, R.; et al. Distribution of cardiovascular disease and retinopathy in patients with type 2 diabetes according to different classification systems for chronic kidney disease: A cross-sectional analysis of the renal insufficiency and

- cardiovascular events (RIACE) Italian multicenter study. *Cardiovasc. Diabetol.*, 2014; *13*: 59.
- 21. Asif, M. The prevention and control the type-2 diabetes by changing lifestyle and dietary pattern. *J. Educ. Health Promot.*, 2014; *3*: 1.
- Russell, W.R.; Baka, A.; Bjorck, I.; Delzenne, N.; Gao, D.; Griffiths, H.R.; Hadjilucas, E.; Juvonen, K.; Lahtinen, S.; Lansink, M.; et al. Impact of Diet Composition on Blood Glucose Regulation. *Crit. Rev. Food Sci. Nutr.*, 2016; 56: 541–590.
- 23. Soares, R.; Costa, C. Oxidative Stress, Inflammation and Angiogenesis in the Metabolic Syndrome; Springer: Heidelberg, Germany, 2009.
- Rahal, A.; Kumar, A.; Singh, V.; Yadav, B.; Tiwari, R.; Chakraborty, S.; Dhama, K. Oxidative Stress, Prooxidants, and Antioxidants: The Interplay. *BioMed Res. Int.*, 2014; 2014: 761264.
- Parthasarathy, S.; Litvinov, D.; Selvarajan, K.; Garelnabi, M. Lipid peroxidation and decomposition—Conflicting roles in plaque vulnerability and stability. *Biochim. Biophys. Acta*, 2008; 1781: 221–231.
- McGrowder, D.; Riley, C.; Morrison, E.Y.; Gordon, L. The role of high-density lipoproteins in reducing the risk of vascular diseases, neurogenerative disorders, and cancer. *Cholesterol*, 2011; 2011: 496925.
- 27. Ferri, N.; Ruscica, M. Proprotein convertase subtilisin/kexin type 9 (PCSK9) and metabolic syndrome: Insights on insulin resistance, inflammation, and atherogenic dyslipidemia. *Endocrine*, 2016.
- 28. Oresic, M.; Vidal-Puig, A. A Systems Biology Approach to Study Metabolic Syndrome; Springer: Heidelberg, Germany, 2014.
- 29. Lee, E.G.; Choi, J.H.; Kim, K.E.; Kim, J.H. Effects of a Walking Program on Self-management and Risk Factors of Metabolic Syndrome in Older Korean Adults. *J. Phys. Ther. Sci.*, 2014; 26: 105–109.
- Bernabe, G.J.; Zafrilla, R.P.; Mulero, C.J.; Gomez, J.P.; Leal, H.M.; Abellan, A.J. Biochemical and nutritional markers and antioxidant activity in metabolic syndrome. *Endocrinol. Nutr.*, 2013; 61: 302–308.
- 31. Bales, C.W.; Kraus, W.E. Caloric restriction: Implications for human cardiometabolic health. *J. Cardiopulm. Rehabil. Prev.*, 2013; *33*: 201–208.
- 32. Grams, J.; Garvey, W.T. Weight Loss and the Prevention and Treatment of Type 2 Diabetes Using Lifestyle Therapy, Pharmacotherapy, and Bariatric Surgery: Mechanisms of Action. *Curr. Obes. Rep.*, 2015; *4*: 287–302.
- 33. Lazo, M.; Solga, S.F.; Horska, A.; Bonekamp, S.; Diehl, A.M.; Brancati, F.L.; Wagenknecht, L.E.; Pi-Sunyer, F.X.; Kahn, S.E.; Clark, J.M. Effect of a 12-month intensive lifestyle intervention on hepatic steatosis in adults with type 2 diabetes. *Diabetes Care*, 2010; *33*: 2156–2163.

- 34. Rossmeislova, L.; Malisova, L.; Kracmerova, J.; Stich, V. Adaptation of human adipose tissue to hypocaloric diet. *Int. J. Obes.*, 2013; *37*: 640–650.
- 35. Wing, R.R.; Lang, W.; Wadden, T.A.; Safford, M.; Knowler, W.C.; Bertoni, A.G.; Hill, J.O.; Brancati, F.L.; Peters, A.; Wagenknecht, L. Benefits of modest weight loss in improving cardiovascular risk factors in overweight and obese individuals with type 2 diabetes. *Diabetes Care*, 2011; *34*: 1481–1486.
- 36. Golay, A.; Brock, E.; Gabriel, R.; Konrad, T.; Lalic, N.; Laville, M.; Mingrone, G.; Petrie, J.; Phan, T.M.; Pietilainen, K.H.; et al. Taking small steps towards targets—Perspectives for clinical practice in diabetes, cardiometabolic disorders and beyond. *Int. J. Clin. Pract.*, 2013; 67: 322–332.
- 37. Fock, K.M.; Khoo, J. Diet and exercise in management of obesity and overweight. *J. Gastroenterol. Hepatol.*, 2013; 28: 59–63.
- 38. Abete, I.; Parra, D.; Martinez, J.A. Energy-restricted diets based on a distinct food selection affecting the glycemic index induce different weight loss and oxidative response. *Clin. Nutr.*, 2008; 27: 545–551.
- 39. Alberti, K.G.; Eckel, R.H.; Grundy, S.M.; Zimmet, P.Z.; Cleeman, J.I.; Donato, K.A.; Fruchart, J.C.; James, W.P.; Loria, C.M.; Smith, S.C., Jr. Harmonizing the metabolic syndrome: A joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity. Circulation, 2009; 120: 1640–1645.
- 40. Fleming, J.A.; Kris-Etherton, P.M. The evidence for alpha-linolenic acid and cardiovascular disease benefits: Comparisons with eicosapentaenoic acid and docosahexaenoic acid. *Adv. Nutr.*, 2014; 5: 863S–876S.
- 41. Gray, B.; Steyn, F.; Davies, P.S.; Vitetta, L. Omega-3 fatty acids: A review of the effects on adiponectin and leptin and potential implications for obesity management. *Eur. J. Clin. Nutr.*, 2013; 67: 1234–1242.
- 42. Wen, Y.T.; Dai, J.H.; Gao, Q. Effects of Omega-3 fatty acid on major cardiovascular events and mortality in patients with coronary heart disease: A meta-analysis of randomized controlled trials. *Nutr. Metab. Cardiovasc. Dis.*, 2014; 24: 470–475.
- 43. Lopez-Huertas, E. The effect of EPA and DHA on metabolic syndrome patients: A systematic review of randomised controlled trials. *Br. J. Nutr.*, 2012; *107*: 185–194.
- 44. Maiorino, M.I.; Chiodini, P.; Bellastella, G.; Giugliano, D.; Esposito, K. Sexual dysfunction in women with cancer: A systematic review with meta-analysis of studies using the Female Sexual Function Index. *Endocrine*, 2016; 54: 329–341.
- 45. EFSA NDA Panel (EFSA Panel on Dietetic Products, Nutrition and Allergies). Scientific Opinion on Dietary Reference Values for fats,

- including saturated fatty acids, polyunsaturated fatty acids, monounsaturated fatty acids, trans fatty acids, and cholesterol1. *EFSA J.*, 2010; 8: 1461–1566.
- 46. Bellastella, G.; Bizzarro, A.; Aitella, E.; Barrasso, M.; Cozzolino, D.; di Martino, S.; Esposito, K.; de Bellis, A. Pregnancy may favour the development of severe autoimmune central diabetes insipidus in women with vasopressin cell antibodies: Description of two cases. *Eur. J. Endocrinol*, 2015; 172: K11–K17.
- 47. Sun, F.H.; Li, C.; Zhang, Y.J.; Wong, S.H.; Wang, L. Effect of Glycemic Index of Breakfast on Energy Intake at Subsequent Meal among Healthy People: A Meta-Analysis. *Nutrients*, 2016; 8: 37.
- 48. Barclay, A.W.; Brand-Miller, J.C.; Wolever, T.M. Glycemic index, glycemic load, and glycemic response are not the same. *Diabetes Care*, 2005; 28: 1839–1840.
- Nakagawa, T.; Hu, H.; Zharikov, S.; Tuttle, K.R.; Short, R.A.; Glushakova, O.; Ouyang, X.; Feig, D.I.; Block, E.R.; Herrera-Acosta, J.; et al. A causal role for uric acid in fructose-induced metabolic syndrome. *Am. J. Physiol. Ren. Physiol.*, 2006; 290: F625–F631.
- 50. Symons Downs, D.; Hausenblas, H.A. Women's exercise beliefs and behaviors during their pregnancy and postpartum. *J. Midwifery Women Health*, 2004; 49: 138–144.
- 51. Brand-Miller, J.; McMillan-Price, J.; Steinbeck, K.; Caterson, I. Dietary glycemic index: Health implications. *J. Am. Coll. Nutr.*, 2009; 28: 446S–449S.
- 52. Thomas, D.; Elliott, E.J. Low glycaemic index, or low glycaemic load, diets for diabetes mellitus. *Cochrane Database Syst. Rev.*, 2009.
- 53. Barrea, L.; Balato, N.; di Somma, C.; Macchia, P.E.; Napolitano, M.; Savanelli, M.C.; Esposito, K.; Colao, A.; Savastano, S. Nutrition and psoriasis: Is there any association between the severity of the disease and adherence to the Mediterranean diet? *J. Transl. Med.*, 2015; *13*: 18.
- 54. Mathias, K.C.; Ng, S.W.; Popkin, B. Monitoring changes in the nutritional content of ready-to-eat grain-based dessert products manufactured and purchased between 2005 and 2012. *J. Acad. Nutr. Diet.*, 2015; *115*: 360–368.
- 55. Serafini, M.; del Rio, D. Understanding the association between dietary antioxidants, redox status and disease: Is the Total Antioxidant Capacity the right tool? *Redox Rep.*, 2004; *9*: 145.
- 56. Bellastella, G.; Maiorino, M.I.; Olita, L.; della Volpe, E.; Giugliano, D.; Esposito, K. Premature ejaculation is associated with glycemic control in Type 1 diabetes. *J. Sex. Med.*, 2015; *12*: 93–99.
- 57. Zulet, M.A.; Moreno-Aliaga, M.J.; Martinez, J.A. Dietary Determinants of Fat Mass and Body Composition. In *Adipose Tissue Biology*; Symonds, M.E., Ed.; Springer: New York, NY, USA, 2012; 271–315.

- 58. Carlsen, M.H.; Halvorsen, B.L.; Holte, K.; Bohn, S.K.; Dragland, S.; Sampson, L.; Willey, C.; Senoo, H.; Umezono, Y.; Sanada, C.; et al. The total antioxidant content of more than 3100 foods, beverages, spices, herbs and supplements used worldwide. *Nutr. J.*, 2010; 9: 3.
- 59. Harasym, J.; Oledzki, R. Effect of fruit and vegetable antioxidants on total antioxidant capacity of blood plasma. *Nutrition*, 2014; *30*: 511–517.
- 60. Maiorino, M.I.; Bellastella, G.; Petrizzo, M.; della Volpe, E.; Orlando, R.; Giugliano, D.; Esposito, K. Circulating endothelial progenitor cells in type 1 diabetic patients with erectile dysfunction. *Endocrine*, 2015; 49: 415–421.
- 61. Bahadoran, Z.; Golzarand, M.; Mirmiran, P.; Shiva, N.; Azizi, F. Dietary total antioxidant capacity and the occurrence of metabolic syndrome and its components after a 3-year follow-up in adults: Tehran Lipid and Glucose Study. *Nutr. Metab.*, 2012; 9: 70.
- 62. Chrysohoou, C.; Esposito, K.; Giugliano, D.; Panagiotakos, D.B. Peripheral Arterial Disease and Cardiovascular Risk: The Role of Mediterranean Diet. *Angiology*, 2015; 66: 708–710.
- 63. De la Iglesia, R.; Lopez-Legarrea, P.; Celada, P.; Sanchez-Muniz, F.J.; Martinez, J.A.; Zulet, M.A. Beneficial effects of the RESMENA dietary pattern on oxidative stress in patients suffering from metabolic syndrome with hyperglycemia are associated to dietary TAC and fruit consumption. *Int. J. Mol. Sci.*, 2013; *14*: 6903–6919.
- 64. Lopez-Legarrea, P.; de la Iglesia, R.; Abete, I.; Bondia-Pons, I.; Navas-Carretero, S.; Forga, L.; Martinez, J.A.; Zulet, M.A. Short-term role of the dietary total antioxidant capacity in two hypocaloric regimes on obese with metabolic syndrome symptoms: The RESMENA randomized controlled trial. *Nutr. Metab.*, 2013; *10*: 22.
- 65. Puchau, B.; Zulet, M.A.; de Echavarri, A.G.; Hermsdorff, H.H.; Martinez, J.A. Dietary total antioxidant capacity is negatively associated with some metabolic syndrome features in healthy young adults. *Nutrition*, 2010; 26: 534–541.
- 66. World Health Organization. *Obesity: Preventing and Managing the Global Epidemic*; Report of a WHO Consultation; World Health Organization Technical Report Series; WHO: Geneva, Switzerland, 2000.
- 67. Tapsell, L.C.; Hemphill, I.; Cobiac, L.; Patch, C.S.; Sullivan, D.R.; Fenech, M.; Roodenrys, S.; Keogh, J.B.; Clifton, P.M.; Williams, P.G.; et al. Health benefits of herbs and spices: The past, the present, the future. *Med. J. Aust.*, 2006; *185*: S4–S24.
- 68. Abete, I.; Astrup, A.; Martinez, J.A.; Thorsdottir, I.; Zulet, M.A. Obesity and the metabolic syndrome: Role of different dietary macronutrient distribution patterns and specific nutritional components on weight loss and maintenance. *Nutr. Rev.*, 2010; 68: 214–231.
- 69. Ebbeling, C.B.; Swain, J.F.; Feldman, H.A.; Wong, W.W.; Hachey, D.L.; Garcia-Lago, E.; Ludwig, D.S.

- Effects of dietary composition on energy expenditure during weight-loss maintenance. *JAMA*, 2012; 307: 2627–2634.
- Abete, I.; Goyenechea, E.; Zulet, M.A.; Martinez, J.A. Obesity and metabolic syndrome: Potential benefit from specific nutritional components. *Nutr. Metab. Cardiovasc. Dis.*, 2011; 21: B1–B15.
- Arciero, P.J.; Ormsbee, M.J.; Gentile, C.L.; Nindl, B.C.; Brestoff, J.R.; Ruby, M. Increased protein intake and meal frequency reduces abdominal fat during energy balance and energy deficit. *Obesity*, 2013; 21: 1357–1366.
- 72. Wikarek, T.; Chudek, J.; Owczarek, A.; Olszanecka-Glinianowicz, M. Effect of dietary macronutrients on postprandial incretin hormone release and satiety in obese and normal-weight women. *Br. J. Nutr.*, 2014; *111*: 236–246.
- 73. Bray, G.A.; Smith, S.R.; de Jonge, L.; Xie, H.; Rood, J.; Martin, C.K.; Most, M.; Brock, C.; Mancuso, S.; Redman, L.M. Effect of dietary protein content on weight gain, energy expenditure, and body composition during overeating: A randomized controlled trial. *JAMA*, 2012; *307*: 47–55.
- 74. Westerterp-Plantenga, M.S.; Nieuwenhuizen, A.; Tome, D.; Soenen, S.; Westerterp, K.R. Dietary protein, weight loss, and weight maintenance. *Annu. Rev. Nutr.*, 2009; 29: 21–41.
- 75. Koppes, L.L.; Boon, N.; Nooyens, A.C.; van Mechelen, W.; Saris, W.H. Macronutrient distribution over a period of 23 years in relation to energy intake and body fatness. *Br. J. Nutr.*, 2009; *101*: 108–115.
- 76. De Jonge, L.; Bray, G.A.; Smith, S.R.; Ryan, D.H.; de Souza, R.J.; Loria, C.M.; Champagne, C.M.; Williamson, D.A.; Sacks, F.M. Effect of diet composition and weight loss on resting energy expenditure in the POUNDS LOST study. *Obesity*, 2012; 20: 2384–2389.
- 77. Stocks, T.; Angquist, L.; Hager, J.; Charon, C.; Holst, C.; Martinez, J.A.; Saris, W.H.; Astrup, A.; Sorensen, T.I.; Larsen, L.H. TFAP2B-dietary protein and glycemic index interactions and weight maintenance after weight loss in the DiOGenes trial. *Hum. Hered.*, 2013; 75: 213–219.
- 78. Giugliano, D.; Maiorino, M.I.; Esposito, K. Linking prediabetes and cancer: A complex issue. *Diabetologia*, 2015; 58: 201–202.
- Bendtsen, L.Q.; Lorenzen, J.K.; Bendsen, N.T.; Rasmussen, C.; Astrup, A. Effect of dairy proteins on appetite, energy expenditure, body weight, and composition: A review of the evidence from controlled clinical trials. Adv. Nutr., 2013; 4: 418–438.
- 80. Heer, M.; Egert, S. Nutrients other than carbohydrates: Their effects on glucose homeostasis in humans. *Diabetes Metab. Res. Rev.*, 2015; *31*: 14–35.
- 81. Layman, D.K.; Evans, E.M.; Erickson, D.; Seyler, J.; Weber, J.; Bagshaw, D.; Griel, A.; Psota, T.; Kris-Etherton, P. A moderate-protein diet produces

- sustained weight loss and long-term changes in body composition and blood lipids in obese adults. *J. Nutr.*, 2009; *139*: 514–521.
- 82. Pedersen, A.N.; Kondrup, J.; Borsheim, E. Health effects of protein intake in healthy adults: A systematic literature review. *Food Nutr. Res.*, 2013; 57: 21245.
- 83. Daly, R.M.; O'Connell, S.L.; Mundell, N.L.; Grimes, C.A.; Dunstan, D.W.; Nowson, C.A. Protein-enriched diet, with the use of lean red meat, combined with progressive resistance training enhances lean tissue mass and muscle strength and reduces circulating IL-6 concentrations in elderly women: A cluster randomized controlled trial. *Am. J. Clin. Nutr.*, 2014; 99: 899–910.
- 84. Arciero, P.J.; Gentile, C.L.; Pressman, R.; Everett, M.; Ormsbee, M.J.; Martin, J.; Santamore, J.; Gorman, L.; Fehling, P.C.; Vukovich, M.D.; et al. Moderate protein intake improves total and regional body composition and insulin sensitivity in overweight adults. *Metab. Clin. Exp.*, 2008; 57: 757–765.
- 85. Gregory, S.M.; Headley, S.A.; Wood, R.J. Effects of dietary macronutrient distribution on vascular integrity in obesity and metabolic syndrome. *Nutr. Rev.*, 2011; *69*: 509–519.
- 86. Consenso FESNAD-SEEDO. Recomendaciones nutricionales basadas en la evidencia para la prevención y el tratamiento del sobrepeso y la obesidad en adultos (Consenso FESNAD-SEEDO). Rev. Esp. Obes., 2011.
- 87. Jakubowicz, D.; Froy, O.; Wainstein, J.; Boaz, M. Meal timing and composition influence ghrelin levels, appetite scores and weight loss maintenance in overweight and obese adults. *Steroids*, 2012; 77: 323–331.
- 88. Schwarz, N.A.; Rigby, B.R.; La Bounty, P.; Shelmadine, B.; Bowden, R.G. A review of weight control strategies and their effects on the regulation of hormonal balance. *J. Nutr. Metab.*, 2011; 2011: 237932.
- 89. Ohkawara, K.; Cornier, M.A.; Kohrt, W.M.; Melanson, E.L. Effects of increased meal frequency on fat oxidation and perceived hunger. *Obesity*, 2013; 21: 336–343.
- 90. Ekmekcioglu, C.; Touitou, Y. Chronobiological aspects of food intake and metabolism and their relevance on energy balance and weight regulation. *Obes. Rev.*, 2011; *12*: 14–25.
- 91. Lioret, S.; Touvier, M.; Lafay, L.; Volatier, J.L.; Maire, B. Are eating occasions and their energy content related to child overweight and socioeconomic status? *Obesity*, 2008; *16*: 2518–2523.
- 92. Bhutani, S.; Varady, K.A. Nibbling versus feasting: Which meal pattern is better for heart disease prevention? *Nutr. Rev.*, 2009; 67: 591–598.
- 93. Leidy, H.J.; Tang, M.; Armstrong, C.L.; Martin, C.B.; Campbell, W.W. The effects of consuming frequent, higher protein meals on appetite and

- satiety during weight loss in overweight/obese men. *Obesity*, 2011; *19*: 818–824.
- 94. Mills, J.P.; Perry, C.D.; Reicks, M. Eating frequency is associated with energy intake but not obesity in midlife women. *Obesity*, 2011; *19*: 552–559.
- 95. Cameron, J.D.; Cyr, M.J.; Doucet, E. Increased meal frequency does not promote greater weight loss in subjects who were prescribed an 8-week equienergetic energy-restricted diet. *Br. J. Nutr.*, 2010; *103*: 1098–1101.
- 96. Smeets, A.J.; Lejeune, M.P.; Westerterp-Plantenga, M.S. Effects of oral fat perception by modified sham feeding on energy expenditure, hormones and appetite profile in the postprandial state. *Br. J. Nutr.*, 2009; *101*: 1360–1368.
- 97. Taylor, M.A.; Garrow, J.S. Compared with nibbling, neither gorging nor a morning fast affect short-term energy balance in obese patients in a chamber calorimeter. *Int. J. Obes. Relat. Metab. Disord.*, 2001; 25: 519–528.
- 98. Smeets, A.J.; Westerterp-Plantenga, M.S. Acute effects on metabolism and appetite profile of one meal difference in the lower range of meal frequency. *Br. J. Nutr.*, 2008; *99*: 1316–1321.
- 99. Heden, T.D.; LeCheminant, J.D.; Smith, J.D. Influence of weight classification on walking and jogging energy expenditure prediction in women. *Res. Q. Exerc. Sport.*, 2012; 83: 391–399.
- 100.Bachman, J.L.; Raynor, H.A. Effects of manipulating eating frequency during a behavioral weight loss intervention: A pilot randomized controlled trial. *Obesity*, 2012; 20: 985–992.
- 101.Perrigue, M.M.; Drewnowski, A.; Wang, C.Y.; Neuhouser, M.L. Higher Eating Frequency Does Not Decrease Appetite in Healthy Adults. *J. Nutr.* 2016; *146*: 59–64.
- 102. Keys, A. Coronary heart disease in seven countries. 1970. *Nutrition*, 1997; *13*: 249–253.
- 103.Keys, A.; Menotti, A.; Aravanis, C.; Blackburn, H.; Djordevic, B.S.; Buzina, R.; Dontas, A.S.; Fidanza, F.; Karvonen, M.J.; Kimura, N.; et al. The seven countries study: 2289 deaths in 15 years. *Prev. Med.*, 1984; *13*: 141–154.
- 104. Davis, C.; Bryan, J.; Hodgson, J.; Murphy, K. Definition of the Mediterranean Diet; a Literature Review. *Nutrients*, 2015; 7: 9139–9153.
- 105.Sofi, F.; Macchi, C.; Abbate, R.; Gensini, G.F.; Casini, A. Mediterranean diet and health status: An updated meta-analysis and a proposal for a literature-based adherence score. *Public Health Nutr.*, 2014; *17*: 2769–2782.
- 106.Mayneris-Perxachs, J.; Sala-Vila, A.; Chisaguano, M.; Castellote, A.I.; Estruch, R.; Covas, M.I.; Fito, M.; Salas-Salvado, J.; Martinez-Gonzalez, M.A.; Lamuela-Raventos, R.; et al. Effects of 1-year intervention with a Mediterranean diet on plasma fatty acid composition and metabolic syndrome in a population at high cardiovascular risk. *PLoS ONE*, 2014; 9: e85202.

- 107. Esposito, K.; Maiorino, M.I.; Bellastella, G.; Chiodini, P.; Panagiotakos, D.; Giugliano, D. A journey into a Mediterranean diet and type 2 diabetes: A systematic review with meta-analyses. BMJ Open, 2015; 5: e008222.
- 108. Kastorini, C.M.; Milionis, H.J.; Esposito, K.; Giugliano, D.; Goudevenos, J.A.; Panagiotakos, D.B. The effect of Mediterranean diet on metabolic syndrome and its components: A meta-analysis of 50 studies and 534,906 individuals. *J. Am. Coll. Cardiol.*, 2011; 57: 1299–1313.
- 109. Schwingshackl, L.; Missbach, B.; Konig, J.; Hoffmann, G. Adherence to a Mediterranean diet and risk of diabetes: A systematic review and meta-analysis. *Public Health Nutr.*, 2015; *18*: 1292–1299.
- 110.Koloverou, E.; Esposito, K.; Giugliano, D.; Panagiotakos, D. The effect of Mediterranean diet on the development of type 2 diabetes mellitus: A meta-analysis of 10 prospective studies and 136,846 participants. *Metab. Clin. Exp.*, 2014; *63*: 903–911.
- 111.Salas-Salvado, J.; Garcia-Arellano, A.; Estruch, R.; Marquez-Sandoval, F.; Corella, D.; Fiol, M.; Gomez-Gracia, E.; Vinoles, E.; Aros, F.; Herrera, C.; et al. Components of the Mediterranean-type food pattern and serum inflammatory markers among patients at high risk for cardiovascular disease. *Eur. J. Clin. Nutr.*, 2008; 62: 651–659.
- 112.Martinez-Gonzalez, M.A.; Garcia-Lopez, M.; Bes-Rastrollo, M.; Toledo, E.; Martinez-Lapiscina, E.H.; Delgado-Rodriguez, M.; Vazquez, Z.; Benito, S.; Beunza, J.J. Mediterranean diet and the incidence of cardiovascular disease: A Spanish cohort. *Nutr. Metab. Cardiovasc. Dis.*, 2011; 21: 237–244.
- 113.Fito, M.; Estruch, R.; Salas-Salvado, J.; Martinez-Gonzalez, M.A.; Aros, F.; Vila, J.; Corella, D.; Diaz, O.; Saez, G.; de la Torre, R.; et al. Effect of the Mediterranean diet on heart failure biomarkers: A randomized sample from the PREDIMED trial. *Eur. J. Heart Fail.*, 2014; *16*: 543–550.
- 114.Estruch, R.; Ros, E.; Salas-Salvado, J.; Covas, M.I.; Corella, D.; Aros, F.; Gomez-Gracia, E.; Ruiz-Gutierrez, V.; Fiol, M.; Lapetra, J.; et al. Primary prevention of cardiovascular disease with a Mediterranean diet. N. Engl. J. Med., 2013; 368: 1279–1290.
- 115.Serra-Majem, L.; Roman, B.; Estruch, R. Scientific evidence of interventions using the Mediterranean diet: A systematic review. *Nutr. Rev.*, 2006; 64: S27–S47.
- 116.Esposito, K.; Kastorini, C.M.; Panagiotakos, D.B.; Giugliano, D. Mediterranean diet and weight loss: Meta-analysis of randomized controlled trials. *Metab. Syndr. Relat. Disord.*, 2011; 9: 1–12.
- 117.Razquin, C.; Martinez, J.A.; Martinez-Gonzalez, M.A.; Mitjavila, M.T.; Estruch, R.; Marti, A. A 3 years follow-up of a Mediterranean diet rich in virgin olive oil is associated with high plasma antioxidant capacity and reduced body weight gain. *Eur. J. Clin. Nutr.*, 2009; 63: 1387–1393.

- 118.Bertoli, S.; Spadafranca, A.; Bes-Rastrollo, M.; Martinez-Gonzalez, M.A.; Ponissi, V.; Beggio, V.; Leone, A.; Battezzati, A. Adherence to the Mediterranean diet is inversely related to binge eating disorder in patients seeking a weight loss program. *Clin. Nutr.*, 2015; *34*: 107–114.
- 119.Rios-Hoyo, A.; Cortes, M.J.; Rios-Ontiveros, H.; Meaney, E.; Ceballos, G.; Gutierrez-Salmean, G. Obesity, Metabolic Syndrome, and Dietary Therapeutical Approaches with a Special Focus on Nutraceuticals (Polyphenols): A Mini-Review. *Int. J. Vitam. Nutr. Res.*, 2014; 84: 113–123.
- 120. Juraschek, S.P.; Guallar, E.; Appel, L.J.; Miller, E.R., 3rd. Effects of vitamin C supplementation on blood pressure: A meta-analysis of randomized controlled trials. *Am. J. Clin. Nutr.*, 2012; *95*: 1079–1088.
- 121.Michels, A.J.; Frei, B. Myths, artifacts, and fatal flaws: Identifying limitations and opportunities in vitamin C research. *Nutrients*, 2013; *5*: 5161–5192.
- 122.Frei, B.; Birlouez-Aragon, I.; Lykkesfeldt, J. Authors' perspective: What is the optimum intake of vitamin C in humans? *Crit. Rev. Food Sci. Nutr.*, 2012; *52*: 815–829.
- 123.Mason, S.A.; della Gatta, P.A.; Snow, R.J.; Russell, A.P.; Wadley, G.D. Ascorbic acid supplementation improves skeletal muscle oxidative stress and insulin sensitivity in people with type 2 diabetes: Findings of a randomized controlled study. *Free Radic. Biol. Med.*, 2016; 93: 227–238.
- 124. Chambial, S.; Dwivedi, S.; Shukla, K.K.; John, P.J.; Sharma, P. Vitamin C in Disease Prevention and Cure: An Overview. *Indian J. Clin. Biochem.*, 2013; 28: 314–328.
- 125.Block, G.; Jensen, C.D.; Dalvi, T.B.; Norkus, E.P.; Hudes, M.; Crawford, P.B.; Holland, N.; Fung, E.B.; Schumacher, L.; Harmatz, P. Vitamin C treatment reduces elevated C-reactive protein. *Free Radic. Biol. Med.*, 2009; 46: 70–77.
- 126.Ashor, A.W.; Siervo, M.; Lara, J.; Oggioni, C.; Afshar, S.; Mathers, J.C. Effect of vitamin C and vitamin E supplementation on endothelial function: A systematic review and meta-analysis of randomised controlled trials. *Br. J. Nutr.*, 2015; *113*: 1182–1194.
- 127.Kim, S.M.; Lim, S.M.; Yoo, J.A.; Woo, M.J.; Cho, K.H. Consumption of high-dose vitamin C (1250 mg per day) enhances functional and structural properties of serum lipoprotein to improve antioxidant, anti-atherosclerotic, and anti-aging effects via regulation of anti-inflammatory microRNA. *Food Funct.*, 2015; 6: 3604–3612.
- 128.Monfared, S.; Larijani, B.; Abdollahi, M. Islet transplantation and antioxidant management: A comprehensive review. *World J. Gastroenterol.*, 2009; *15*: 1153–1161.
- 129.German Nutrition Society (DGE). New Reference Values for Vitamin C Intake. *Ann. Nutr. Metab.*, 2015; 67: 13–20.
- 130.Mamede, A.C.; Tavares, S.D.; Abrantes, A.M.; Trindade, J.; Maia, J.M.; Botelho, M.F. The role of

- vitamins in cancer: A review. *Nutr. Cancer*, 2011; 63: 479–494.
- 131.Moser, M.A.; Chun, O.K. Vitamin C and Heart Health: A Review Based on Findings from Epidemiologic Studies. *Int. J. Mol. Sci.*, 2016; *17*: 1328.
- 132. Vilaplana-Perez, C.; Aunon, D.; Garcia-Flores, L.A.; Gil-Izquierdo, A. Hydroxytyrosol and potential uses in cardiovascular diseases, cancer, and AIDS. *Front. Nutr.*, 2014; *1:* 18.
- 133.Achmon, Y.; Fishman, A. The antioxidant hydroxytyrosol: Biotechnological production challenges and opportunities. *Appl. Microbiol. Biotechnol.*, 2015; 99: 1119–1130.
- 134.Bulotta, S.; Celano, M.; Lepore, S.M.; Montalcini, T.; Pujia, A.; Russo, D. Beneficial effects of the olive oil phenolic components oleuropein and hydroxytyrosol: Focus on protection against cardiovascular and metabolic diseases. *J. Transl. Med.*, 2014; 12: 219.
- 135.EFSA NDA Panel (EFSA Panel on Dietetic Products, Nutrition and Allergies). Scientific Opinion on the substantiation of health claims related to polyphenols in olive and protection of LDL particles from oxidative damage (ID 1333, 1638, 1639, 1696, 2865), maintenance of normal blood HDL cholesterol concentrations (ID 1639). EFSA J., 2011; 9: 2033–2058.
- 136.Scoditti, E.; Nestola, A.; Massaro, M.; Calabriso, N.; Storelli, C.; De Caterina, R.; Carluccio, M.A. Hydroxytyrosol suppresses MMP-9 and COX-2 activity and expression in activated human monocytes via PKCalpha and PKCbeta1 inhibition. *Atherosclerosis*, 2014; 232: 17–24.
- 137.Giordano, E.; Dangles, O.; Rakotomanomana, N.; Baracchini, S.; Visioli, F. 3-*O*-Hydroxytyrosol glucuronide and 4-*O*-hydroxytyrosol glucuronide reduce endoplasmic reticulum stress in vitro. *Food Funct.*. 2015; *6*: 3275–3281.
- 138.Granados-Principal, S.; Quiles, J.L.; Ramirez-Tortosa, C.L.; Sanchez-Rovira, P.; Ramirez-Tortosa, M.C. Hydroxytyrosol: From laboratory investigations to future clinical trials. *Nutr. Rev.*, 2010; 68: 191–206.
- 139. Carluccio, M.A.; Siculella, L.; Ancora, M.A.; Massaro, M.; Scoditti, E.; Storelli, C.; Visioli, F.; Distante, A.; De Caterina, R. Olive oil and red wine antioxidant polyphenols inhibit endothelial activation: Antiatherogenic properties of Mediterranean diet phytochemicals. *Arterioscler. Thromb. Vasc. Biol.*, 2003; 23: 622–629.
- 140. Visioli, F.; Bernardini, E. Extra virgin olive oil's polyphenols: Biological activities. *Curr. Pharm.*, *Des.*, 2011; *17*: 786–804.
- 141. Nabavi, S.F.; Russo, G.L.; Daglia, M.; Nabavi, S.M. Role of quercetin as an alternative for obesity treatment: You are what you eat! *Food Chem.*, 2015; *179*: 305–310.

- 142. Vinayagam, R.; Xu, B. Antidiabetic properties of dietary flavonoids: A cellular mechanism review. *Nutr. Metab.*, 2015; *12*: 60.
- 143. Shibata, T.; Nakashima, F.; Honda, K.; Lu, Y.J.; Kondo, T.; Ushida, Y.; Aizawa, K.; Suganuma, H.; Oe, S.; Tanaka, H.; et al. Toll-like receptors as a target of food-derived anti-inflammatory compounds. *J. Biol. Chem.*, 2014; 289: 32757–32772.
- 144.Ahn, J.; Lee, H.; Kim, S.; Park, J.; Ha, T. The antiobesity effect of quercetin is mediated by the AMPK and MAPK signaling pathways. *Biochem. Biophys. Res. Commun.*, 2008; *373*: 545–549.
- 145.Fang, X.K.; Gao, J.; Zhu, D.N. Kaempferol and quercetin isolated from Euonymus alatus improve glucose uptake of 3T3-L1 cells without adipogenesis activity. *Life Sci.*, 2008; 82: 615–622.
- 146.Clark, J.L.; Zahradka, P.; Taylor, C.G. Efficacy of flavonoids in the management of high blood pressure. *Nutr. Rev.*, 2015; 73: 799–822.
- 147.D'Andrea, G. Quercetin: A flavonol with multifaceted therapeutic applications? *Fitoterapia*, 2015; *106*: 256–271.
- 148.Larson, A.; Witman, M.A.; Guo, Y.; Ives, S.; Richardson, R.S.; Bruno, R.S.; Jalili, T.; Symons, J.D. Acute, quercetin-induced reductions in blood pressure in hypertensive individuals are not secondary to lower plasma angiotensin-converting enzyme activity or endothelin-1: Nitric oxide. *Nutr. Res.*, 2012; *32*: 557–564.
- 149.Tome-Carneiro, J.; Gonzalvez, M.; Larrosa, M.; Yanez-Gascon, M.J.; Garcia-Almagro, F.J.; Ruiz-Ros, J.A.; Tomas-Barberan, F.A.; Garcia-Conesa, M.T.; Espin, J.C. Resveratrol in primary and secondary prevention of cardiovascular disease: A dietary and clinical perspective. *Ann. N. Y. Acad. Sci.*, 2013; 1290: 37–51
- 150.Leonard, S.S.; Xia, C.; Jiang, B.H.; Stinefelt, B.; Klandorf, H.; Harris, G.K.; Shi, X. Resveratrol scavenges reactive oxygen species and effects radical-induced cellular responses. *Biochem. Biophys. Res. Commun.*, 2003; *309*: 1017–1026.
- 151.Ren, Z.; Wang, L.; Cui, J.; Huoc, Z.; Xue, J.; Cui, H.; Mao, Q.; Yang, R. Resveratrol inhibits NF-κB signaling through suppression of p65 and IκB kinase activities. *Die Pharm.*, 2013; 68: 689–694.
- 152.Latruffe, N.; Lancon, A.; Frazzi, R.; Aires, V.; Delmas, D.; Michaille, J.J.; Djouadi, F.; Bastin, J.; Cherkaoui-Malki, M. Exploring new ways of regulation by resveratrol involving miRNAs, with emphasis on inflammation. *Ann. N. Y. Acad. Sci.*, 2015; *1348*: 97–106.
- 153.Hausenblas, H.A.; Schoulda, J.A.; Smoliga, J.M. Resveratrol treatment as an adjunct to pharmacological management in type 2 diabetes mellitus—Systematic review and meta-analysis. *Mol. Nutr. Food Res.*, 2015; 59: 147–159.
- 154.Liu, K.; Zhou, R.; Wang, B.; Mi, M.T. Effect of resveratrol on glucose control and insulin sensitivity:

- A meta-analysis of 11 randomized controlled trials. *Am. J. Clin. Nutr.*, 2014; *99*: 1510–1519.
- 155.Bitterman, J.L.; Chung, J.H. Metabolic effects of resveratrol: Addressing the controversies. *Cell. Mol. Life Sci.*, 2015; 72: 1473–1488.
- 156.Han, S.; Park, J.S.; Lee, S.; Jeong, A.L.; Oh, K.S.; Ka, H.I.; Choi, H.J.; Son, W.C.; Lee, W.Y.; Oh, S.J.; et al. CTRP1 protects against diet-induced hyperglycemia by enhancing glycolysis and fatty acid oxidation. *J. Nutr. Biochem.*, 2016; 27: 43–52.
- 157.Gambini, J.; Ingles, M.; Olaso, G.; Lopez-Grueso, R.; Bonet-Costa, V.; Gimeno-Mallench, L.; Mas-Bargues, C.; Abdelaziz, K.M.; Gomez-Cabrera, M.C.; Vina, J.; et al. Properties of Resveratrol: In Vitro and In Vivo Studies about Metabolism, Bioavailability, and Biological Effects in Animal Models and Humans. Oxid. Med. Cell. Longev., 2015; 2015: 837042.
- 158. Yang, C.S.; Suh, N. Cancer prevention by different forms of tocopherols. *Top. Curr. Chem.*, 2013; *329*: 21–33.
- 159. Jiang, Q. Natural forms of vitamin E: Metabolism, antioxidant, and anti-inflammatory activities and their role in disease prevention and therapy. *Free Radic. Biol. Med.*, 2014; 72: 76–90.
- 160. Witting, P.K.; Upston, J.M.; Stocker, R. The molecular action of alpha-tocopherol in lipoprotein lipid peroxidation. Pro- and antioxidant activity of vitamin E in complex heterogeneous lipid emulsions. In *Fat-Soluble Vitamins*; Quinn, P.J., Kagan, V.E., Eds.; Springer: New York, NY, USA; 345–390.
- 161.Saboori, S.; Shab-Bidar, S.; Speakman, J.R.; Yousefi Rad, E.; Djafarian, K. Effect of vitamin E supplementation on serum C-reactive protein level: A meta-analysis of randomized controlled trials. *Eur. J. Clin. Nutr.*, 2015; 69: 867–873.
- 162. Azzi, A.; Meydani, S.N.; Meydani, M.; Zingg, J.M. The rise, the fall and the renaissance of vitamin E. *Arch. Biochem. Biophys.*, 2016; 595: 100–108.
- 163.Raederstorff, D.; Wyss, A.; Calder, P.C.; Weber, P.; Eggersdorfer, M. Vitamin E function and requirements in relation to PUFA. *Br. J. Nutr.*, 2015; *114*: 1113–1122.
- 164.Loffredo, L.; Perri, L.; Di Castelnuovo, A.; Iacoviello, L.; De Gaetano, G.; Violi, F. Supplementation with vitamin E alone is associated with reduced myocardial infarction: A meta-analysis. Nutr. Metab. Cardiovasc. Dis., 2015; 25: 354–363.
- 165. Giampieri, F.; Tulipani, S.; Alvarez-Suarez, J.M.; Quiles, J.L.; Mezzetti, B.; Battino, M. The strawberry: Composition, nutritional quality, and impact on human health. *Nutrition*, 2012; 28: 9–19.
- 166.Amiot, M.J.; Riva, C.; Vinet, A. Effects of dietary polyphenols on metabolic syndrome features in humans: A systematic review. *Obes. Rev.*, 2016; *17:* 573–586.
- 167. Smeriglio, A.; Barreca, D.; Bellocco, E.; Trombetta, D. Chemistry, Pharmacology and Health Benefits of

- Anthocyanins. *Phytother.* Res., 2016; 30: 1265–1286.
- 168.Lila, M.A. Anthocyanins and Human Health: An In Vitro Investigative Approach. *J. Biomed. Biotechnol.*, 2004; 2004: 306–313.
- 169.Stull, A.J.; Cash, K.C.; Johnson, W.D.; Champagne, C.M.; Cefalu, W.T. Bioactives in blueberries improve insulin sensitivity in obese, insulin-resistant men and women. *J. Nutr.*, 2010; *140*: 1764–1768.
- 170.Zhu, Y.; Xia, M.; Yang, Y.; Liu, F.; Li, Z.; Hao, Y.; Mi, M.; Jin, T.; Ling, W. Purified anthocyanin supplementation improves endothelial function via NO-cGMP activation in hypercholesterolemic individuals. *Clin. Chem.*, 2011; *57*: 1524–1533.
- 171.Qin, Y.; Xia, M.; Ma, J.; Hao, Y.; Liu, J.; Mou, H.; Cao, L.; Ling, W. Anthocyanin supplementation improves serum LDL- and HDL-cholesterol concentrations associated with the inhibition of cholesteryl ester transfer protein in dyslipidemic subjects. *Am. J. Clin. Nutr.*, 2009; *90*: 485–492.
- 172.Zhu, Y.; Ling, W.; Guo, H.; Song, F.; Ye, Q.; Zou, T.; Li, D.; Zhang, Y.; Li, G.; Xiao, Y.; et al. Anti-inflammatory effect of purified dietary anthocyanin in adults with hypercholesterolemia: A randomized controlled trial. *Nutr. Metab. Cardiovasc. Dis.*, 2013; 23: 843–849.
- 173.Zhu, Y.; Huang, X.; Zhang, Y.; Wang, Y.; Liu, Y.; Sun, R.; Xia, M. Anthocyanin supplementation improves HDL-associated paraoxonase 1 activity and enhances cholesterol efflux capacity in subjects with hypercholesterolemia. *J. Clin. Endocrinol. Metab.*, 2014; 99: 561–569.
- 174.Karlsen, A.; Retterstol, L.; Laake, P.; Paur, I.; Bohn, S.K.; Sandvik, L.; Blomhoff, R. Anthocyanins inhibit nuclear factor-kappaB activation in monocytes and reduce plasma concentrations of proinflammatory mediators in healthy adults. *J. Nutr.*, 2007; *137*; 1951–1954.
- 175.Keske, M.A.; Ng, H.L.; Premilovac, D.; Rattigan, S.; Kim, J.A.; Munir, K.; Yang, P.; Quon, M.J. Vascular and metabolic actions of the green tea polyphenol epigallocatechin gallate. *Curr. Med. Chem.*, 2015; 22: 59–69.
- 176.Johnson, R.; Bryant, S.; Huntley, A.L. Green tea and green tea catechin extracts: An overview of the clinical evidence. *Maturitas*, 2012; 73: 280–287.
- 177. Huang, J.; Wang, Y.; Xie, Z.; Zhou, Y.; Zhang, Y.; Wan, X. The anti-obesity effects of green tea in human intervention and basic molecular studies. *Eur. J. Clin. Nutr.*, 2014; 68: 1075–1087.

178. Hursel, R.; Westerterp-Plantenga, M.S. Catechinand caffeine-rich teas for control of body weight in humans. *Am. J. Clin. Nutr.*, 2013; *98*: 1682S–1693S.

دور التغذية في الوقاية من وإدارة متلازمة الأيض: مقاربات قائمة على الأدلة المخص: الملخص:

الخلفية: تشمل متلازمة الأيض مجموعة من الاضطرابات الأيضية المتشابكة، بما في ذلك السمنة، ارتفاع السكر في الدم، اضطراب الدهون، وارتفاع ضغط الدم. أصبحت الحالة أكثر انتشارًا عالميًا، مما يتماشى مع العوامل المرتبطة بنمط الحياة مثل العادات الغذائية السيئة وقلة النشاط البدني. تسهم متلازمة الدم. أصبحت الحالة أكثر انتشارًا عالميًا، مما يتماشى مع العوامل المرتبطة بنمط الحياة مثل العادات الغذائية المسكري من النوع 2.

الهدف: تهدف هذه المراجعة إلى تقييم دور أنماط التغذية المختلفة والمركبات البيولوجية النشطة في الوقاية من وإدارة متلازمة الأيض، باستُخدام مقاربات قائمة على الأدلة.

الطرق: أجرينا مراجعة شاملة للأدبيات، مع التركيز على تأثير الحميات المقيدة للطاقة، الأحماض الدهنية أوميغا-3، حميات منخفضة المؤشر الجلايسيمي/التحميل الجلايسيمي، السعة الإجمالية لمضادات الأكسدة، الحميات العالية البروتين، أنماط تناول الوجبات المتكررة، النظام الغذائي المتوسطي، والمواد الغذائية المحددة مثل فيتامين C وهيدروكسي تيروسول على متلازمة الأيض.

النتائج: الحميات المقيدة للطاقة فعالة في تقليل الوزن وتحسين المؤشرات الأيضية، بما في ذلك خفض مستويات الكوليسترول LDL والدهون الثلاثية في المؤشر الدهنية أوميغا-3 أدلة متوسطة على تقليل مخاطر الأمراض القلبية والالتهابات. تساعد الحميات منخفضة المؤشر

الجلايسيمي/التحميل الجلايسيمي في استقرار مستويات السكر في الدم، بينما تحسن الحميات الغنية بمضادات الأكسدة من الاستجابة للأكسدة والالتهابات. قد تعزز الحميات العالية البروتين الشبع والنتائج الأيضية، على الرغم من أن النتائج غير متسقة يرتبط النظام الغذائي المتوسطي بغوائد ملحوظة، بما في ذلك تقليل مخاطر مرض السكري من النوع 2 والأمراض القلبية الوعائية. تقدم المركبات البيولوجية النشطة مثل فيتامين C وهيدروكسي تيروسول فوائد مضادة نقليل مخاطر مرض السكري من النوع 2 والأمراض القلبية الوعائية. تقدم المركبات البيولوجية النشطة مثل فيتامين C وهيدروكسي تيروسول فوائد مضادة للالتهابات.

الاستنتاج: تلعب التدخلات الغذائية دورًا حيويًا في إدارة متلازمة الأيض. بينما تُظهر الحميات المقيدة للطاقة والنظام الغذائي المتوسطي فوائد كبيرة، تتفاوت فعالية الأنماط الغذائية الأخرى. يمكن أن تعزز استراتيجيات التغذية الشخصية التي تشمل المركبات البيولوجية النشطة من إدارة المتلازمة والوقاية منها. الكلمات المفتاحية: متلازمة الأيض، أنماط التغذية، المركبات البيولوجية النشطة، السمنة، ارتفاع السكر في الدم، اضطراب الدهون، ارتفاع ضغط الدم، المتوسطي. النظام الغذائي المتوسطي.

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