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Review Article

The Effect of Fibre Intervention on Serum and Faecal Short-Chain Fatty Acids in Human with Overweight or Obesity: A Systematic Review of Human Intervention Studies

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Abstract
Overweight/ obesity is associated with many related comorbidities, such as type 2 diabetes, cardiovascular disease, and nonalcoholic fatty liver disease (NAFLD). Nutritional interventions focusing on dietary fibre and prebiotics interventions have been implemented. Fibre has been suggested to modulate gut-derived metabolites short-chain fatty acid (SCFA). We conducted a systematic review on fibre (including prebiotics) interventions to depict its effect on SCFA from faecal and blood using standard methodologies. Pubmed, Cochrane, Embase, CINAHL, and Scopus databases were systematically searched to yield peer-reviewed articles published until 31 October 2021. We included 17 articles describing fibre (including prebiotics) intervention in adult individuals with overweight/obesity. These interventions were broadly described into 3 groups: (i) fibre type food items (n = 8); (ii) fibre supplementations (i.e. prebiotics) (n = 8); (iii) prebiotic supplementation combined with CRD (n = 1). Fibre type food items intervention mostly affected the changes of acetate in faecal, whilst propionate mostly changed in the blood. Interestingly, intervention with fibre supplementation affects more the increase in faecal and blood acetate. Furthermore, fiber intervention might have an impact on the gut microbiota. Nevertheless, more well-controlled human studies are needed, with a more personalized approach perhaps based on obesity phenotype and gut microbiota profiles.

Keywords: *fibre; prebiotics; SCFA; obesity; gut microbiota*
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INTRODUCTION

Over the last decades, the prevalence of obesity was about 13% of the adult population (11% of men and 15% of women) were obese.[1] According to the Organization for Economic Cooperation and Development report data, obesity has reached epidemic proportions in developed and developing countries.[2] An imbalance between energy intake and energy expenditure results in obesity.[3] More recently, dietary content of high-fat and low fibre, sedentary lifestyle, and the gut microbiome are also involved in the development of obesity.[4–6]

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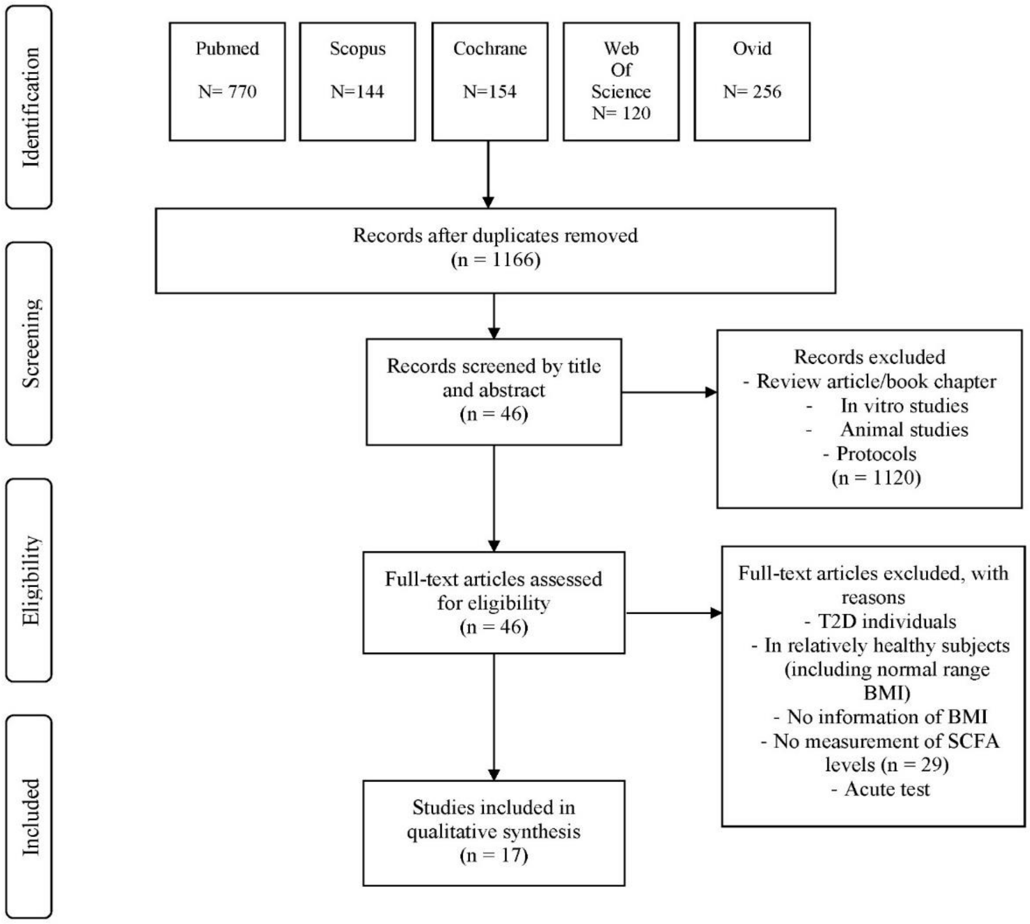

Figure 1. PRISMA 2020 flow chart delineating the study selection process

Obesity is strongly associated with many related comorbidities, such as type 2 diabetes, cardiovascular disease, and nonalcoholic fatty liver disease (NAFLD).[7] Bodyweight control by increasing physical activity and dietary-induced weight loss is still an important strategy to prevent obesity-related disorders.[8–10] Of interest, various dietary components, such as fibre, that modulate metabolic health have been of growing interest in recent years. Dietary fibre may be contributed to additional mechanisms to maintain a bodyweight that may not be mediated solely by caloric content.[11]

Growing evidence supports the critical role of dietary fibre intake as a major contributor to gut microbiota-accessible carbohydrates in managing obesity-related metabolic disorders.[12] The positive interaction between dietary fibre and the gut microbiome might improve metabolic health in humans with overweight or obese. These mechanisms may partly be explained by the beneficial metabolites of fermentation (i.e. short-chain fatty acids (SCFAs) acetate, propionate, and butyrate).[13] More interestingly, It has been reported that the SCFAs can also be transported across the gut into the circulation.[14]

Animal studies suggest that SCFAs have an important role in preventing and treating obesity-associated disorders.[15,16] However, the effect of dietary fibre on SCFAs concentration in humans with overweight/obesity is not entirely consistent. For instance, Van der Beek et al., 2018 have demonstrated that prebiotic inulin increases only serum acetate but not with other SCFAs, and does not affect on faecal SCFAs.[17] In contrast, other fibre supplementation studies have increased acetate and propionate levels in faecal samples of humans overweight or obesity.[18,19]

Of the two types of dietary fibre, water-soluble and insoluble, most soluble fibre are more fermentable and produces higher amounts of SCFAs compared to insoluble fibre.[20] For example, mixed fibre, such as yellow pea fibre, is composed of cellulose, hemicellulose, and pectin and contains a mixture of soluble and insoluble fibre with a more significant proportion of insoluble.[21] In addition to that, more recent definitions have included oligosaccharides as dietary fibre. Prebiotics is a selectively fermented ingredient that allows specific changes, both in the composition and/or activity in the gut microbiota that benefits the host's metabolic health.[22] Prospective cohort studies indicate clearly that high fibre intakes are associated with a low risk of cardiovascular diseases (CVDs).[23] However, data on adult individuals with obesity is relatively mixed.[24] Thus, it may be that the physiological effects of dietary fibre related metabolite SCFAs might not be uniform in obesity. Although the link between dietary fibre and SCFAs levels has been indicated, its effect on faecal and serum concentrations from different intervention studies is still not wholly overviewed. The current systematic review was aimed to determine the effect of fibre interventions that may modulate faecal and serum SCFAs of adult individuals with overweight or obesity.

METHODS

Study design

We utilized a systematic review design to comprehensively describe dietary fibre interventions for modulating SCFAs in adult individuals with overweight or obesity and determine pertinent knowledge gaps in this critical research area. This systematic review was guided using an approach based on the methodological framework by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses/PRISMA.[25] Ethical approval was not sought as we have only used published data for this review.

The PICOS (Patients, Intervention, Comparison/Control, Outcome, Study design) framework was also used to develop inclusion criteria.[26] We included only studies with adult individuals with overweight or obesity as participants. This review has operationalized intervention definition as dietary fibre or fibre type prebiotics supplementation. The group comparison in included studies was placebo/control. The outcome was the levels of SCFAs in faecal and serum from adult individuals with overweight or obesity following dietary fibre/fibre supplementation intervention. We included only studies with broad types of intervention study design.

Exclusion criteria were as follows: (1) any observational studies/ review/ acute test; (2) studies in animal models; (3) study intervention non-dietary fibre/fibre supplementation; (4) patient/participants were healthy and already developed type 2 diabetes (T2D); (5) study performed in children and adolescents (<18 years).

Literature search strategy and study selection

We conducted our systematic review according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines and used the newest version of the checklist.[26] The outcome of interest was the faecal and serum SCFAs levels in adults with overweight or obesity as a result of dietary fibre types intervention.

A comprehensive literature search PubMed/Medline (Medical Literature Analyses and Retrieval System Online), Cochrane Library, Web of Science, Embase database (OVID), and SCOPUS (ScienceDirect) was performed to identify articles until the 31st of October 2021. The main keywords used were "short-chain fatty acids", "scfa", "dietary fibre", "prebiotic", "obesity", and "overweight". These keywords were combined with Boolean operators (e.g. OR, AND, NOT), and All Fields or Medical subject subheading (Mesh) terms. The search terms for PubMed were: ((((("fiber"[All Fields]) OR ("dietary fiber"[All Fields]))) AND ("scfa"[All Fields])) OR ("short chain fatty acids"[All Fields])) AND ("obesity"[All Fields]).

Following the search, duplicates were removed. Two authors (A.P. and R.A.) independently screened titles and abstracts. Based on the inclusion criteria, the final study selection was done by two authors (A.P and R.A.) and approved by other authors (E.R.N., M.M., D.N.A., A.C.K). All stages from searching and data extraction and qualitative/quantitative synthesis are described in (**Figure 1)**. Any disagreements between the authors were resolved through discussion between authors.

Data extraction and management

By using standardized forms, data were extracted regarding study characteristics, all PICOS details including patients, inclusion criteria of subjects, sample size, description of intervention of each study (either dietary fibre or fibre supplementation), comparison/control, SCFA measurements, all outcome measures of the intervention (serum and faecal SCFA), as well as other relevant outcomes. Data were extracted by two authors (A.P. and R.A.). The studies were subsequently classified according to the focus and outcomes to establish key discussion areas of this review.

RESULTS

Study characteristics

Study identification and selection are detailed in the PRISMA diagram for systematic reviews (**Figure 1**). The initial search strategy generated 1444 articles, out of which 278 were excluded as duplicates. After analysis of titles and abstracts, 843 records were excluded, including review articles or book chapters, in vitro studies, animal studies, and protocols, and 46 articles were selected for full-text review. Among these, 29 studies were excluded according to exclusion criteria. Thus, a total of 17 studies were included in the qualitative synthesis (**Table 1**).[18,19,35–41,27–34]

The majority of studies (14 studies) included both sexes (male and female); the remaining three studies only included male (2 studies) or female (1 study) participants. BMI cut-offs vary between studies, 1 study included participants with BMI <28.7 kg/m^2,[27] 1 study with BMI ≤32 kg/m^2,[29] and the remaining studies (15 studies) included BMI ranging from 25 – 45 kg/m^2.[18,19,37–41,28,30–36] Furthermore, the majority of studies (11 out of 17) included adults individual with overweight/ obesity without comorbidities, whereas six studies included adults overweight/obesity with comorbidities such as hypercholesterolemia,[27,29] hypertriglyceridemia,[28] metabolic syndrome,[31] prediabetes,[32] and non-alcoholic fatty liver disease/NAFLD.[33] Three studies have conducted the research with a randomized crossover design.[28,29,40] However, two out of 3 crossover trials did not conduct a washout period. In addition, thirteen studies were designed to parallel randomized trials, and one study by Bridges et al, 1992 was a non-randomized intervention.

Types of fibre intervention for the adult individuals with overweight and obesity mostly can be grouped into (i) fibre type food items; (ii) fibre supplementation (i.e. prebiotics); and (iii) prebiotic supplementation and calorie restriction diet mode of intervention. The dietary fibre (including prebiotics supplementation) was provided alone or combined with other modes of intervention such as a caloric restriction diet (CRD). Eight studies provided fibre type food items (e.g., wheat bran, oat bran, fruit (avocado; juçara berry), whole-grain cereal, yaçon flour, Mediterranean diet, RS2-enriched wheat roll).[27,28,31,34–36,38,40] Meanwhile, eight studies used fibre supplementation only (i.e. prebiotics). The types of fibre supplementation in these eight studies consisted of inulin, galactooligosaccharides (GOS), inulin-propionate ester, yellow pea fibre, arabinoxylan, inulin-type fructans (ITF), resistant starch, and wheat bran with reduced particle size (WB RPS) fraction.[18,19,29,30,32,33,37,41] Dosages used for fibre supplementation had ranged from 10 g/d to 20 g/d, whereas food type dietary fibre doses ranged from 14 g/d to 34 g/d. Duration of intervention ranged from 1 to 12 weeks. The most common intervention duration was 12 weeks (n = 8), followed by 6 weeks (n = 4), 3 weeks (n = 2) and 1/ 4/ 8 weeks (n = 1 for each study time) (**Table 1**).

Ten studies analyzed short-chain fatty acids (SCFAs) only in faecal samples, four studies only in the serum, and the three others analyzed both in faecal and serum. Analysis techniques used to determine faecal as well as serum SCFAs, including gas chromatography (GC), gas chromatography equipped with a flame ionization detector (GC-FID), liquid chromatography-mass spectrometry (LC-MS/MS), gas chromatography-mass spectrometry (GC-MS), and high-performance liquid chromatography (HPLC). Similar techniques were used to characterize the serum (serum) SCFAs, except for 1 study that examined using a direct enzymatic spectrophotometer for acetate analysis.[27]

Type of fibre for supplementation based on fermentation rate in colon

Eight out of the nine studies that used fibre supplementation/ combined with CRD were analyzed SCFAs in the faecal. They were further classified based on the degree of fermentation of the type of fibre used, according to Wang et al. 2019.[42] Seven studies employed inulin, GOS, or arabinoxylan, all of which had fast fermentation rates, whereas one used pea fibre containing resistant starch, which had slow fermentation rates. From 5 studies that reported significant changes in faecal SCFA levels, it used fibre and prebiotics supplementation with a fast fermentation rate type. In contrast, only one study reported an elevation in acetate levels, which have used a fibre intervention with a slow fermentation rate type (**Table 2**).

The effect of fibre type food items on the blood SCFAs in human overweight/ obesity

Three studies used fibre type food items and analyzed SCFA levels in the blood.[27,31,36] The intervention group in one study had a significant increase in serum acetate. Only one study found a significant increase in serum propionate levels,[31] even though two studies reported a change in serum propionate levels. The intervention group's postprandial plasma butyrate levels were also found to be significantly increased.[36] Based on these findings, it can be summarized that fibre from food items intervention can raise blood SCFA levels, including acetate, propionate, and butyrate (**Table 3)**.

The effect of fibre type food items on the faecal SCFAs in human overweight/ obesity

Five out of eight studies that used fibre type food items, measured faecal SCFA levels. Two studies found a substantial rise in acetate,[34,35] while one study by Noakes et al, 1996 found a significant increase in butyrate among the three that showed an increase in SCFA in the intervention group. In two other research,[38,40] SCFA levels were found to be lower or there was no difference between the intervention and control groups (**Table 3**).

The effect of fibre supplementation/ combined with CRD on the blood SCFAs in human overweight/ obesity

There were four studies that analyzed blood SCFA out of the total of nine that used fiber supplementation. Only one study reported a positive effect on SCFA, an increase in acetate levels and total SCFA in the intervention group.[41] Two other research showed a decrease in butyrate levels[33] or no change in the blood SCFA levels[32], while one study could not detect the presence of SCFA in blood samples[43] (**Table 3**).

The effect of fibre supplementation/ combined with CRD on the faecal SCFAs in human overweight/obesity

There were eight studies that used fibre supplements and measured faecal SCFA levels. Three of eight studies showed a significant increase in acetate levels.[18,29,37] In contrast to faecal propionate levels which were reported to be increased by two studies[19,43], none of the studies reported changes in faecal butyrate levels (**Table 3**).

The effect of fibre intervention on gut microbiota

Furthermore, some studies (not all) have also demonstrated the gut microbiota change following fibre interventions. **Table 3** described the eleven studies (out of 17) that have investigated the gut microbiota changes. Interestingly, the acetate bacteria producer such as *Bifidobacterium*, *Akkermansia*, *Faecalibacterium*, *Lachnospira*, as well as the butyrate bacteria producer such as *Ruminococcus* and *Bacteroides*, were among the gut microbiota genus that was altered following fibre intervention in the adult individuals with overweight/ obesity. The majority of the changes in SCFA levels may be partly explained by alteration of the gut microbiota, depending on the duration of intervention. This suggests that fibre supplementation, through the gut microbiota, could stimulate the production of SCFA, particularly acetate, which is thought to play a role with metabolic regulation in overweight or obese individuals.

DISCUSSION

This review aimed to describe and determine the effect of dietary fibre/ prebiotics intervention on faecal or serum short-chain fatty acids (SCFAs) production in adult individuals with overweight or obesity. About seventeen studies were identified and deemed appropriate for inclusion in our systematic review, highlighting the dearth of recent interventional modes undertaken to modulate SCFAs levels for adult individuals with overweight or obesity. Obesity, per se, may alter the gut microbial composition, with a marked reduction in some microbiota and commensal strains, reducing the production of its metabolites.[44] The consumption of dietary fibre from diet or supplements has been proposed as an effective dietary strategy for obesity control.[45]

In our review, fibre supplementation (i.e. prebiotics) comprised approximately 50% (9 studies) of interventions discussed. They were representative of the best options available in their respective dietary supplement categories. For instance, inulin, galactooligosaccharides (GOS), and resistant starch are fibre supplement options. Roughly 40% (8 studies) of the included articles, the interventions were administered as fibre type food intervention such as wheat bran, oat bran, fruit (avocado; juçara berry), whole-grain cereal, and Mediterranean diet are among of the diet can be prescribed due to high fibre content.

Benefits of dietary fibre can be observed in a recent systematic review and meta-analysis of data from 185 prospective studies and 58 clinical trials with 4635 adult participants were included in the analyses, demonstrating a 15-30% decrease in all-cause and cardiovascular-related mortality and incidence of coronary heart disease, stroke incidence and mortality, type 2 diabetes, and colorectal cancer.[46] Furthermore, it has been suggested that adherence to dietary patterns focusing attention on fibre and polyphenols can modulate human gut microbiota.[47] Indeed, it has been shown that fibre plays a role in alleviating obesity-related health issues, potentially by modulating gut-derived metabolites SCFAs.[48]

Our outcome analysis focused only on SCFA levels, either from faecal and serum samples of adult individuals with overweight or obesity. The majority SCFAs in the form of acetate, butyrate, and propionate have been widely investigated and may have relevance in overweight or obesity interventions. It has been suggested that a decrease in absorption or greater SCFAs utilization by colonocytes may contribute to increased transport of SCFAs to the systemic circulation.[49] Furthermore, these parameters may be altered, potentially due to modulation of the gut microbiota following specific dietary fibre intervention.[48]

However, not all outcomes of SCFAs levels showed similar improvements following dietary fibre interventions in adult individuals with overweight or obesity. In this review, it seems that acetate level was predominantly increased as compared with other SCFAs following dietary fibre interventions in overweight or obese individuals. Interestingly, this increased acetate level was observed in the faecal and serum samples, followed by propionate and butyrate. An improvement in this acetate, propionate, and butyrate might be partly explained by modulation of microbiota acetate, propionate, and butyrate producer (e.g. *Bifidobacterium*, *Firmicutes*, *Prevotella*, *Akkermansia*) following fibre supplementation in individuals with overweight and obesity as shown in gut microbiota data of included studies.[18,19,30,35,36]

Of note, differential responses to SCFA levels might also be attributable to the baseline characteristics of gut microbiota. Indeed, a recent human study showed that microbiota characteristics prior to prebiotic intervention determined the outcome of gut-derived metabolites (i.e. SCFAs).[50] Next to that, the cross-feeding mechanisms during dietary fibre intervention may also play a role in the SCFAs modulation by gut microbiota.[51] Thus may argue that the fibre (including prebiotics) are not "one size fits all"; it may be due to variation in the SCFA production capacity of individuals' gut microbiota across the tested fibre (including prebiotics).

Furthermore, the mode of administration or colonic fermentation site of fibre (including prebiotics) is a crucial determinant of the metabolic response.[52] It has been shown that slowly fermentable fibres have a higher potential for influencing host metabolism, given the much higher SCFA release by the distal intestines.[53] Next to that, in this systematic review, many included studies have used faecal SCFA as a biomarker of gut-derived SCFA production. However, the body rapidly absorbs gut microbially produced SCFA. Consequently, faecal measurements may not represent *in vivo* colonic production, which is influenced by prebiotics or other colonic substrates (i.e. dietary fibre), colonic pH and microbiota composition. This may have implications for developing nutritional strategies to modulate SCFA production and improve metabolic health. Perhaps further studies should be focused on dietary fibres/ prebiotics intervention that can reach the distal colon and based on more personalized baseline gut microbiota characteristics.

Our systematic review possesses a few strengths. The number of articles included is relatively modest (17 studies), with substantial total sample size and includes only human interventional studies, ensuring recent evidence is presented. We have made every effort to incorporate relevant articles by not imposing limitations on the types of dietary fibre interventions and definitions. The review process is rigorously detailed in the Methods section to ensure the transparency and clarity of the systematic review.

On the other hand, a few limitations to our review can be identified. Systematic reviews generally involve a broad range of sources, including online databases, grey literature, electronic search engines, data archives and written scientific texts. We have performed only from major database searches, which may reduce the number of studies under consideration. The systematic review framework utilized for the review recommended electronic databases and manual hand searching of reference lists, which has been performed extensively in our review. This review only includes studies written in English, allowing a possibility of language bias. The included studies were also not subjected to critical appraisal; hence, the individual studies quality is unknown.

CONCLUSION

Various dietary fibre interventions compasses of food type fibre and prebiotics supplementation to improve metabolic health among adult individuals with overweight or obesity have been attempted. The majority of studies result in improved SCFA levels in faecal and serum samples. Particularly acetate levels are predominantly elevated following the dietary fibre intervention. Future research should focus on the fibre (including prebiotics) supplementation mode that can reach the distal colonic site and a more personalized approach by considering baseline individual phenotype and gut microbiota characteristics. The findings of this review might be used as a reference for the community, particularly Indonesians who have low fibre intake, to increase fibre consumption through dietary fibre intake or fibre supplementation.

Table 1. Characteristics of human intervention studies included in the systematic review on the effect of fibre interventions on short-chain fatty acids

Author (year)	**N[1]**	**Participants (Gender; Age (years); BMI (kg/m^2); Comorbidities)**	**Study design**	**Types of intervention**	**Intervention (Type of Fibre; dosage; duration)**	**Comparison (placebo/control)**	**SCFA samples**	**SCFA measurements**
Bridges et al. 1992	20	(Men; mean age 61; BMI <28.7; hypercholesterolemic)	Intervention with parallel design	Fibre type food items	(Wheat bran & oat bran; total Fibre 34g; soluble Fibre 7.8g & 13.4g, respectively; 3 weeks)	Control (Control Diet with 14gr total Fibre with 3gr soluble Fibre)	Blood	For acetate: direct enzymatic by spectrophotometer For other SCFA using Gas Chromatography
Noakes et al. 1996	29	(Men and Women; Age ranged 44 – 64; mean BMI 29; high Triglyceride, mild hypertension)	RCT cross over design (no washout period)	Fibre type food items	(High amylose & oat bran; different doses by gender; High amylose men = 74g, women 50g; Oat bran men = 121g, women 87g; 12 weeks)	Low amylose (Dose 11-13g both men and women)	Fecal	Capillary Gas Chromatography
Causey et al. 2000	12	(Men; Age ranged 27-49; BMI $\leq$ 32; mild hypercholesterolemia)	RCT double blind cross over design (no washout period)	Fibre supplementa tion	(Inulin; 20g; 3 weeks)	Control	Fecal	Gas Chromatography
Salazar et al. 2014	30	(Women; Age ranged 18-65; BMI > 30; no comorbid)	RCT double blind parallel design	Fibre supplementa tion	(Inulin-type fructans Fibre; 16g; 12 weeks)	Placebo (maltodextrin)	Fecal	Gas chromatography-flame ionization detector (GC-FID)

Table 1. Continued (1)

Author (year)	N[1]	Participants (Gender; Age (years); BMI (kg/m^2); Comorbidities)	Study design	Types of intervention	Intervention (Type of Fibre; dosage; duration)	Comparison (placebo/control)	SCFA samples	SCFA measurements
Vetrani et al. 2016	54	(Men & Women; mean Age intervention group 57.2 vs. control 58.4; mean BMI intervention group 32.1 vs. control 31.5; Metabolic Syndrome)	RCT open-label design	Fibre type food items	(whole grain; not specify the dose; 12 weeks)	Control	Blood	Gas Chromatography
Canfora et al. 2017	44	(Men & Women; Age ranged 45-70; BMI ranged 28-40; prediabetic)	RCT double-blind parallel design	Fibre supplementa tion	(Galactooligosaccharides (GOSs); 15g; 12 weeks)	Placebo (maltodextrin)	Blood and Fecal	Gas Chromatography for fecal SCFA Liquid Chromatography-Mass Spectrophotometry for plasma SCFA
Cham bers et al. 2018	20	(Men & Women; mean Age 51; mean BMI intervention 31.5 vs control 29.5; with NAFLD)	RCT double-blind, parallel design	Fibre supplementa tion	(Inulin-propionate ester; 20g; 6 weeks)	Placebo (Inulin)	Blood	Gas Chromatography
Mayeng bam et al. 2019	53	(Men & Women; Age ranged 18-70; BMI ranged 25-38; no comorbid)	RCT double-blind design	Fibre supplementa tion	(Pea Fibre; 15gr; 12 weeks)	Control (isocaloric of wafers)	Fecal	Gas Chromatography
Jamar et al. 2020	35	(Men & Women; Age ranged 31-59; BMI ranged obesity I and II; no comorbid)	RCT double-blind design	Fibre type food items	(juçara group (5 g lyophilized juçara); 6 weeks)	Placebo group (5 g of maltodextrin)	Fecal	Gas Chromatography

Table 1. Continued (2)

Author (year)	N[1]	Participants (Gender; Age (years); BMI (kg/m^2); Comorbidities)	Study design	Types of intervention	Intervention (Type of Fibre; dosage; duration)	Comparison (placebo/control)	SCFA samples	SCFA measurements
Nguyen et al. 2020	38	(Men & Women; Age ranged 19-50; mean BMI 32.9; no comorbid)	RCT double-blind parallel design	Fibre supplementation	(arabinoxylan isolated from corn bran; 25gr for women & 35gr for men; 6 weeks)	Placebo (microcrystalline cellulose)	Fecal	Gas Chromatography
Thompson et al. 2020	163#	(Men & Women; Age ranged 25-45; mean BMI 32.8; no comorbid)	RCT double-blind parallel design	Fibre type food items	(fruit fibre/avocado; 175gr men & 140gr women; 12 weeks)	Control	Fecal	Gas Chromatography – Mass Spectrophotometry
Vitale et al. 2020	33	(Men & Women; Age ranged 20-60; BMI ranged 25-35; no comorbid)	RCT double-blind parallel design	Fibre type food items	(Mediterranean-formulated diet; 25.2gr; 8 weeks)	Control	Blood	Gas-Chromatography/Flame Ionization Detector
Neyrinck et al. 2021	24	(Men & Women; Age ranged 18-65; BMI >30; no comorbid)	RCT single-blind design	Fibre supplementation	(Inulin; 16gr; 12 weeks)	Placebo (maltodextrin)	Fecal	Gas Chromatography with flame ionization detector
Machado et al. 2021	30	(Men & Women; Age ranged 20-45; BMI ranged 25-35; no comorbid)	RCT double-blind design	Fibre type food items	(Yacon flour; 25gr; 6 weeks)	Control	Fecal	High Performance Liquid Chromatography (HPLC)

Table 1. Continued (3)

Author (year)	N[1]	Participants (Gender; Age (years); BMI (kg/m^2); Comorbidities)	Study design	Types of intervention	Intervention (Type of Fibre; dosage; duration)	Comparison (placebo/control)	SCFA samples	SCFA measurements
Benítez -Páez et al. 2021	80	(Men & Women; Age ranged 18-60; BMI ranged 28-45; no comorbid)	RCT double-blind parallel design	Combined with CRD	(Calorie Restriction Diet/CRD + Inulin 10gr + Resistant Maltodextrin 10gr; 12 weeks)	Placebo (CRD + maltodextrin)	Blood and Fecal	Liquid Chromatography-Mass Spectrophotometry/ Mass Spectrophotometry (LC-MS/MS)
Deroov er et al. 2021	14	(Men & Women; Age ranged 18-65; BMI ≥30; no comorbid)	RCT single-blind parallel design	Fibre supplementa tion	(Wheat bran RPS fraction; 20 g; 1 months)	Placebo (maltodextrin)	Blood and Fecal	Gas Chromatography – Mass Spectrophotometry
Hughes et al. 2021	37	(Men & Women; Age ranged 40-65; BMI ranged 18.5-39.9; no comorbid)	RCT double-blind cross over design (with washout period)	Fibre type food items	(RS2-enriched wheat; 14-19 g; 7 days)	Control (wild-type wheat)	Fecal	Gas Chromatography – Mass Spectrophotometry

[1] Number of participants at baseline/ randomizations; [#] Faecal samples were analyzed only from 45 individuals

Table 2. Type of fibre for supplementation based on fermentation rate in colon as proposed by Wang et al. 2019

Type of fibre for supplementation	**Fermentation rate**	**Key findings on SCFA levels**	**Author (year)**
Inulin	Fast	Acetate levels tended to increase (p=0.08) in inulin group as compared to control	Causey et al. 2000
Inulin-type fructans	Fast	Total SCFA, acetate and propionate levels were decreased significantly in inulin-type fructans group	Salazar et al. 2014
Galactooligosaccharides	Fast	No effect of intervention on fecal SCFA	Canfora et al. 2017
Pea Fibre (contains oligosaccharides and resistant starches)	Slow	- Significantly increased acetate levels - Significantly decreased isovalerate concentrations	Mayengbam et al. 2019
Arabinoxylan	Fast	An increased in propionate concentration in intervention group as compared to control	Nguyen et al. 2020
Inulin	Fast	Acetate significantly increased in the placebo group	Neyrinck et al. 2021
Wheat bran (contain 70% arabinoxylan)	Fast	- Isovalerate significantly decreased at the end of intervention period in WB RPS group, but increased in the placebo group - Total SCFA, acetate, propionate, butyrate, and isobutyrate were not changed	Deroover et al. 2021
Inulin	Fast	An increased on propionate (based on multi-omics analysis)	Benítez-Páez et al. 2021

Table 3. Key findings of the effect of fibre on the blood and faecal SCFA level and modulation of the gut microbiota in the adult individuals with overweight/obesity

Types of intervention	SCFA samples	Author (year)	Key findings on SCFA levels	Other relevant findings
Fibre type food items	Blood	Bridges et al. 1992	- Fasting serum acetate values were significantly higher after the oat-bran than after the control diets but not for wheat-bran compared with control diets - Fasting serum propionate concentrations for the six subjects increased slightly but not significantly on the oat-bran diet compared with control diets	NA
		Vetrani et al. 2016	- After the intervention, fasting plasma propionate concentration increased in respect to baseline in the whole-grain group, whereas a reduction was detected in the control group - The absolute changes in fasting plasma propionate concentration between 12 weeks and the baseline values were significantly different between the whole grain and the control group	NA
		Vitale et al. 2020	Postprandial plasma butyric acid levels significantly increased at the end of the intervention only in the intervention group	- A significant decrease in the relative abundance of *Ruminococcus torques*, *Coprococcus comes*, *Streptococcus gallolyticus* and *Flavonifractor plautii* ($p < 0.05$) - A significant increase in the relative abundance of *Intestinimonas butyriciproducens* and *Akkermansia muciniphila* ($p < 0.05$) in the intervention group vs control - The increase in butyric acid was positively correlated to the relative abundance of *Bacteroides xylanisolvens* and *Roseburia hominis*
	Fecal	Noakes et al. 1996	Butyrate significantly higher in high-amylose group compared with control and oat bran group	NA
		Jamar et al. 2020	Significantly increased acetate	A relative abundance of *Akkermansia muciniphila*, *Bifidobacterium spp*. and *Clostridium coccoides* were observed
		Thompson et al. 2020	Fecal acetate levels were significantly higher in intervention group vs. control after intervention	At the genus level, the relative abundances of *Faecalibacterium*, *Lachnospira*, and *Alistipes* were enriched in the intervention group, while the relative abundances of *Roseburia* and *Ruminococcus* were decreased

Table 3. Continued (1)

Types of intervention	SCFA samples	Author (year)	Key findings on SCFA levels	Other relevant findings
Fibre type food items	Fecal	Machado et al. 2019	Significantly decreased SCFA (acetate, butyrate, and propionate)	NA
		Hughes et al. 2021	No significant differences were detected in absolute concentrations of fecal SCFAs after the intervention and between groups	- RS intake significantly altered alpha and beta diversity - The composition of the fecal microbiota was significantly different after RS2 consumption - RS intervention also decreased both Shannon diversity and Chao1 richness of the gut microbial community - RS intervention was associated with an increase in *Ruminococcus* and *Gemmiger* compared to Control and baseline (Pre-RS) - *Faecalibacterium*, *Roseburia*, and *Bifidobacterium* were also increased after RS compared to baseline, though these effects were not significant compared to Control - *Bifidobacterium* was increased after Control compared to baseline, suggesting that the bifidogenic effect was not specific to the RS2-enriched wheat - Butyrate and total SCFAs were positively correlated with relative abundance of *Faecalibacterium*, *Ruminoccocus*, *Roseburia*, and *Barnesiellaceae*
Fiber supplementation	Blood	Canfora et al. 2017	No effect of GOS on blood SCFA levels	- *Bifidobacterium* was significantly higher in GOS group as compared to placebo after the intervention. - Other taxa *Prevotella oralis et rel.*, *Prevotella melaninogenica et rel.*, *Bacteroides stercoris et rel.*, *Sutterella wadsworthia et rel*. was higher in GOS - However, the effect of GOS much higher, increasing *Bifidobacterium* as compared to other taxas
		Chambers et al. 2018	A reduced fasting butyrate levels as compared to the inulin-control group	NA
		Deroover et al. 2021	- Acetate and total SCFA concentrations increased after WB RPS intervention, but decreased after placebo intervention - The effect of WB RPS on postprandial ^{13}C-SCFA concentrations was not different from placebo	NA

Table 3. Continued (2)

Types of intervention	SCFA samples	Author (year)	Key findings on SCFA levels	Other relevant findings
Fiber supplementation	Fecal	Causey et al. 2000	Acetate levels tended to increase (p=0.08) in inulin group as compared to control	NA
		Salazar et al. 2014	Total SCFA, acetate and propionate levels were decreased significantly in inulin-type fructans group	- *Bifidobacterium longum*, *Bifidobacterium pseudocatenulatum and Bifidobacterium adolescentis* were significantly increased at the end of the treatment in the prebiotic group - Acetate and propionate positively correlated with BMI, fasting insulin and HOMA - Butyrate and total SCFA significantly correlated with fasting insulin and HOMA
		Canfora et al. 2017	No effect of intervention on fecal SCFA	NA
		Mayengbam et al. 2019	- Significantly increased acetate levels - Significantly decreased isovalerate concentrations	An increase in *Lachnospira* (*Phyla Firmicutes*) in the intervention group vs. placebo
		Nguyen et al. 2020	An increased in propionate concentration in intervention group as compared to control	*Bifidobacterium longum*, *Blautia obeum*, and *Prevotella copri* were significantly increased
		Neyrinck et al. 2021	Acetate significantly increased in the placebo group	*Erysipelotrichaceae* (UCG003) was the sole bacteria negatively correlated with changes in fecal acetate
		Deroover et al. 2021	- Isovalerate significantly decreased at the end of intervention period in WB RPS group, but increased in the placebo group - Total SCFA, acetate, propionate, butyrate, and isobutyrate were not changed	- Microbial load of the fecal samples was not affected by WB RPS or placebo intervention - Higher numbers of *Butyricicoccus*, *Streptococcus*, and some unspecified genera belonging to the class of the bacilli were identified as characteristic for the WB RPS intervention

Table 3. Continued (3)

Types of intervention	SCFA samples	Author (year)	Key findings on SCFA levels	Other relevant findings
Combined with CRD	Blood	Benítez-Páez et al. 2021	No SCFA was detected in the blood samples	NA
	Fecal	Benítez-Páez et al. 2021	An increased on propionate (based on multi-omics analysis)	- vfDifferent Clostridial species exhibited negative associations with faecal acetate, propionate, and butyrate (r = -0.30 to -0.43, FDR $p < 1.50\text{-}4$ for all comparisons). - In men received CRD + Fibre, butyrate producers (*Faecalibacterium prausnitzii* and *Bacteroides caccae*) was deeply reduced - Increase in faecal propionate following the fibre supplementation, matching with the enrichment of propanoate metabolism genes identified in the metagenome analysis, were higher in men than women

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