Weight Loss

Subjects: Primary Health Care

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Overweight and obesity are related pathological conditions with a significant impact at the cardiovascular, metabolic, musculoskeletal, and oncological levels, representing a significant global public health problem. The traditionally proposed therapeutic approaches act at the nutritional, psychological, lifestyle (abolishing sedentary lifestyle and promoting physical exercise), and pharmacological levels, in combination with the consumption of food supplements.

microbiota prebiotic weight loss food supplements botanicals nutraceutical

1. Introduction

Overweight and obesity are related pathological conditions with a significant impact at the cardiovascular, metabolic, musculoskeletal, and oncological levels, representing a significant global public health problem [1]. The traditionally proposed therapeutic approaches act at the nutritional, psychological, lifestyle (abolishing sedentary lifestyle and promoting physical exercise), and pharmacological levels, in combination with the consumption of food supplements [2]. Watanabe et al. recently identified and examined 33 food supplements most used for weight loss, dividing them according to the main effect and depending on the primary impact on nutrient absorption, appetite regulation, energy expenditure modulation, and fat and carbohydrate metabolism [2]. Substances considered prebiotic, which specifically stimulate components of the microbiota capable of providing positive effects, such as increasing immune function and protection from pathogens, improve host metabolism and nutrient absorption [3]. This can have a significant impact on the metabolism of various substances used as food supplements.

2. Results

The retrieved data indicated that many different food supplements, both herbal and not, have been investigated in humans for their prebiotic effect and their capacity to modulate gut microbiota. (**Table 1**). In detail, we found robust data for the following: Supplements with the main goal of nutrient absorption (green tea, ginseng, chitosan, β-glucans, psyllium, guar gum, and inulin); Supplements with the main goal of appetite regulation (whey proteins and chlorogenic acid); Supplements with the main goal of energy expenditure modulation (curcumin and L-carnitine); Supplements with the main goal of fat metabolism (resveratrol and flaxseed).

Table 1. Summary of clinical trials reporting prebiotic effects of these natural substances and their impact on gut microflora.

Substance	Subjects	Intervention	Clinical Outcome	Gut Microflora Modifications
Substances with Evidence of Weight Loss Associated with Modifications of the Microbiota				
Chlorogenic Acid [4]	26 patients with diabetes and non-alcoholic fatty liver disease (NAFLD)	3 months of 200 mg caffeine plus 200 mg chlorogenic acid supplementation	Significant decrease in body weight	Non-significative bifidobacteria increase in the caffeine plus chlorogenic acid group
Inulin [5][6][7][8][9][10]	44 healthy adults with mild constipation	12 g/day inulin intake	Gut function improvement	Changes in relative abundances of *Anaerostipes*, *Bilophila*, and *Bifidobacterium* spp.
	26 healthy individuals	9 g/die inulin intake	Greater satiety	Greater proportions of the genus *Bifidobacterium*, a reduced level of non-classified Clostridiales. and a tendency to decrease Oxalobacteraceae
	30 obese women	Inulin/oligofructose 50/50 mix 16 g/day for 3 months	Slight decrease in fat mass and plasma levels of lactate and phosphatidylcholine	*Bifidobacterium* spp. and *Faecalibacterium prausnitzii* increase and *Bacteroides intestinalis, Bacteroides vulgatus.* and *Propionibacterium* spp. reduction
	12 overweight adults	20 g/day of inulin-propionate ester		Increase in Actinobacteria, decrease in Clostridia; decrease in the proportion of Clostridiales order. *Anaerostipes hadrus*, *Bifidobacterium faecale. Bacteroides caccae*, *Bacteroides uniformis*, *Bacteroides xylanisolvens*, and *Fusicatenibacter saccharivorans* higher percentage and a lower percentage of *Blautia obeumin*, *Blautia lutea* and *Bacillius fluminis*, *Blautia obeum*, *Eubacterium ruminantium*, *Anaerostipes hadrus*, and *Prevotella copri*
	42 12-year-old overweight	8 g/day of oligofructose	Significant decreases in body	*Bifidobacterium* spp. increase and decrease in

Substance	Subjects	Intervention	Clinical Outcome	Gut Microflora Modifications
	subjects	enriched inulin for 16 weeks	weight and serum triglycerides	*Bacteroides vulgatus* and *Faecalibacterium prausnitzii*
P. ginseng [11]	10 obese women	8 g dry extract for 8 weeks	Weight loss effect and slight modifications of gut microbiota	In effective weight loss group, change in levels of *Blautia, Faecalibacterium* spp. In ineffective weight loss group, change in levels of *Bifidobacterium*, *Blautia*, and *Clostridium* at the genus level
Substances with Evidence of Metabolic Modifications Potentially Favorable to Weight Loss Associated with Modifications of the Microbiota				
Resveratrol (RSV) [12]	37 overweight and obese men and women	Supplementation of epigallocatechin-3-gallate and RSV (282 and 80 mg/day, respectively, for 12 weeks)	Increased fat oxidation and skeletal muscle mitochondrial oxidative capacity	Reduced abundance of Bacteroidetes phylum in men but not in women
Flaxseed [13]	58 obese postmenopausal women	Flaxseed mucilage (10 g) for 6 weeks	Improved insulin sensitivity related to the decrease in the serum C-peptide and insulin response	24 decreased species *in Faecalibacterium* genus and 8 increased species in *Clostridium* genus
Substances with Evidence of Changes in the Microbiota Associated with Other Effects (Which in the Animal Model are Associated with Weight Loss)				
β-glucans [14]	26 healthy subjects	2 months of 3 g/day of barley β-glucans	Marked increase in levels of the main SCFA	Increased levels of *Roseburia hominis*, Clostridiaceae (*Clostridium orbiscindens* and other *Clostridium* spp.), *Ruminococcus* spp. and reduced abundance of Firmicutes and Fusobacteria
Chitosan and COS [15] [16]	10 healthy volunteers	3 g chitosan/day before meal for 28-day supplement period		Increased level of *Bacteroides* spp.

Substance	Subjects	Intervention	Clinical Outcome	Gut Microflora Modifications
	120 Chinese coronary heart disease patients	COS consumption of 1-2 g/day for 6 months	Improved blood urea nitrogen and serum creatinine. Higher circulating antioxidant levels. Increased SOD and GSH serum levels. Reduced levels of ALT and AST. Improved lipid profiles	Decreased *Faecalibacterium, Alistipes*, and *Escherichia* spp. abundance. *Bacteroides*, *Megasphaera*, *Roseburia*, *Prevotella*, and *Bifidobacterium* spp., increased abundance of *Lactobacillus*, *Lactococcus*, and *Phascolarctobacterium* spp.
Curcumin [17]	30 healthy subjects (14 analyzed)	1000 mg curcumin plus 1.25 mg extract of piperine every tablet—3 times/day		Increase in *Clostridium*, *Bacteroides.*, *Citrobacter*, *Cronobacter*, *Enterobacter*, *Enterococcus*, *Klebsiella*, *Parabacteroides*, and *Pseudomonas* spp. and decreased abundance of *Blautia* and *Ruminococcus* spp.
Green Tea [18]	Healthy subjects: 8 males, 4 females	400 mL per day for two weeks	Elevation in SCFA, and reduction in bacterial LPS synthesis in feces	Increased Firmicutes to Bacteroidetes ratio, reduced fecal levels of *Fusobacterium* spp.
Guar Gum [19][20][21][22][23]	20 healthy volunteers	5 g of guar gum three times/day for 3 weeks	Improvement in defecation frequency; stool consistency; and abundance of butyrate, acetate, and amino acids	Increase in *Ruminococcus*, *Fusicatenibacter*, *Faecalibacterium*, and *Bacteroides* spp. and a reduction in *Roseburia*, *Lachnospiracea*, and *Blautia* spp.
	44 healthy volunteers	5 g/day guar gum for 3 months	Altered stool consistency	*Bifidobacterium*, *Ruminococcus*, and *Megasphaera* spp. increase and *Bacteroides* and *Phascolarctobacterium* spp. inhibited growth
	31 healthy volunteers	3.4 g/day guar gum for 21 days		Transitory bifidobacterial increase
	13 children suffering from autism spectrum disorder with concomitant	6 g/day guar gum	Increased defecation frequency and reduced irritability	Increased *Acidaminococcus* spp. and reduced genera *Streptococcus*,

Substance	Subjects	Intervention	Clinical Outcome	Gut Microflora Modifications
	dysbiosis and constipation			*Odoribacter*, and *Eubacterium* spp.
	15 hemodialysis patients with concomitant constipation	5.1 g/day guar gum for 4 weeks	Improved the individual stool form and decreased the constipation	Increase in bifidobacteria, *Bacteroides* spp. and lactobacilli and reduction in the *Clostridium* XVIII cluster
L-carnitine [24]	15 Japanese patients receiving hemodialysis	L-carnitine tablets (900 mg) for 3 months	Improved muscle discomfort, gastrointestinal disorders	Decrease in the abundance of genus *Clostridia* subcluster 4
Whey Proteins [25]	24 cross-country runners	10 weeks 20 g isolated WP + 10 g hydrolyzed WP		Increased abundance of Bacteroidetes phylum; decreased presence of health-related taxa, including *Roseburia*, *Blautia* spp., and *Bifidobacterium longum*
Psyllium [26]	8 healthy volunteers and 16 constipated patients	7 days of 7 g/day psyllium	Increased acetate, propionate, and butyrate, correlated with increased fecal water	Healthy adults increased *Veillonella* and decreased *Subdoligranulum* spp. In constipated subjects, increased levels of *Lachnospira*, *Faecalibacterium*, *Phascolarctobacterium*, *Veillonella*, and *Sutterella* spp., decreased uncultured Coriobacteria and *Christensenella* spp.

3. Discussion

The evaluation of the effectiveness and related biological mechanisms of natural products mainly used in the management of overweight depicts different targets and underlined mechanisms, including carbohydrate and fat metabolism and/or increased energy expenditure. Interestingly, current evidence suggests that the modulation of gut microflora provided by some nutraceuticals and herbal food supplements may play a relevant role in intestinal homeostasis. The analysis performed in this review underlines the effect on overweight and related pathological conditions exerted by nutraceuticals and herbal food supplements intervening in the gut microbiota structure and their reshaping abilities. In particular, this work highlights the complexity of specific modifications of the microbial environment produced by natural products. It is worth noting that in a recent review, which comprehensively took

into account the most used food supplements for the management of overweight [2], all natural products with a demonstrated prebiotic effect were included. In vivo and in vitro studies have evidenced a prebiotic effect of top selling food supplements, such as white kidney bean, glucomannan, agar, caralluma, spirulina, coffee/caffeine/guaranà, bitter orange, capsaicin, capsaicinoids and capsinoids, pyruvate, dyacilglycerol, liquorice, conjugated linoleic acid, aloe vera, grapefruit, mangosteen, chromium and lipoic acid, whereas more sound data could be retrieved for some natural products investigated in clinical trials. This review depicts the up-to-date state of the art of the fascinating complexity of gut microbiota modulation exerted by nutraceuticals and herbal food supplements investigated in clinical trials. Some of these substances have been shown to be able to act on *Bifidobacterium*; *Lactobacillus*; *Akkermansia*; and productive butyrate species, such as Faecalibacterium and *Roseburia spp.* The ability to favor the development of bifidobacteria is considerably relevant for a series of different effects, including the immuno-modulation processes and protection against pathogens; cross-talk with the butyrate producers, such as *Faecalibacterium prausnitzii* and *Roseburia spp.*; and the ability to intervene in the metabolism of macro- and micronutrients with lysis of indigestible carbohydrates, vitamin B group synthesis and antioxidants substances [27]. Furthermore, the ability to positively modulate butyrate-producing bacteria potentially confers other metabolic benefits, favoring the modulation of adipose organ function, liver and skeletal muscle function, with the amelioration of glucose levels and improved insulin sensitivity [28]. The upregulation of Lactobacillus spp. is a potentially favorable element in the management of various conditions, such as the health maintenance of reproductive [29] and urological [30] systems. Crovesy et al. also described numerous benefits in relation to weight control for different *Lactobacillus spp.*, both taken individually and combined with other nutraceutical products. [31]. Several nutraceuticals show the ability to favor the modulation of Akkermansia muciniphila , a strain actively investigated in recent years. Akkermansia muciniphila is related to a series of extremely favorable effects in the context of weight control, reduction in body fat, and the management of many of metabolic problems. Everard et. al. reported that Akkermansia muciniphila can act by increasing endocannabinoids gut levels, which play a relevant role in inflammation, gut barrier and gut peptide secretion, reverting fat-mass gain, adipose tissue inflammation, insulin resistance, and metabolic endotoxemia [32]. Xu et al. proposed that Akkermansia muciniphila also intervenes favorably in the modulation of liver and metabolic disorders related to lipid metabolism, modifying the metabolic pathways present in an obesity condition [15]. Abuqwider et. al, starting from the analysis of 804 studies, focused on 10 randomized controlled trials that showed that Akkermansia muciniphila balances the dynamics of energy management, favoring a better balance of carbohydrate metabolism with a consequent reduction in low-grade inflammatory processes, and contributed to weight management and to the improvement of the metabolic parameters related to obesity [33]. *Faecalibacterium prausnitzii* and *Rosaeburia spp.* are described as being the main producer of butyrate [34], an essential short chain fatty acid for maintaining gut homeostasis and intestinal barrier function. Their presence is correlated with a better management of inflammatory processes and immune tolerance, especially in allergy-based disorders [35].

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