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Role of phytochemicals in the management of metabolic syndrome

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ABSTRACT

Background: The World Health Organization (WHO) for some years has been focusing on what is now commonly referred to as an "epidemic of obesity and diabetes" ("diabesity"): behind this outbreak, there are several risk factors grouped in what is called "metabolic syndrome" (MetS). The basis of this "epidemic" is either a diet too often characterized by excessive consumption of saturated and trans-esterified fatty acids, simple sugars and salt, either a sedentary lifestyle.
Purpose: The aim of this review is to focus on the phytochemicals that have a more positive effect on the treatment and/or prevention of MetS.
Chapters: Treatment strategies for MetS include pharmacologic and non-pharmacologic options, with varying degrees of success rate. The first is indicated for patients with high cardiovascular risk, while the second one is the most cost-effective preventive approach for subjects with borderline parameters and for patients intolerant to pharmacological therapy. MetS non-pharmacological treatments could involve the use of nutraceuticals, most of which has plant origins (phytochemicals), associated with lifestyle improvement. The chapter will discuss the available evidence on soluble fibres from psyllium and other sources, cinnamaldehyde, cinnamic acid and other cinnamon phytochemicals, berberine, corosolic acid from banaba, charantin from bitter gourd, catechins and flavonols from green tea and cocoa. Vegetable omega-3 polyunsaturated fatty acids, alliin from garlic, soy peptides, and curcumin from curcuma longa.
Conclusion: Some nutraceuticals, when adequately dosed, should improve a number of the MetS components.

Introduction

Metabolic syndrome (MetS) is a clinical entity substantially heterogeneous, represented by the coexistence of multiple alterations, in particular abdominal obesity, insulin-resistance, hypertension and dyslipidaemia (high TG and low HDL-C values), associated with an increased risk to develop cardiovascular diseases, type 2 diabetes and for all-cause mortality (Wu et al. 2010).

The most commonly accepted definition of MetS includes three or more of the following signs: waist circumference > 102 cm (male) or > 88 cm (female), TG > 1.7 mmol/l, HDL cholesterol < 1.0 mmol/l (male) or <1.3 mmol/l (female), blood pressure > 135/85 mmHg on medication, fasting plasma glucose (FPG) > 6.1 mmol/l (Malik et al. 2004; Grundy et al. 2005).

The cornerstone in the treatment of MetS is based on an improvement of lifestyle, promoting physical activity and a balanced low-energy diet, which is also the most cost-effective approach to this condition. When life-style modification has improved the MetS features, but further improvement is required, before to begin a (often multiple) pharmacological therapy, some phytochemicals could be also useful tools in the treatment of one or more MetS components (Table 1) (Graf et al. 2010). In some cases, the use of nutraceuticals could also be considered in already pharmacologically treated patients in support to drugs when the therapeutic target has not been reached (Grundy et al. 2005; NCEP expert panel 2001).

Giving the large number of phytochemicals with proposed positive effects on Mets, the purpose of this review is to analyse those that have had a demonstrated impact on more than one MetS components in clinical trials, and in particular those having an effect on insulin-resistance, the pathophysiological background of MetS.

Abbreviations: ACE, angiotensin converting enzyme; ALA, alpha-linoleic acid; AMPK, AMP-activated protein kinase; DHA, docosahexaenoic acid; EPA, eicosapentaenoic acid; FPG, fasting plasma glucose; GLP-1, glucagon like peptide-1; GLUT, glucose transporter; HbA1c, glycated haemoglobin; HBF-4-alpha, hepatic nuclear factor 4-alpha, HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol; MAPK, mitogen-activated protein kinase; MetS, metabolic syndrome; NF-kB, nuclear factor Kappa-B; NO, nitric oxide; OGTT, 75-g glucose tolerance test; PCSK9, proprotein convertase subtilisin/kexin type 9; PGG, penta-O-galloyl-glucopyranose; PPAR, peroxisome proliferator-activated receptor; PUFAs, polyunsaturated fatty acids; RBP-4, retinol binding protein-4; TG, triglcyerides; TGF-beta, transforming growth factor-beta; WMD, weighted mean difference.

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Table 1
Clinical studies on nutraceuticals in diabetes mellitus and metabolic syndrome.

Reference	Intervention	Participants (n)	Duration of intervention	Outcome measures	Main results
Vitamin C (ascorbic acid)					
Chen et al. (2006)	Vitamin C (800 mg/day)	Subjects with T2DM with low plasma vitamin C (<40 μM) (32)	4 weeks	FPG, FPI, Forearm blood flow	No significant effect
Dakhale et al. (2011)	Vitamin C (1 g/day) with metformin or placebo with metformin	Type 2 DM subjects (70)	12 weeks	FPG, PPBG, HBA1c	Significant reduction in all parameters
Vitamin E (α-tocopherol)					
The Heart Outcomes Prevention Evaluation Study Investigators (2000)	Vitamin E (400 IU daily) or placebo and an angiotensin-converting–enzyme inhibitor (ramipril) or placebo	Subjects with high risk for cardiovascular disease, in particular with cardiovascular disease or diabetes in addition to one other risk factor. (9541)	4,5 years	Major CV events	No apparent effect on cardiovascular outcomes.
Sesso et al. (2008)	Vitamin E (400 IU every other day) vs. placebo or Vitamin C (500 mg daily) vs. placebo	Male physicians (14,641)	10 years	CV events	The supplementation doesn't reduce the risk of major CV events
Vitamin D					
Pittas et al. (2007)	Calcium citrate (500 mg) + vitamin D3 (700 IU daily)	Non diabetic Caucasian adults aged > 65 years (314)	3 years	FPG, IS	The supplementation attenuates the increases in glycemia and IR
Pilz et al. (2015)	Vitamin D3 (2800 IU daily as oily drops) or placebo	Subjects with arterial hypertension and 25-hydroxyvitamin D levels below 30 ng/mL (200)	8 weeks	BP, Cardiovascular risk factors	No significant effects on blood pressure and CV risk factors
Zhou et al. (2014)	Vitamin D3 (0.50 μg daily)	Subjects with T2DM (164)	12 weeks	BMI, WC, FPG, FPI, HbA1C, HOMA-IR, IR	Significant improvement in all parameters
Flavonoids					
Dower et al. (2015)	Epicatechin (100 mg/d), quercetin-3-glucoside (160 mg/d) or placebo	Subjects with BP between 125-160 mm Hg (37)	4 weeks	Vascular function and cardiometabolic health	Epicatechin improved FPI and IR. There were not other significant results neither with the supplementation with epicatechin either with quercetin-3-glucoside.
West et al. (2014)	Active group: 37 g/d of dark chocolate and a sugar-free cocoa beverage (total cocoa = 22 g/d, total flavanols (TF) = 814 mg/d); control group: low-flavanol chocolate bar and a cocoa-free beverage with no added sugar (TF = 3 mg/d)	Overweight adults(30)	4 weeks	CVD risk Endothelial function	Enhanced vasodilation and significant reductions in arterial stiffness in women.
Mink et al. (2007)	Total flavonoids intake: 0.6–133.1 mg/day 133.2–201.8 mg/day 201.9–281.9 mg/day 282.0–425.2 mg/day 425.3–3524.4 mg/day	Postmenopausal women (34,489)	16 years	CV and all-cause mortality	Reduced risk in death due to CV and all causes
Omega-3 fatty acids					
Tsitouras et al. (2008)	Fatty fish (720 g/week) + sardine oil (15 mL/day; 4–5 g n-3) or olive and corn oil	Healthy men and women (12)	8 weeks	FPG, Insulin concentration	No change in FPG and insulin Improved IR in 3 h OGTT

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