Dietary fibres and appetite

comparing apples and oranges?

Anne J. Wanders

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General Abstract

Background and objective: Dietary fibre can contribute in the prevention of overweight and obesity. However, different classes of dietary fibre may have different effects on appetite and energy intake regulation. The aim of this thesis was to investigate the effect of different dietary fibre classes on appetite, and its underlying mechanisms. Both acute and long term effects of dietary fibre classes were explored by diverse study designs, comprising a systematic review, three intervention studies and an observational study.

Methods: First, we systematically reviewed available literature on the relationship between dietary fibre types, satiety, acute and long term energy intake and body weight. Next, in two intervention studies we investigated whether bulking, viscous, and gel forming properties of fibre could be related to satiation (n=121) or satiety (n=29), and whether fibre consumed in different food matrices could be related to satiety (n=29). Then, in a third intervention study (n=32), the role of acute and long term exposure (16 days) to gel forming fibre on satiety and energy intake was explored. Finally, long term (6.4 year) associations between the intake of dietary fibre classes and change in body weight were studied in an elderly population-based prospective cohort (n=1,859).

Results: The literature review of studies in acute settings showed that dietary fibres with viscous properties and dietary fibres consumed in a liquid food matrix increased satiety and lowered subsequent energy intake. In the intervention studies we observed that foods containing a high-dose of gel forming fibre induced earlier satiation and increased satiety. Foods containing bulking and viscous fibres did not affect satiation or satiety. We observed that the earlier satiation and increased satiety were likely mediated by the increased time that was needed to eat the foods. Satiety, but not earlier satiation, was related to a slowed down gastric emptying rate.

The literature review of studies on long term effects indicated that dietary fibre may lower energy intake and body weight, and that not all dietary fibre types are equally effective. Long term changes could, however, not be associated with viscosity, solubility, fermentability or with food matrix properties. In the intervention study we found that a gelled fibre persistently increased satiety compared to control, but did not decrease energy intake or body weight. In the prospective cohort study, a higher intake of total fibre, fibre from different food sources and fibre types were not associated with changes in body weight or waist circumference, although in general inverse associations were observed.

Conclusions: We conclude that fibre classes that are hydrated and thickened result in earlier satiation and increased satiety. These effects are likely mediated by an increased oro-sensory exposure time and a slowed down gastric emptying rate. Dietary fibres may decrease long term energy intake and body weight, yet, we were not able to associate the effects with specific dietary fibre classes or underlying mechanisms.

Keywords: dietary fibre, satiation, satiety, appetite, energy intake, body weight, viscosity, eating time, gastric emptying, fermentation.

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General Introduction

Across Europe the prevalence of obesity (BMI >30 kg/m^2) in adults aged 18 years and over varies between 8% and 25%. Moreover, the prevalence of overweight or obesity (BMI >25 kg/m^2) in adults varies between 37% and 69% (1). Being obese or overweight puts people at an increased risk of heart disease, type 2 diabetes mellitus, hypertension and certain cancers. Measures that contribute to the prevention of obesity are physical activity and dietary factors, among others dietary fibre (2).

'Dietary fibre' is a collective term for a wide range of components, primarily carbohydrates, that are not digested in the small intestine (3). Different fibre types are for example: cellulose, hemicellulose, pectin, guar gum, psyllium and dextrin. It is generally considered that fibres may have an array of physiological effects in humans, for example: a decreased intestinal transit time, increased stool bulk, improved weight management, reduced blood cholesterol levels, and reduced post-prandial blood glucose and insulin levels (4-6). Yet, not all components covered by the collective term 'dietary fibre' are equally effective. Summarizing the wide range of components into 'total dietary fibre', which is common practice in the field of nutrition and health (7-9), may therefore lead to inconsistent findings.

Over the past number of years, nutrition scientists more and more acknowledge that each dietary fibre has unique characteristics that may determine its physiological effects (4, 10, 11). However, investigating all different and newly developed types of dietary fibre for its physiological effects requires substantial amounts of time and financial resources. It would therefore be highly valuable to identify the characteristics of dietary fibres that determine the physiological effects, which then can be used for fibre classification.

Comparing apples and oranges?
The saying 'comparing apples and oranges' as a subtitle to the title of this thesis requires some explanation. The saying is generally used when two items are compared that cannot be validly compared. When studying the effects of 'total dietary fibre' on health outcomes, nutrition scientists are aware that they are summing 'apples and oranges' (12-14). Yet, it is not clear which fibre characteristics, the 'apples' and the 'oranges', determine its health outcomes. Hence, a question mark is added to the saying. Moreover, in two chapters in this thesis apples and oranges are actually compared. In chapter 4 we compare pectin originating from apples with pectin originating from citrus, and in chapter 6 different fibre types from fruit are studied.

The research described in this thesis explores the effect of different dietary fibre classes on appetite, and its underlying mechanisms. This chapter starts with the definition of dietary fibre and the recommended and actual intakes. This is followed by an overview of dietary fibre classification methods and an overview of mechanisms how dietary fibres can affect appetite. Finally, the aim and the outline of the thesis are presented.

Dietary fibre

Dietary fibre definition and intake

In the year 1953, Hipsly (15) was the first to use the term dietary fibre for non-digestible components of plant cell walls. Twenty years later, Trowell (16) adopted the term and defined dietary fibre as the remnants of plant components that are resistant to hydrolysis by human alimentary enzymes, comprising celluloses, hemicelluloses, gums, lignins, waxes and cutins (16). Since then, the dietary fibre definition has been much debated. It has been related to the array of physiological effects and the different analytical methods for dietary fibre analysis. Meanwhile, many local authorities agreed on their own definitions (17, 18). In 2009 the worldwide community, as represented by the Codex Alimentarius Commission, agreed on the definition presented in Textbox 1.1 (3, 19).

Textbox 1.1: Codex Committee on Nutrition and Foods for Special Dietary Uses (CCNFSDU) definition of dietary fibre (3, 19).

Dietary fibre means carbohydrate polymers[1] with ten or more monomeric units[2], which are not hydrolysed by the endogenous enzymes in the small intestine of humans and belong to the following categories:

- Edible carbohydrate polymers naturally occurring in the food as consumed,
- Carbohydrate polymers, which have been obtained from food raw material by physical, enzymatic or chemical means and which have been shown to have a physiological effect of benefit to health as demonstrated by generally accepted scientific evidence to competent authorities,
- Synthetic carbohydrate polymers which have been shown to have a physiological effect of benefit to health as demonstrated by generally accepted scientific evidence to competent authorities.

[1] When derived from a plant origin, dietary fibre may include fractions of lignin and/or other compounds associated with polysaccharides in the plant cell walls. These compounds also may be measured by certain analytical method(s) for dietary fibre. However, such compounds are not included in the definition of dietary fibre if extracted and re-introduced into a food.

[2] Decision on whether to include carbohydrates from 3 to 9 monomeric units should be left to national authorities.

A number of international and national authorities have set dietary reference values for the intake of dietary fibre. The Health Council of the Netherlands has set an intake of 3.4 grams per megajoule as a guideline for adults in the Netherlands, with no upper limit. This intake refers to an average of 30 gram fibre per day for women and 40 gram fibre per day for men aged 31 to 50 years (17). The European Food Safety Authority (EFSA) considers a fibre intake of 25 gram per day to be adequate

(4). The World Health Organisation (WHO) advises a dietary fibre intake of at least 25 grams per day, which should originate from fruits, vegetables and wholegrain foods (2).

Based on food consumption survey data in the Netherlands in 2010, median daily intake of dietary fibre was respectively 2.1 and 2.3 gram per megajoule (23 and 18 gram per day) for men and women aged 31 to 50 years (20). Food sources contributing the most to fibre intake in the Netherlands were cereals and cereal products (42%), vegetables (14%), fruits, nuts and olives (11%) and potatoes and other tubers (10%). Across countries, the intake of dietary fibre and its food sources varies largely (21). For example, between 1995 and 2000, the proportion of fibre obtained from cereals and cereal products was highest in Denmark (about 57%) and lowest in Spain (about 22%). The proportion of fibre from fruit was highest in Spain, France and Italy (about 30%) and lowest in the UK (about 14%).

Dietary fibre classification

Dissimilar dietary fibre types may affect appetite differently (4-6). It is, therefore, not correct to make a general statement about the effect of 'dietary fibre' on appetite. At present, fibre classifications are made based on fibre source, physico-chemical properties, and on food matrix. Below, several classification methods are listed.

In observational studies fibre intake is often classified by food origin or source, (e.g. 12-14, 22, 23). Food sources that are commonly studied are cereal fibre, vegetable fibre and fruit fibre, less commonly studied are legume fibre and fibre from nuts and seeds. The dietary fibre composition between food sources is heterogeneous. For example, in perspective to the other food sources, cereals are high in hemicellulose and lignin and very low in pectin, and vegetables and fruits are high in pectin and very low in lignin (24).

The basic chemical dietary fibre classes are: resistant oligosaccharides; resistant starch; and resistant non-starch polysaccharides (NSP). Oligosaccharides are molecules containing two to nine monosaccharides (i.e. sugar components). Polysaccharides are molecules with complex arrangements of ten or more monosaccharides. Resistant starch is regarded a separate class because it actually is a digestible polysaccharide, but resists digestion due to varying reasons. Apart from the variation in monosaccharides, dietary fibres also vary in the conformation of the molecules and the linkages between the molecules. Due to this variation, dietary fibre types may vary in physico-chemical properties, such as solubility, viscosity, fermentation, water holding capacity and bile-acid binding (25), that can also vary within dietary fibre types. A good example is pectin; pectins can have very heterogeneous molecules that vary with the food source and extraction conditions. The variation in molecular weight and degree of esterification can, as a result, lead to differences in solubility, viscosity and gelling ability (26).

The food matrix in which dietary fibres are consumed may affect the physico-chemical properties of the fibre. The extent of pre-processing, such as grinding, cooking or hydrating, or the addition of other nutrients, can change the physico-chemical properties. For example, insoluble fibres from bran retain water in a network of pores. When increasing the particle size, for example by grinding

a food, water holding capacity may increase due to the greater number of pores and voids in the sponge-like cells (25). Another possible effect of the food matrix is the level of hydration of the dietary fibre before consumption. Hydration is essential before viscous solutions can be formed. Some fibres hydrate instantaneous upon mixing whereas others take hours to be fully hydrated (27).

Dietary fibre and appetite

Maintaining a long term balance between energy intake and energy expenditure is critical to human health and survival (28). Over the course of a day humans typically have a number of eating occasions, which include meals, drinks and snacks. The regulation of this food intake is a complex interplay involving a wide range of internal signals in the brain, gastrointestinal tract and adipose tissue. Moreover, food intake is also affected by external signals, as people may eat when satiated and refrain from eating when hungry (29-31).

In order to regulate the energy intake from a single eating occasion towards long term energy balance, both short and long term appetite signals have to interact (28, 30). In the complex system of appetite and energy intake regulation, satiation and satiety play an important role. Satiation refers to the amount of food consumed during an eating occasion, and satiety refers to the period of time between subsequent eating occasions (29).

Whereas short term signals influence how much is eaten during and between eating occasions, long term signals, such as insulin and leptin concentrations in blood, relate to the amount and distribution of body fat (28, 32). After integration of these signals in the brain, these signals can modulate the sensitivity to short term satiety signals (28, 33). For example, after a period of overeating, increased brain insulin and leptin signalling makes neural circuits more sensitive to satiation signals, and may lead to smaller meals before feeling full.

Fruits, vegetables, cereals and other foods naturally rich in dietary fibre generally have a high water content, a low energy density and have a more rough structure than foods low in fibre (34, 35). Earlier studies have suggested that dietary fibre content in foods naturally rich in dietary fibre is positively associated to earlier satiation (36, 37) and increased satiety (36). Furthermore, prospective observational studies showed an inverse association between total dietary fibre intake and BMI or body weight (12, 13, 38-40). However, randomized controlled trials have resulted in either no, or positive effects of dietary fibre on appetite (41-43), suggesting that not all types of dietary fibre are equally effective.

Different types of dietary fibre may affect appetite via diverse processes, which origin from sensory, gastric, nutrient, hormonal and colonic signals. These processes are described in the next section.

Mechanisms by which dietary fibres may affect appetite

Sensory signals

Regulation of food intake starts already before the actual ingestion with the thought about food and the anticipation of the body to its ingestion. Responses to sensory signals, such as taste, odour and texture provoke a cascade of physiological, hormonal and autonomic responses, which are often referred to as cephalic phase responses (44, 45). Cephalic phase responses prepare the gastro-intestinal tract for the optimal digestion and absorption of nutrients, with the aim to maintain energy homeostasis (44-46). Foods that provide more sensory signals lead to more cephalic stimulation, which indicates a greater disturbance of energy homeostasis and may lead to a decrease in meal size (46, 47). Foods high in fibre may provide more sensory signals by their effects on texture (5), as high fibre foods generally have a more rough structure than low fibre foods and need more chewing (35). More chewing provides more sensory signals, which may lead a subsequent decrease in meal size (48).

Palatability of a food is related to a preferred combination of sensory signals such as taste, odour and texture in a food (49). An enhanced palatability of a food may result in an increased intake of the food (50), even beyond the subjects homeostatic needs (51). Whereas foods high in dietary fibre generally are less liked (34), they may result in a decrease in meal size.

Gastric signals

The gastric phase of the regulation of food intake starts with the first bite of food with the release of gastric and pancreatic juices and hormones (46). Although the stomach can sense nutrients, gastric satiation signals primarily arise from gastric mechanoreceptor stimulation (33). Meal volume or meal weight has a larger effect on meal termination than the amount of energy in a meal (52, 53). This implies that a lower energy density can lead to a lower total energy intake. Dietary fibre can increase the water holding capacity of foods and intestinal content. This may result in an increase of the intestinal volume and lowers the energy density. The emptying of foods from the stomach usually starts immediately with liquids, whereas solids are emptied when they have reached a sufficiently small particle size (54, 55). By the increased water holding capacity of foods and intestinal content, and by the more rough structure of high fibre foods, dietary fibre may affect gastric motility and as a result slow down the gastric emptying rate. A reduced gastric emptying enhances gastric mechanoreceptor stimulation and gastric satiety signals, which may result in a decrease in meal size (56) and a longer sensation of satiety.

Nutrient and hormonal signals

Whereas gastric satiety signals are primary of mechanical origin, intestinal satiety signals are typically nutrient-dependent (57), and may for example act as a feedback system to slow down gastric emptying rate (56). Dietary fibre can induce thickening of the intestinal content, which may slow down the rate by which nutrients enter the circulation. Moreover, dietary fibre can induce thickening of the unstirred water layer which then forms a greater barrier to absorption. Therefore, dietary fibre may prolong the release of nutrients and lead to a longer sensation of satiety (10, 58).

Dietary fibre can, furthermore, entrap or bind nutrients in the intestinal content, which lowers the bioavailability of fatty acids and proteins and results in a reduced energy absorption and an increased faecal loss of nutrients (59-61). As a consequence of the slower uptake of nutrients, blood glucose concentrations tend to be lower after high fibre diets (58, 62). Lower postprandial blood glucose concentrations blunt insulin secretion, that is suggested to be related to an increased satiety (5, 63).

Satiety signals are also suggested to be regulated by the release of gastrointestinal peptides by endocrine cells. Some of the best studied peptides are: ghrelin, cholecystokinin (CCK), peptide tyrosin tyrosin (PYY), and glucagon-like peptide 1 (GLP-1) (64, 65). These peptides are released in the circulation and may act to increase satiety and decrease energy intake, with the exception of ghrelin, which increases before meals and decreases with eating. The release of gastrointestinal peptides is primarily nutrient stimulated, but can also occur by non-nutrient processes like neural regulation or gastric mechanoreceptor stimulation (33, 64). The presence of dietary fibre may slow down the rate by which nutrients enter the circulation and may prolong the release of gastrointestinal peptides and lead to a longer sensation of satiety. However, research also showed that dietary fibre may lead to greater postprandial releases of peptides (32).

Colonic signals

By definition, dietary fibres are resistant to endogenous enzymes and are not absorbed in the small intestine of humans (3, 19). After entering the colon largely unmodified, many types of dietary fibre are subject to anaerobic fermentation by the colonic microflora. Fermentation end products may be absorbed in the colon, and may therefore contribute to the metabolisable energy content of the diet. The average energy content of dietary fibre is 8 kJ (2 kcal) per gram (18, 66, 67) and is lower compared to digestible carbohydrates (17 kJ per gram). It is important to note that the energy content of dietary fibre is an estimate, and may vary between 0 and 13 kJ per gram (67), as the extent of fermentation depends on both type of dietary fibre and host characteristics. The relatively low energy content of dietary fibre contributes to a lower energy density of foods. Foods high in dietary fibre are therefore said to have a 'bulky' nature.

The main end products of fermentation of dietary fibre are gases such as hydrogen and carbon dioxide, and short-chain fatty acids (SCFA) such as acetate, propionate, and butyrate (68). These by-products of bacterial fermentation acidify the colonic content, modify the microflora composition and are metabolized by human tissues (68, 69). There are indications that bacterial fermentation may play a role in the regulation of food intake (70, 71), but the processes are unclear. It was suggested that butyrate and propionate may enter the circulation via the portal blood system and stimulate GLP-1 and PYY secretion (70, 72, 73). Furthermore, SCFAs may slow down gastrointestinal transit time of intestinal content (72), they may affect satiety by changes in glucose and lipid metabolism (5), and oxidation of SCFAs may provide long-lasting energy and may lead to a longer sensation of satiety (74).

Aim and outline of the thesis

Different types of dietary fibre may differently affect appetite. Therefore, it is highly valuable to investigate whether it is possible to identify classes of dietary fibre with consistent effects on appetite. At present, fibre classifications are made based on fibre source, chemical properties, and on food matrix. These classes, however, have not been systematically studied for their effects on appetite. The aim of this thesis therefore was to explore the effect of different dietary fibre classes on appetite, and its underlying mechanisms. Acute and long term effects of dietary fibre classes were investigated by diverse study designs comprising a systematic review, three intervention studies and an observational study.

Figure 1.1 presents an overview of fibre classification methods and their potential effects on appetite and underlying mechanisms. The dietary fibre classification methods are based on physico-chemical properties, food matrix and fibre source. The fibre classes may differently affect acute and long term effects. These effects may work via diverse mechanisms which origin from sensory, gastric, nutrient/hormonal and colonic signals.
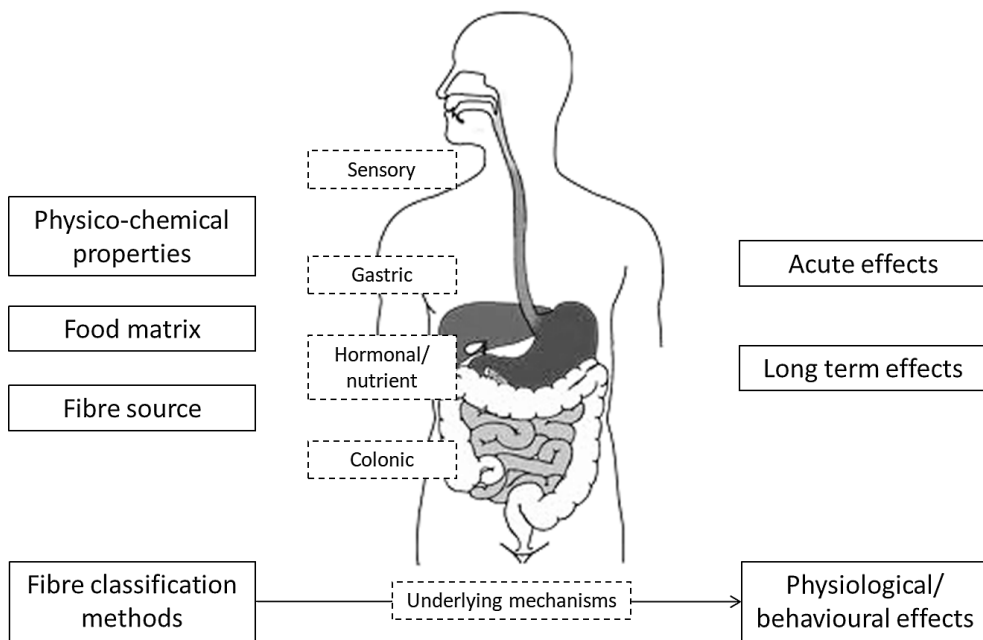

Figure 1.1: Dietary fibre classification methods and their possible effects on appetite and underlying mechanisms.

In this thesis we primarily focus on classifying dietary fibres according to their physico-chemical properties. This was chosen because in current available research on dietary fibre and appetite these properties are most frequently reported, and therefore regarded as an appropriate starting point. However, we also explored classification of fibres by food matrix, polymer structure and fibre source.

This thesis is structured according the following outline. First, a comprehensive literature review **(chapter 2)** was conducted to systematically investigate the available literature on the relationship between dietary fibre, acute effects on satiety and long term energy intake and body weight. In the review fibres were classified according to monosaccharide composition and the physico-chemical properties viscosity, solubility and fermentability. Chapters 3 to 6 consist of original studies, three interventions studying the range from satiation to long term energy intake, and the fourth one being an observational study. In **chapter 3** we aimed to determine the effects of three distinctive physico-chemical properties of dietary fibre, i.e. bulking, viscous, and gel forming fibre, on satiation. Satiation was determined by measuring *ad libitum* intake of test foods, supplemented with the fibres, in a semi-real life setting. In **chapter 4** we aimed to investigate the effect of these three distinctive physico-chemical properties of dietary fibre on satiety. Satiety was determined before ingestion of the dietary fibre and after fixed time intervals, as well as by an *ad libitum* lunch after 3 hours. To further investigate the role of the food matrix, we investigated the effect of the gel forming fibre in three different food matrices (gel, liquid, capsules) on satiety within the same design. **Chapter 5** describes an intervention study in which we investigated whether consumption of a test food with either gel forming dietary fibre or a gel forming non-fibre control affects satiety and energy intake differently. This was investigated after single exposure and after 2 weeks of daily exposure. In **chapter 6**, associations between different fibre sources, fibre types and body weight change in an observational cohort study among Dutch elderly subjects are described. In the last chapter **(chapter 7)**, the findings are summarized and discussed in the view of the used methodology and perspectives of other studies.

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Effects of dietary fibre on subjective appetite, energy intake and body weight:

A systematic review of randomized controlled trials

Authors

Anne J. Wanders

Joost J.G.C. van den Borne

Cees de Graaf

Toine Hulshof

Melliana C. Jonathan

Mette Kristensen

Monica Mars

Henk A. Schols

Edith J.M. Feskens

Abstract

Dietary fibres are believed to reduce subjective appetite, energy intake and body weight. However, different types of dietary fibre may affect these outcomes differently. The aim of this review was to systematically investigate the available literature on the relationship between dietary fibre types, appetite, acute and long-term energy intake, and body weight. Fibres were grouped according to chemical structure and physicochemical properties (viscosity, solubility and fermentability). Effect rates were calculated as the proportion of all fibre-control comparisons that reduced appetite (n=58 comparisons), acute energy intake (n=26), long term energy intake (n=38) or body weight (n=66). For appetite, acute energy intake, long term energy intake and body weight there were clear differences in effect rates depending on chemical structure. Interestingly, fibres characterized as being more viscous (e.g. pectins, β-glucans and guar gum) reduced appetite more often than those less viscous fibres (59% vs. 14%), which also applied to acute energy intake (69% vs. 30%). Overall, effects on energy intake and body weight were relatively small and distinct dose-response relationships were not observed. Short and long term effects of dietary fibres appear to differ and multiple mechanisms relating to their different physicochemical properties seem to interplay. This warrants further exploration.

Introduction

The increased prevalence of overweight and obesity has led to many studies examining the influence of diet composition on energy intake and body weight. Epidemiological studies have shown that a higher intake of dietary fibre is associated with smaller body weight and waist circumference (1, 2). Additionally, controlled intervention studies indicate that a high dietary fibre intake may prevent weight gain by reducing appetite and energy intake (3-6).

Multiple mechanisms by which dietary fibres affect appetite, energy intake and body weight have been suggested. Dietary fibres reduce the energy density of foods, which may directly lead to reduced energy intake and indirectly to reduced appetite (7). Fibre rich foods generally take longer to chew, which may increase sensory satiety and reduce meal size (8-10). Furthermore, fibres may decrease intestinal passage rates, leading to a more gradual nutrient absorption and prolonged feelings of satiety (11). They may also decrease energy absorption by lowering the bioavailability of fatty acids and proteins (12, 13). Finally, dietary fibres can be fermented in the colon, which increases the concentration of short chain fatty acids, which may enhance satiety via various mechanisms (14).

It is thought that inhibition of subjective appetite, energy intake and body weight by fibre-rich diets may depend on the chemical structure of the fibre and their physicochemical properties rather than on total fibre intake (15-17). Physicochemical properties of fibres associated with appetite, energy intake and body weight, include solubility, viscosity, water holding capacity and fermentability. Such properties may not only affect the satiating capacity of dietary fibres, but could also impact long term appetite and, as a consequence, the regulation of energy intake.

Despite the recognition of these possible associations, a systematic overview of effects of dietary fibres is lacking. We therefore conducted a systematic review to summarize the available literature on the relationship between specific dietary fibre types and three outcome variables: subjective appetite, energy intake and body weight.

Methods

Selection of literature

A systematic literature search was conducted to identify randomized clinical trials with dietary fibres on subjective appetite, energy intake, and body weight in humans. Databases searched were PubMed and Food Science and Technology Abstracts (FSTA). Titles, abstracts and keywords were searched from inception up to 17 February, 2010. Search terms included comprehensive (MeSH) terms and synonyms for the intervention (i.e. constituents of dietary fibre according to AACC (18)) and for the three outcomes (i.e. appetite, energy intake and body weight). The detailed search question is included in Appendix 1. The search was restricted to papers in English. All papers that were found were screened by two reviewers. Each reviewer screened 45% of the articles and the remaining 10% was screened by both. Inclusion criteria were: adult human population,

randomized intervention, isolated dietary fibre or bran, parallel control group, non-fibre control group, and measures of subjective appetite, energy intake or body weight. Studies that did not report quantitative data were excluded.

Extraction of variables

Data from included papers were extracted on the fibres of study (type, physicochemical properties, dosage, food/drink or supplement, liquid or solid), study design (crossover, parallel), subject characteristics, diet and lifestyle advice for subjects (no limitation, advice not to change diet/lifestyle, advice to change diet/lifestyle), the three outcomes, i.e. subjective appetite, energy intake and body weight, and whether or not the outcome was a primary endpoint.

Effects on subjective appetite

In general, many different methodologies are used to measure appetite (19). We only included studies with a preload study design with ratings of subjective appetite expressed on Visual Analogue Scales (VAS) measured up to 4 hours after the fibre preload. Ratings of subjective appetite are often measured by one or more of the following six items: hunger, fullness, satiety, desire to eat, appetite and prospective consumption. We extracted hunger ratings, because these were most often reported. If hunger ratings were not available, reverse fullness, reverse satiety, or appetite, in this order, were used alternatively. An effect of fibre on appetite was considered to be present if either one or both of the two following criteria were fulfilled; if not the effect was considered to be absent. The first criterion was a significantly smaller area under the curve (AUC) for fibre compared to control. The second criterion was a reduction of 10% in mean appetite ratings (19, 20). To calculate this, data were extracted at 1,2,3 and 4 hours after ingestion of the preload. Not all studies provided data at exactly these time points, therefore measurements at 1 hour comprised data between 30-60 minutes and 2, 3, and 4 hour measurements comprised data after respectively 90-120, 150-180, and 210-240 minutes. Hunger ratings were transformed to a 100% scale with ratings from 0% 'not at all hungry' to 100% 'extremely hungry'. Differences in subjective appetite ratings between fibre and control were then calculated from raw data; if raw data were not available, changes from baseline data were used. A negative value means 'suppressed subjective appetite after fibre administration compared to control'.

Effects on energy intake

Energy intake studies were evaluated as two categories: acute studies and long-term studies. The first category comprised studies in which a single preload with fibre was provided and *ad libitum* energy intake was measured after a fixed time interval. The second category comprised studies in which daily fibre supplementation was given over a period of $\geq$ 1 week, during which energy intake was voluntary, and intake was measured with recalls (24h food recall, 7d diet history, food frequency questionnaire), records (daily food record, weighed food record), or *ad libitum* meals. When measurements were repeated on multiple time intervals, only the final measurement was included in the review. Changes in energy intake after fibre supplementation were calculated as absolute changes (MJ) and relative changes (%) compared to the control treatment. For long term

energy intake, data were calculated relative to baseline values when these were available. A negative value means 'less energy consumed after fibre administration than after the control treatment'. For both acute and long term energy intake any absolute reduction was used to evaluate the effect rate of fibre, independent from whether it was a significant reduction or not.

Effects on body weight

Studies on body weight were included only if energy intake during the intervention was voluntary and body weight was measured by the researchers. When measurements were repeated on multiple time intervals, only the final measurement was included in the review. Changes in body weight were calculated as absolute changes (kg) and relative changes (%) compared to baseline body weight. Additionally, changes in body weight were calculated per 4 weeks of intervention and per gram of dietary fibre. For body weight, any absolute reduction was used to evaluate the effect rate of fibre, independent from whether it was a significant reduction or not.

Fibre groups

Fibres were grouped primarily based on their chemical structure (Figure 2.1). The groups were as follows: glucose polymers with alpha-1,4 linkages (resistant starch), other alpha linkages (dextrins) and beta linkages (glucans), as well as polymers mainly consisting of mannose (mannans), fructose (fructans), xylose (xylans) and galacturonic acid (pectins). Marine polysaccharides (alginate, carrageenan, agar) and chitosan were grouped according to their unique origin and chemical properties. For analysis on physicochemical properties fibres were divided in groups according to viscous, soluble and fermentable properties. In this review, fermentability relates to whether the fibres are fermented by anaerobic bacteria in the large intestine. Most intervention studies limitedly reported physicochemical properties of the fibres, thus we estimated them by screening the literature on fibre properties (21-24). We then identified the range for each property, and set the categories accordingly. In addition, this was matched with expert knowledge from our food chemists. Two categories were made per property: fibres which are more viscous and fibres which are less viscous; more soluble and less soluble fibres; and more fermentable and less fermentable fibres (Figure 2.1).

Reporting data

Effect rates were calculated as the proportion (%) of all available comparisons that reduced subjective appetite, energy intake or body weight. Effect sizes were calculated as an average (%/MJ/kg), weighted by the number of subjects who completed the study.
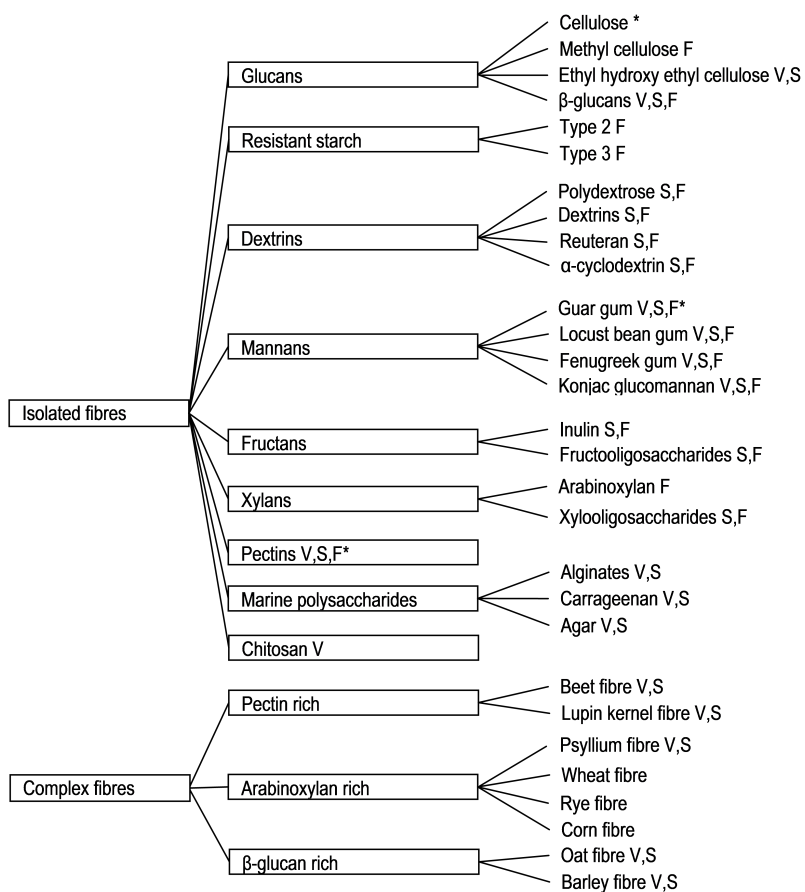
Figure 2.1: Grouping of fibres and their assumed physicochemical properties. V = more viscous fibres; S = more soluble fibres; F = more fermentable fibres; * = these fibres are often modified to adjust their physicochemical properties.

Results

A total of 7,829 abstracts were retrieved and reviewed on title, abstract and full text. The inclusion criteria were met by 104 original randomized controlled studies. Many of the studies reported effects of more than one fibre source (n=17) or had multiple outcomes (n=31), the total number of available fibre-control comparisons was 188. For subjective appetite, 34 papers with 58 fibre-control comparisons were included, for studies on acute energy intake 14 papers with 26 comparisons, for long term energy intake 30 papers with 38 comparisons, and for body weight 59 papers with 66 comparisons were included.

Short term studies

Effects on subjective appetite

Study characteristics and effects of fibres on subjective appetite ratings by fibre group are shown in Table 2.1a and 2.1b. Out of 58 fibre-control comparisons, 25 comparisons (43%) relevantly reduced appetite (>10% reduction). Irrespective of the fibre group, fibre reduced appetite on average with 5% over the 4 h time interval. Fibre groups with the largest proportion of appetite-reducing effects were pectins (4 out of 4 comparisons: 100%), pectin-rich fibres (100%), glucans (62%), mannans (50%) and marine polysaccharides (50%).

When fibres were grouped according to their physicochemical properties, 22 out of 37 comparisons (59%) with more viscous fibres reduced appetite and 3 out of 21 comparisons (14%) with less viscous fibres reduced appetite. Averaged over the 4 h time interval, more viscous fibres reduced appetite with 7.4%, at a mean fibre dose of 8.1g, whereas less viscous fibres reduced appetite with 1.3% at a mean fibre dose of 8.4g. For more soluble fibres, similar but less pronounced effects were found. Out of 46 comparisons with more soluble fibres, 22 (48%) relevantly reduced appetite, whereas out of 12 comparisons with less soluble fibres, 3 (25%) reduced appetite. For fermentability, effects were similar for both classes (42% vs. 44%). The effect rate was not different between liquids and solids (both 43%). However, with respect to the effect size, fibres provided as liquids reduced appetite with 6.6%, over 4 h, compared to 3.1% when fibres were provided as solids. Figure 2.2a shows the mean change in subjective appetite ratings by fibre dose, weighted by number of subjects per comparison, for all comparisons that reported dose and effect size (n=44). Across fibre groups, when dose-response lines were forced through the origin, appetite ratings decreased with 0.18% per gram increase in fibre intake. For more viscous fibres, this reduction was 0.41%.

Effects on acute energy intake

Study characteristics and effects of the different groups of fibre on acute energy intake are shown in Table 2.2a and 2.2b. Fourteen out of 26 comparisons (54%) showed an absolute reduction in energy intake. Fibre types with the highest effect rate for energy intake reduction were β-glucan-rich fibres (100%), resistant starch (100%), dextrins (100%), and pectin (100%). All β-glucan-rich fibres, however, originated from oat sources and were tested in a single study (25), and for resistant starch, dextrins and pectins only one comparison was available.

When fibres were grouped according to their physicochemical properties, 11 out of 16 comparisons (69%) with more viscous fibres reduced acute energy intake, whereas 3 out of 10 comparisons (30%) with less viscous fibres reduced energy intake. More soluble fibres were more effective than less soluble fibres in reducing acute energy intake (59% vs. 25%), but only four comparisons with less soluble fibres were available. We found small differences between classes for more fermentable vs. less fermentable (56% vs. 50%) and liquids versus solids (58% vs. 50%).

Long term studies

Long term effects on energy intake

Study characteristics and effects of different groups of fibres on long term energy intake are shown in Table 2.3a and 2.3b. Out of 38 fibre-control comparisons, 24 showed an absolute reduction in long term energy intake (63%). Irrespective of fibre group, fibre intake reduced energy intake by 2.6% (0.15 MJ per day). Fibre with the greatest number of comparisons showing a reduction in energy intake were arabinoxylan-rich fibres (88%), mannans (83%), fructans (80%), and resistant starch (67%).

When fibres were grouped according to physicochemical properties, differences between classes were found for more viscous versus less viscous fibres (50% vs. 69%) and more fermentable versus less fermentable fibres (67% vs. 57%). Small differences were found for more soluble versus less soluble fibres (61% vs. 67%). For study design characteristics, differences were also found for fibres provided as liquids versus solids (69% vs. 59%), no difference was found for fibre in food versus fibre in supplement (63% vs. 64%). In 12 comparisons (32%) energy intake was the primary endpoint of the study. Of these, 75% showed reduced long term energy intake after fibre supplementation, compared to 58% when energy intake was not the primary endpoint. Regarding methods of long term energy intake assessment, energy intake was reduced in 7 out of 14 (50%) comparisons with food recalls, compared to 14 out of 21 (67%) comparisons with with food records, and 3 out of 3 (100%) comparisons with *ad libitum* intake measurements.

Long term effects on body weight

The study characteristics and effects of different groups of fibre on body weight are shown in Table 2.4a and 2.4b. Out of 66 fibre-control comparisons, 39 showed an absolute reduction in body weight (59%). Irrespective of the fibre group, fibre reduced body weight with 1.3% over the complete study period (on average 0.72 kg), which corresponds to a reduction of 0.4% per 4 weeks. All comparisons on dextrins (100%) and marine polysaccharides (100%) reduced body weight. Other fibres with a high effect rate on weight loss were chitosan (86%), fructans (67%), and arabinoxylans (67%). When fibres were grouped according to physicochemical properties, differences between classes were found for more viscous versus less viscous fibres (53% vs. 71%); more soluble versus less soluble fibres (53% vs. 74%) and more fermentable versus less fermentable fibres (56% vs. 63%). Of the 20 comparisons in which weight loss was measured as the primary endpoint of the study, 70% resulted in body weight reduction, compared to 54% when weight loss was not a primary endpoint. For other study design characteristics, we found differences for liquids

versus solids (54% vs. 65%) and small differences for fibre in food versus fibre in supplement (53% vs. 62%). Figure 2.2b shows the mean change in body weight per 4 weeks by fibre dose for all fibre-control comparisons, weighted by number of subjects per comparison, specified for viscosity and fermentability. Across fibre groups, dose-response lines showed a reduction in body weight of 0.014% per 4 weeks per gram increase of fibre intake. For fibre groups, clear dose-response relations were only seen for chitosan and fructans, with a reduction of respectively 0.13% and 0.08% per 4 weeks per gram. However, the chitosan studies used relatively low dosages of fibre (1.2-3 g/d), and one extreme finding on fructo-oligosaccharides (26) contributed disproportionally to the finding for fructans. Effects of dose on weight loss were similar between classes for viscosity and fermentability.

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Table 2.1a: Study characteristics of different fibre groups on subjective appetite ratings in a preload study design.

fibre group	Comparisons[1] (n)	Studies (n)	Subjects (n)	Blinding (n) nb/b/db/?[2]	Crossover/ parallel (n) x/p[2]	Food/ supplement (n) f/sup[2]	Liquid/ solid (n) l/s[2]	Mean fibre dose[3] (g)	References
Pectin	4	1	74	4/0/0/0	4/0	4/0	0/4	14.2	(54)
Pectin rich	1	1	33	0/1/0/0	1/0	1/0	1/0	3.6	(55)
Glucan	13	10	265	1/8/3/1	12/1	11/2	9/4	3.6	(25,56-59) (31-33,60,61)
β-Glucan	9	6	131	0/7/1/1	8/1	9/0	7/2	6.2	
Cellulose	4	4	134	1/1/2/0	4/0	2/2	2/2	0.6	
Mannan	8	7	123	2/2/1/3	8/0	8/0	0/8	9.1	(34,57,62-66)
Guar gum	6	6	87	2/0/1/3	6/0	6/0	0/6	10.7	
Marine polysaccharide	2	1	24	0/0/0/2	2/0	2/0	0/2	3.3	(62)
Arabinoxylan rich	16	11	236	0/11/4/1	16/0	12/4	11/5	12.0	(57,67-76)
Rye bran	3	1	48	0/3/0/0	3/0	3/0	3/0	8.3	
Psyllium gum	9	7	120	0/6/3/0	9/0	5/4	5/4	13.6	
β-glucan rich	2	2	34	0/1/1/0	2/0	2/0	2/0	9.0	(75,76)
Dextrin	3	3	66	0/0/2/1	3/0	3/0	1/2	8.7	(76-78)
Fructan	6	4	190	0/3/3/0	5/1	5/1	3/3	5.8	(4,55,58,79)
Resistant starch	3	3	50	1/1/1/0	3/0	3/0	1/2	22.2	(76,80,81)
Total fibre	58	43	1095	8/27/15/8	56/2	51/7	28/30	8.5	

[1] Number of fibre vs. control comparisons, 1 study can result in multiple comparisons.

[2] Abbreviations used for study design characteristics: nb=not blind; b=blind; db=double blind; ?=missing. x=crossover; p=parallel. F=food or drink; sup=supplement; l=liquid; s=solid.

[3] Mean fibre dose, weighted by the number of subjects per comparison.

Table 2.1b: Effects of different fibre groups on subjective appetite ratings in a preload study design.

fibre group	Overall effect rate[1] (%)	Effect rate[2] (n_effect/n_total)					Effect size[3] (%)			
		AUC	1 h	2 h	3 h	4 h	1 h	2 h	3 h	4 h
Pectin	100	0/0	4/4	4/4	3/4	3/4	-17.2	-19.5	-16.2	-14.6
Pectin rich	100	1/1	0/1	0/1	0/1	0/1	-4.0	-8.0	-7.3	-6.0
Glucan	62	7/8	1/9	1/8	1/5	0/4	-3.2	-4.1	-1.9	-4.3
β-Glucan	78	6/6	0/5	1/5	1/3	0/2	0.3	-2.9	-4.2	1.2
Cellulose	50	1/2	1/4	0/3	0/2	0/2	-5.2	-4.8	-0.9	-6.0
Mannan	50	3/6	2/5	1/5	2/3	1/1	-7.2	-6.1	-12.7	-17.0
Guar gum	50	2/4	2/5	1/5	2/3	1/1	-7.2	-6.1	-12.7	-17.0
Marine polysaccharide	50	1/2	1/2	1/2	1/2	1/2	-7.5	-9.0	-13.5	-14.5
Arabinoxylan rich	44	3/5	2/15	5/15	3/10	2/8	-4.0	-5.9	-5.6	-5.0
Rye bran	100	3/3	0/3	1/3	2/3	1/3	-5.6	-9.8	-9.4	-8.1
Psyllium gum	44	0/0	2/9	4/9	1/6	1/4	-4.7	-5.6	-3.9	-8.4
β-glucan rich	0	0/1	0/1	0/1	0/1	0/1	1.0	7.0	8.0	19.0
Dextrin	0	0/3	0/1	0/1	0/1	0/1	6.1	3.0	7.1	2.7
Fructan	0	0/2	0/5	0/5	0/3	0/3	-1.0	-1.6	-3.8	-1.0
Resistant starch	0	0/1	0/2	0/2	0/2	0/1	3.5	4.3	4.7	10.0
Total fibre	43	15/29	10/45	12/44	10/32	7/26	-4.2	-5.3	-5.3	-5.2

[1] If a comparison had at least one relevant reduction in appetite ratings (for 1,2,3,4 hours or for AUC), the overall comparison was rated as an effect. The overall effect rate is given as n_{effect}/n_{total} in %.

[2] If an individual comparison had a relevant reduction in appetite ratings of >10% after 1,2,3,4 hours or if the area under the curve (AUC) for fibre resulted in significantly lower appetite ratings than the control, the comparison was rated as an effect. Here the proportion of the number of comparisons with a relevant effect is given relative to the total number of comparisons for that fibre group (n_{effect}/n_{total}).

[3] Change in appetite ratings in %, weighted by the number of subjects per comparison, a negative effect size means a reduction in subjective appetite ratings after fibre treatment.

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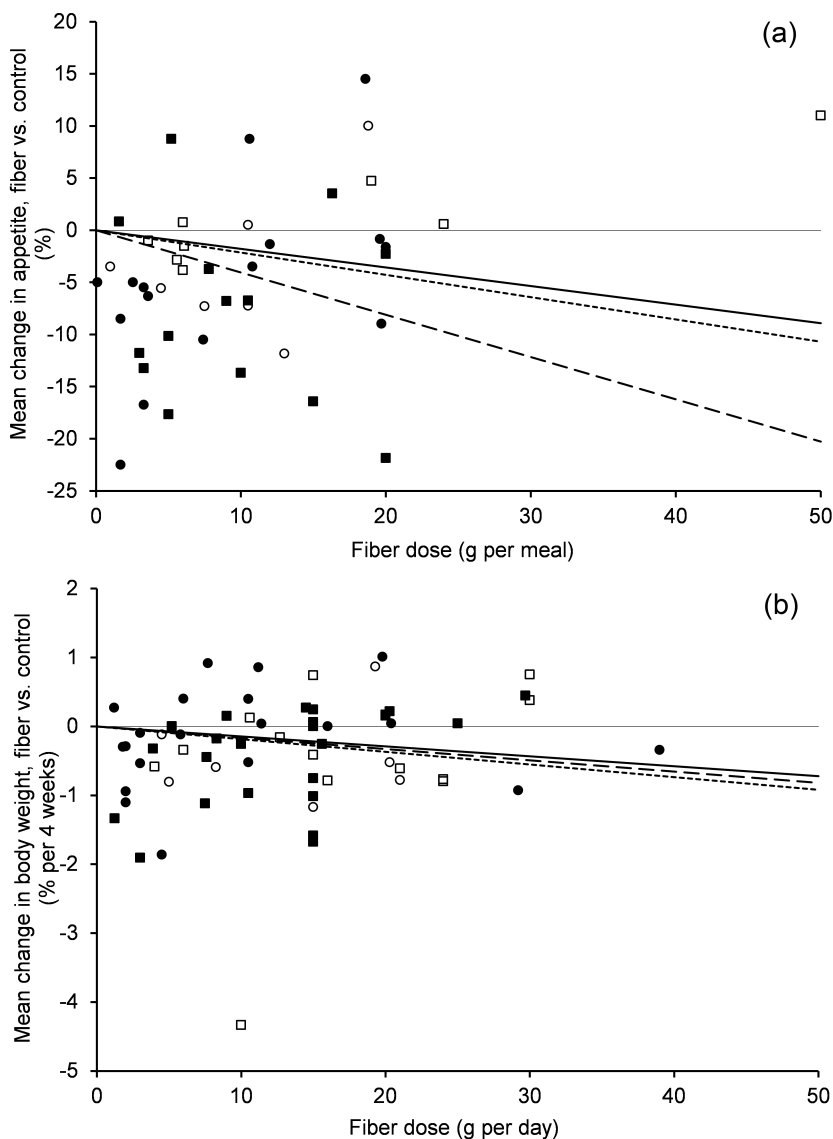
Figure 2.2: Mean changes in subjective appetite and body weight by fibre dose, viscosity and fermentability. Black symbols = more viscous fibres; White symbols = less viscous fibres. Squares = more fermentable fibres; Circles = less fermentable fibres. Regression lines: ——— = overall; – – – = more viscous fibres; · · · ·= more fermentable fibres. Regression lines were forced through the origin because a zero change in diet should produce a zero change in appetite or body weight. Regression lines were weighted for number of subjects per study. (a): Mean change in subjective appetite for all comparisons reporting dose and effect size (n=44). The slope of the overall regression line is -0.178x; the slope of the more viscous fibres regression line is -0.406x; the slope of the more fermentable fibres regression line is -0.214x. (b): Mean change in body weight per 4 weeks for all comparisons (n=66). The slope of the overall regression line is -0.014x; the slope of the more viscous fibres regression line is -0.016x; the slope of the more fermentable fibres regression line is -0.018x.

Table 2.2a: Study characteristics of different fibre groups on acute energy intake in a preload study design.

fibre group	Comparisons[1]	Studies	Subjects	Blinding	Crossover/ parallel	Food/ supplement	Liquid/ solid	Mean fibre dose[3]	Mean study duration[4]
	(n)	(n)	(n)	(n)	(n)	(n)	(n)	(g)	(h)
				nb/b/db/?[2]	x/p[2]	f/sup[2]	l/s[2]		
β-glucan rich	4	1	56	0/4/0/0	4/0	4/0	0/4	5.8	4.0
Pectin	1	1	58	1/0/0/0	1/0	1/0	1/0	4.8	0.3
Dextrin	1	1	15	0/1/0/0	1/0	1/0	1/0	25.0	1.5
Resistant starch	1	1	20	0/1/0/0	1/0	1/0	1/0	48.0	7.0
Mannan	6	3	145	3/2/0/1	6/0	6/0	6/0	9.9	3.7
Glucan	5	4	80	0/2/1/2	5/0	5/0	1/4	3.4	1.6
Fructan	4	2	118	0/0/0/0	4/0	4/0	2/2	5.9	2.7
Arabinoxylan rich	4	2	50	0/4/0/0	4/0	4/0	0/4	11.9	2.5
Total fibre	26	15	542	4/16/3/3	26/0	26/0	12/14	9.1	2.8

[1] Number of fibre vs. control comparisons, 1 study can result in multiple comparisons.

[2] Abbreviations used for study design characteristics: nb=not blind; b=blind; db=double blind; ?=missing. x=crossover; p=parallel. f=food or drink; sup=supplement; l=liquid; s=solid.

[3] Mean fibre dose, weighted by the number of subjects per comparison.

[4] Mean study duration in hours, weighted by the number of subjects per comparison.

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Table 2.2b: Effects of different fibre groups on acute energy intake in a preload study design.

fibre group	Effect rate[1] (%)	Effect size[2] (MJ)			Effect size[2] (%)			References
		mean	min	max	mean	min	max	
β-glucan rich	100	-0.42	-0.5	-0.4	-10.1	-11.9	-8.6	(25)
Pectin	100	-0.10	-0.1	-0.1	-2.7	-2.7	-2.7	(82)
Dextrin	100	-0.18	-0.2	-0.2	-5.9	-5.9	-5.9	(5)
Resistant starch	100	-0.37	-0.4	-0.4	-6.5	-6.5	-6.5	(80)
Mannan	50	-0.07	-0.6	0.4	-0.5	-17.1	17.0	(64, 65, 83)
Glucan	40	-0.05	-0.7	0.2	-1.3	-19.1	6.1	(33, 58, 59, 84)
Fructan	25	0.05	-0.1	0.2	2.2	-3.6	5.7	(58, 79)
Arabinoxylan rich	25	0.32	-0.1	0.8	20.0	-3.1	52.2	(68, 69)
Total fibre	54	-0.06	-0.7	0.8	0.3	-19.1	52.2	

[1] If fibre treatment reduced energy intake compared to control this was rated as an effect. The effect rate is given as n_{effect}/n_{total} in %.

[2] Change in energy intake in MJ and percent, weighted by number of subjects per comparison. A negative effect size means a reduction in energy intake after fibre treatment.

Table 2.3a: Study characteristics of different fibre groups on long term energy intake.

fibre group	Comparisons[1]	Studies	Subjects	Blinding	Crossover/ parallel	Food/ supplement	Liquid/ solid	Body/ weight	Diet and lifestyle advice	Assessment	Mean fibre dose[3]	Mean study duration[4]
	(n)	(n)	(n)	(n)	(n)	(n)	(n)	(n)	(n)	(n)	(g)	(h)
				nb/b/db/?[2]	x/p[2]	f/sup[2]	l/s[2]	no/ov[2]	nl/an/ac[2]	ra/ro/ad[2]		
Arabinoxylan rich	8	6	239	4/2/2/0	6/2	8/0	0/8	1/4	3/2/3	2/4/2	15.5	5.2
Psyllium gum	2	2	80	0/1/1/0	2/0	2/0	0/2	0/2	0/0/2	0/1/1	15.8	4.0
Wheat bran	6	5	159	4/1/1/0	4/2	6/0	0/6	1/2	3/2/1	2/3/1	15.4	5.8
Mannan	6	6	127	3/0/3/0	3/3	3/3	3/3	1/5	3/2/1	1/5/0	18.4	19.7
Fructan	5	5	150	0/1/4/0	3/2	1/4	4/1	3/2	5/0/0	0/5/0	15.5	6.7
Resistant starch	6	3	210	0/6/0/0	6/0	6/0	4/2	6/0	4/2/0	6/0/0	28.2	2.3
Arabinoxylan	2	2	26	0/2/0/0	2/0	2/0	0/2	0/2	1/1/0	0/2/0	15.0	5.4
Dextrin	4	3	118	0/1/3/0	1/3	1/3	3/1	3/1	1/3/0	3/0/1	15.1	7.7
Marine polysaccharide	2	2	96	2/0/0/0	1/1	2/0	1/1	0/2	0/1/1	1/1/0	9.6	11.2
β-glucan rich	3	2	102	1/2/0/0	0/3	3/0	0/3	0/3	0/0/3	0/3/0	20.7	12.7
Glucan	1	1	43	0/1/0/0	0/1	1/0	1/0	0/1	0/1/0	0/1/0	5.2	5.0
Chitosan	1	1	56	0/0/1/0	0/1	0/1	0/1	0/1	0/0/1	1/0/0	2.0	17.3
Total fibre	38	31	1167	10/15/13/0	22/16	27/11	16/22	14/21	17/12/9	14/21/3	17.0	8.4

[1] Number of fibre vs. control comparisons, 1 study can result in multiple comparisons.

[2] Abbreviations used for study design characteristics: nb=not blind; b=blind; db=double blind; ?=missing. x=crossover; p=parallel. f=food or drink; sup=supplement. l=liquid; s=solid. no=normal weight; ov=overweight or obese. nl=no lifestyle advice; an=advice not to change; ac=advice to change. ra=diet recall; ro=diet record; ad=ad libitum meal.

[3] Mean fibre dose, weighted by the number of subjects per comparison.

[4] Mean study duration in weeks, weighted by the number of subjects per comparison.

2

Table 2.3b: Effects of different fibre groups on long term energy intake.

fibre group	Effect rate[1] (%)	Effect size[2] (MJ)			Effect size[2] (%)			References
		mean	min	max	mean	min	max	
Arabinoxylan rich	88	-0.64	-2.0	0.2	-7.6	-23.6	2.5	(85-90)
Psyllium gum	100	-0.43	-0.7	-0.4	-4.9	-7.1	-4.5	
Wheat bran	83	-0.74	-2.0	0.2	-8.9	-23.6	2.5	
Mannan	83	-0.38	-1.3	0.7	-4.1	-19.4	6.3	(91-96)
Fructan	80	-0.25	-0.7	0.5	-2.6	-7.8	6.3	(4, 6, 97-99)
Resistant starch	67	-0.22	-0.7	0.2	-1.9	-5.8	1.3	(85, 100, 101)
Arabinoxylan	50	-0.03	-0.2	0.1	-0.2	-2.2	1.2	(102, 103)
Dextrin	50	0.39	-1.0	1.6	-5.8	-13.4	0.6	(5, 104, 105)
Marine polysaccharide	50	-0.34	-0.7	0.8	-4.0	-8.1	11.8	(3, 106)
β-glucan rich	0	0.49	0.0	0.9	3.3	0.5	7.8	(107, 108)
Glucan	0	0.60	0.6	0.6	8.1	8.1	8.1	(56)
Chitosan	0	0.40	0.4	0.4	3.4	3.4	3.4	(109)
Total fibre	63	-0.15	-2.0	1.6	-2.6	-23.6	11.8	

[1] If fibre treatment reduced energy intake compared to control this was rated as an effect. The effect rate is given as n_{effect}/n_{total} in %.

[2] Change in energy intake in MJ and percent, weighted by number of subjects per comparison. A negative effect size means a reduction in energy intake after fibre treatment.

Table 2.4a: Study characteristics of different fibre groups on body weight.

fibre group	Comparisons[1] (n)	Studies (n)	Subjects (n)	Blinding (n) nb/b/db/?[2]	Crossover/ parallel (n) x/p[2]	Food/ supplement (n) f/sup[2]	Liquid/ solid (n) l/s[2]	Body/ weight (n) no/ov[2]	Diet and lifestyle advice (n) nl/an/ac[2]	Mean fibre dose[3] (g)	Mean study duration[4] (wk)
Dextrin	3	2	103	0/0/3/0	0/3	0/3	2/1	2/1	0/3/0	13.7	8.7
Marine polysaccharide	2	2	96	1/1/0/0	1/1	1/1	1/1	0/2	0/1/1	9.6	11.2
Chitosan	7	7	536	0/1/6/0	0/7	1/6	1/6	0/4	1/3/3	2.3	13.5
Fructan	3	3	101	0/0/3/0	1/2	0/3	3/0	0/3	2/1/0	14.4	12.9
Arabinoxylan	3	3	52	0/2/1/0	2/1	2/1	1/2	0/3	1/2/0	9.5	6.7
Mannan	26	25	705	8/2/16/0	15/11	4/22	16/10	4/20	6/15/5	11.9	12.7
Glucomannan	3	3	135	0/0/3/0	1/2	0/3	0/3	0/3	0/2/1	2.7	5.0
Guar gum	23	22	570	8/2/13/0	14/9	4/19	16/7	4/17	6/13/4	14.1	14.5
Arabinoxylan rich	12	11	498	10/1/1/0	3/9	5/7	6/6	0/7	2/4/6	14.2	10.4
Wheat bran	6	5	181	5/0/1/0	3/3	4/2	1/5	0/2	2/3/1	14.5	6.4
Psyllium gum	6	6	317	5/1/0/0	0/6	1/5	5/1	0/5	0/1/5	13.9	12.6
β-glucan rich	4	3	143	1/3/0/0	0/4	3/1	0/4	0/3	0/1/3	13.6	10.2
Glucan	2	2	100	0/1/1/0	0/2	1/1	2/0	0/2	0/1/1	4.8	6.7
Resistant starch	3	2	139	0/0/3/0	2/1	2/1	3/0	2/1	0/3/0	28.9	3.0
Pectin rich	1	1	13	1/0/0/0	1/0	0/1	0/1	0/1	0/0/1	16.0	6.0
Total fibre	66	61	2486	21/11/34/0	25/41	19/47	35/31	8/47	12/34/20	11.1	11.1
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[1] Number of fibre vs. control comparisons, 1 study can result in multiple comparisons.

[2] Abbreviations used for study design characteristics: nb=not blind; b=blind; db=double blind; ?=missing. x=crossover; p=parallel. f=food or drink; sup=supplement. l=liquid; s=solid. no=normal weight; ov=overweight or obese. nl=no lifestyle advice; an=advice not to change; ac=advice to change.

[3] Mean fibre dose, weighted by the number of subjects per comparison.

[4] Mean study duration in weeks, weighted by the number of subjects per comparison.

Table 2.4b: Effects of different fibre groups on body weight.

fibre group	Effect rate[1] (%)	Effect size[2] (kg)	Effect size[2] (%)			Effect size / 4 weeks[2] (%)	References
			mean	min	max		
Dextrin	100	-1.0	-1.0	-1.1	-1.0	-0.58	(104, 105)
Marine polysaccharide	100	-3.5	-4.8	-5.6	-1.9	-1.67	(3, 106)
Chitosan	86	-1.0	-1.2	-4.8	0.5	-0.30	(109-115)
Fructan	67	-6.3	-7.1	-18.5	0.3	-1.70	(4, 26, 98)
Arabinoxylan	67	-0.3	-0.5	-1.2	1.1	-0.25	(102, 103, 116)
Mannan	54	-0.3	-1.2	-6.3	2.9	-0.61	(91-93, 95, 96, 117-136)
Glucomannan	100	-1.1	-1.4	-3.8	-0.3	-0.95	
Guar gum	48	-0.1	-1.2	-6.3	2.9	-0.53	
Arabinoxylan rich	50	-0.1	-0.8	-3.4	1.7	-0.05	(86, 87, 90, 122, 137-143)
Wheat bran	83	-0.7	-1.3	-2.6	0.4	-0.60	
Psyllium gum	17	0.3	-0.5	-3.4	1.7	0.26	
β-glucan rich	50	0.1	0.2	-2.1	1.8	0.21	(107, 141, 144)
Glucan	50	-0.2	-0.1	-0.2	0.0	-0.07	(56, 145)
Resistant starch	33	0.2	0.2	-0.6	0.6	0.32	(101, 146)
Pectin rich	0	0.0	0.0	0.0	0.0	0.00	(147)
Total fibre	59	-0.7	-1.3	-18.5	2.9	-0.39	

[1] If fibre treatment reduced body weight compared to control this was rated as an effect. The effect rate is given as n_{effect}/n_{total} in %.

[2] Change in body weight in kg and percent, weighted by number of subjects per comparison. A negative effect size means a reduction in body weight after fibre treatment.

[3] Change in body weight (%), per comparison recalculated to 4 weeks, weighted by number of subjects per comparison.

Discussion

This review shows that different dietary fibres affect subjective appetite, acute energy intake, long term energy intake, and body weight differently. The physicochemical properties of fibres may contribute to such variation. Viscosity likely explains reductions in subjective appetite and acute energy intake to a greater extent than solubility or fermentability. Viscosity, solubility or fermentability could, however, not exclusively explain reductions in long term energy intake or body weight. Table 2.5 provides an overall summary of these findings.

Other quantitative reviews on the effect of dietary fibres on appetite, energy intake and body weight have been published (8, 27, 28). The current review is, however, the first quantitative overview of the effects of dietary fibre on appetite, energy intake and body weight which focuses on differences between fibres according to structure and physicochemical properties. Most intervention studies limitedly reported physicochemical properties of the fibres used, thus we made assumptions on their degree of solubility, fermentability and viscosity. Due to the high heterogeneity even within fibre types, we did not attempt to estimate molecular weight and water holding capacity. We decided to conduct a systematic review rather than a meta-analysis because many included studies did not report any measure of variance (e.g. standard deviations or confidence intervals). Meta-analyses on effects of guar gum (29) and chitosan (30) on body weight, however, showed changes in body weight comparable to our review.

Short term effects

Pectins and most glucans were the types of fibres which exhibited the largest proportion of appetite reducing effects over a 4 h time interval. For mannans and marine polysaccharides, half of the comparisons exhibited relevant appetite reducing effects. A reduction of 10% compared to a control food has been proposed as a relevant effect size (19). Smaller changes might not affect future energy intake and body weight. Variations in effects between fibres with the same chemical structure can likely be explained by differences in composition of the fibres, which also affects their physicochemical properties. For example cellulose (a glucan) is usually insoluble and non-viscous (31), whereas ethylhydroxyethyl cellulose and microcrystalline cellulose (32, 33) are both soluble and viscous. Similarly, guar gum (a mannan) can be chemically modified to reduce its viscous properties and improve its practical applications without alteration of the polymer structure (34).

We showed that the majority of fibres which reduced subjective appetite had viscous properties. These findings were confirmed by the findings on acute energy intake, despite the limited data on acute energy intake. Several mechanisms of action for effects of viscous fibres have been proposed. Viscous solutions may increase sensory delivered satiety by increased exposure time in the oral cavity (10). Because viscous dietary fibres can hold large quantities of water, they can increase stomach distension which may trigger afferent vagal signals of fullness (35). They may also delay gastric emptying and thereby prolong the absorption of nutrients (11, 36). Furthermore, the increased viscosity of digesta in the small intestine can also result in prolonged presence of nutrients in the small intestine which in turn affects the release of appetite-regulating peptides throughout the

Table 2.5: Summarized effects of dietary fibre on subjective appetite, acute and long term energy intake and body weight.

Fibre group	Subjective appetite		Acute energy intake		Long term energy intake		Body weight	
	Comparisons	Effect	Comparisons	Effect	Comparisons	Effect	Comparisons	Effect
Arabinoxylan					2	+	3	+
Arabinoxylan rich	16	+	1	–	8	++	12	–
Chitosan					1	–	7	++
Dextrin	3	–	1	++	4	–	3	++
Fructan	6	–	4	–	5	++	3	+
Glucan	13	++	5	–	1	–	2	–
β-glucan rich	2	–	4	++	3	–	4	–
Mannan	8	+	6	–	6	++	26	+
Marine polysaccharide	2	+			2	–	2	++
Pectin rich	1	++					1	–
Pectin	4	++	1	++				
Resistant starch	3	–	1	++	6	+	3	–
More viscous	37	++	16	+	12	–	45	+
Less viscous	21	+	10	–	26	+	21	+
More soluble	46	+	22	+	23	+	47	+
Less soluble	12	+	4	–	15	+	19	+
More fermentable	33	+	16	+	24	+	39	+
Less fermentable	25	+	10	–	14	+	27	+
Total fibre	58	+	26	+	38	+	66	+

Effects are recoded from effect rates. For subjective appetite an effect rate of 0% is recoded to '–'; 1% to 50% is recoded to '+'; and 51% to 100% is recoded to '++'. For acute energy intake, long term energy intake and body weight an effect rate of 0% is recoded to '–'; 51% to 75% is recoded to '+'; and 76% to 100% is recoded to '++'.

intestine, such as cholecystokinin (CCK) in the duodenum and peptide tyrosine tyrosine (PYY) and glucagon-like peptide 1 (GLP-1) in the distal ileum and proximal colon (37). As a result, subjective appetite may be reduced.

When fibres were provided as liquids they appeared to have stronger appetite reducing effects compared to solids. We hypothesize that hydration of the dietary fibres may differ depending on the food matrix. Furthermore, the rate of hydration might also explain differences in physiological effects within the group of viscous fibres, as some fibres are hydrated immediately upon mixing whereas others take hours to be fully hydrated (38, 39). With these quantitative data we confirm findings from previous reviews (8, 17, 27) that fibres with viscous properties are an important regulator of short term appetite as well as acute energy intake.

The current review does not include long-term studies on subjective appetite. Long-term fibre supplementation may, however, affect appetite via specific routes, such as affecting microbiota composition (40), SCFA production (17, 41) and gastrointestinal hormone release (42, 43). Our search retrieved only a limited number of studies assessing long-term effects on subjective appetite (n=14). Hence, mutual comparison of these studies was hampered by a lack of common methodology.

Long term effects

The results from this review suggest that dietary fibres may reduce long term energy intake and body weight. Across fibre groups, the overall average reduction in body weight was 0.4% per 4 weeks, which is 300 g per 4 weeks for an average participant of 79 kg. For energy intake the average reduction was 0.15 MJ per day. However, not all fibres appeared to be equally efficient for long term effects. Dextrins, marine polysaccharides, and chitosan showed the highest effect rates in body weight reduction, whereas arabinoxylan rich fibres, mannans, and fructans showed the highest effect rates in long term energy intake reduction. Due to the greater number of studies and more uniform methodology of measuring body weight, we think that the studies on body weight better represent the long-term effects of fibres.

As reflected in the overall average for both energy intake and body weight, effect sizes were relatively small in many studies and differed largely between studies. Nonetheless, even small differences may be of clinical relevance, as an average yearly weight gain of 0.5-1.0 kg with an estimated positive energy balance of less than 0.2 MJ per day is considered to account for the weight gain in 90% of the adult American population (44).

Long term energy intake or body weight reduction could not be associated with the physicochemical properties viscosity, solubility and fermentability. These findings suggest that for long term body weight management not one single mechanism predominates, but rather that multiple mechanisms come into play, as also suggested by others (8, 45-47). On the long term viscous fibres might be primarily effective as an appetite suppressor when it is used in a healthy lifestyle. This relation was not studied in this review. Besides the mechanisms proposed for acute appetite suppression, insulin sensitivity may play a role in long term effects both through changes in appetite regulation

as well as altered adipocyte metabolism (48). Furthermore, fermentation of dietary fibres in the large intestine may alter the growth of specific gut microbiota and affect short chain fatty acid production and composition. These short chain fatty acids may affect the secretion of appetite-regulating peptides or may be used as an energy source after absorption (14). Fibres can also reduce the bioavailability of nutrients, for example by entrapping fat in the intestine, which is a well-known mechanism of action of chitosan (49). Combinations of these and other putative mechanisms should be considered. The interplay of multiple working mechanisms also likely explains why we did not find clear dose-response effects of fibre on body weight.

Importance of study design

Several critical factors in study design, other than the type of fibre, should be carefully considered when designing and evaluating effects of dietary fibre on appetite, energy intake and body weight. First, the strategy of fibre supplementation may affect the outcomes. Fibre can be administered as isolated fibres in supplements, as isolated fibres processed in foods, or as drinks or foods naturally containing high amounts of fibre. If isolated fibres are ingested as supplements, hydration may not yet have occurred within the time frame of a postprandial study (38), and therefore found to be less effective. Foods naturally rich in dietary fibres also contain other bioactive compounds; the latter might also change findings related to appetite and food intake which make comparisons with isolated fibres or a placebo product more complex.

Second, adding fibre to a diet implies either exchanging the fibre with a nutrient, which affects the macronutrient content of the diet, or adding the fibre on top of a diet, which results in excess energy intake and a change in meal volume. Effects of fibre may be confounded with effects of macronutrients and meal size (35, 37, 50). All these decisions on which fibres to use and how to provide them have their limitations; therefore direct comparisons should be done with some caution.

Third, and in contrast to acute appetite studies, long term studies are usually not designed primarily to measure long term energy intake and body weight, but rather effects on blood lipids or insulin resistance. Therefore, they may lack power, study duration, quality of measurements, or the appropriate study population to be able to find clear effects (51). In this review 30% of the long term studies were primary aimed at studying energy intake or body weight. The effect rate of these studies was 15% higher compared to studies that were not primary aimed to study energy intake or body weight.

The regulation of food intake and body weight involves complex physiological and psychological features, and differs in the short and long term (19 , 52). Physiological adaptation to a changed dietary pattern (e.g. adaptation of gastric distention or gut microbiota), together with psychological and external aspects such as anticipating and building on external stimuli at moment of consumption, play an important role in long term effects on energy intake and body weight regulation (53). Hence, it is very difficult to compare studies and to extrapolate findings in short term appetite research to longer term effects. Most of our current knowledge on satiating properties of dietary fibres is

based on short term studies. The challenge for future research will be to identify the relationship between those short term appetite sensations and longer term changes in energy intake and body weight.

In conclusion, different types of fibre affect subjective appetite, acute energy intake, long term energy intake, and body weight differently. More viscous fibres presumably affect subjective appetite and acute energy intake, whereas no evident association between physicochemical properties and long term energy intake or body weight was found. The quality of the long term studies and the complex physiological influence of fibres on long term energy intake and body weight limit extrapolation of findings in short term studies. Additional research on fibres and their short-term and long-term subjective appetite, energy intake and body weight is necessary, and a thorough characterization of the fibres used in terms of physicochemical properties is encouraged.

Funding

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Appendix 1

Research question as searched in PubMed on 17-2-2010

Fibre

(Dietary fibre [mesh]) OR (Non-starch polysaccharide* [tiab]) OR (Resistant oligosaccharide* [tiab]) OR (Beta-glucans [mesh] OR Beta-glucans [tiab]) OR (Cellulose [mesh] OR Cellulose* [tiab]) OR (Hemicellulose* [tiab]) OR (Arabinoxylan* [tiab]) OR (Arabinogalactan* [tiab]) OR (Polyfructose* [tiab]) OR (Inulin* [tiab]) OR (Oligofructan* [tiab]) OR (Galacto-oligosaccharide* [tiab] OR Galactooligosaccharide* [tiab]) OR (Plant gums [mesh] OR Plant gum* [tiab]) OR (Mucilage* [tiab]) OR (Pectin* [tiab]) OR (Analogous carbohydrate* [tiab]) OR (Indigestible dextrin* [tiab]) OR (Resistant maltodextrin* [tiab]) OR (Resistant potato dextrin* [tiab]) OR (Synthesized carbohydrate compound* [tiab]) OR (Polydextrose [tiab]) OR (Resistant starch* [tiab]) OR (Lignin* [tiab]) OR (Wax* [tiab]) OR (Phytate* [tiab]) OR (Cutin* [tiab]) OR (Saponin* [tiab]) OR (Suberin* [tiab]) OR (Tannin* [tiab]) OR (Alginate* [tiab]) OR (Carrageenan* [tiab]) OR (Chitin [mesh] OR Chitin* [tiab]) OR (Fructans [mesh] OR Fructan* [tiab]) OR (Galactans [mesh] OR Galactan* [tiab]) OR (Amylose* [tiab]) OR (Dextrins [mesh] OR Dextrin* [tiab]) OR (Trehalose* [tiab]) OR (Glycosaminoglycans [mesh] OR Glycosaminoglycan* [tiab]) OR (Mannan* [tiab]) OR (Trisaccharides [mesh] OR Trisaccharide* [tiab]) OR (Xylan* [tiab]) OR (Fructooligosaccharide* [tiab] OR Fructo-oligosaccharide* [tiab]) OR (Oligofructose* [tiab]) OR (Glucooligosaccharide* [tiab] OR Gluco-oligosaccharide* [tiab]) OR (Cyclodextrin* [tiab]) OR (Xylooligosaccharide* [tiab] OR Xylo-oligosaccharide* [tiab]) OR (Guar gum* [tiab]) OR (Locust bean gum* [tiab]) OR (Psyllium* [tiab]) OR (Mannanoligosaccharide [tiab] OR Mannan-oligosaccharide* [tiab]) OR (Bran [tiab]) OR (brans [tiab]) OR (Pulp [tiab]) OR (pulps [tiab]) OR (Whole grain [tiab] OR wholegrain [tiab]) OR ((fiber* [tiab] OR fibre* [tiab]) AND (diet [tiab] OR diets [tiab] OR dietary [tiab] OR intake* [tiab] OR consumption [tiab] OR fruit* [tiab] OR vegetable* [tiab] OR food* [tiab] OR soluble [tiab] OR insoluble [tiab] OR fermentable [tiab])) OR (prebiotic* [tiab])

Outcomes

(Satiation [mesh]) OR (satiat* [tiab]) OR (Hunger [mesh]) OR (Appetite [tiab]) OR (Appetite Depressant [mesh]) OR (Personal Satisfaction [mesh]) OR (Personal Satisf* [tiab]) OR (satisfaction* [tiab]) OR (satiet* [tiab]) OR (hunger [tiab]) OR (Desire to eat [tiab]) OR (prospective food consumption [tiab]) OR (Fullness [tiab]) OR (subjective feeling* [tiab]) OR (energy intake [mesh]) OR (energy intake* [tiab]) OR (caloric restriction [mesh]) OR (caloric restrict* [tiab]) OR (Caloric intake* [tiab]) OR (Ingestion [tiab]) OR (Food intake [tiab]) OR (Food intakes [tiab]) OR (Food consumption* [tiab]) OR (Food consuming [tiab]) OR (Eating behav* [tiab]) OR (Water Consumption [tiab]) OR (Water Consuming [tiab]) OR (Water Intake [tiab]) OR (Water drinking [tiab]) OR (Ad libitum intake* [tiab]) OR (Ad libitum [tiab] AND intake [tiab]) OR (Body Weight Changes [mesh]) OR (Body Weight Change* [tiab]) OR (Body weight [tiab]) OR (Bodyweight [tiab]) OR (Body weight [mesh]) OR (weight gain [tiab]) OR (weight gaining [tiab]) OR (weight gains [tiab]) OR (weight loss [tiab]) OR (body mass index [mesh]) OR (body mass index [tiab]) OR (bmi [tiab]) OR (Quetelet* index [tiab]) OR (Weight management [tiab]) OR (Weight regulat* [tiab]) OR (Weight reduc* [tiab]) OR (Negative energy balance [tiab]) OR (energy expend* [tiab]) OR (obesity treatment [tiab])

Combine

(FIBRE) AND (OUTCOMES)

Limitations

[(RESULS) NOT ((rat OR Rats OR Mouse OR Mice OR pig OR pigs OR cow OR cows OR sheep OR chicken* OR dog OR dogs) NOT human [mesh])

Limit: Only English

3

The effects of bulking, viscous and gel forming dietary fibres on satiation

Authors

Anne J. Wanders

Melliana C. Jonathan

Joost J.G.C. van den Borne

Monica Mars

Henk A. Schols

Edith J.M. Feskens

Cees de Graaf

Abstract

The objective was to determine the effects of dietary fibre with bulking, viscous and gel forming properties on satiation, and to identify the underlying mechanisms. We conducted a randomized crossover study with 121 men and women. Subjects were healthy, non-restrained, aged 18-50 years, and with normal BMI (18.5-25 kg/m^2). Test products were cookies containing either: no added fibre (control), cellulose (bulking, 5 g/100 g), guar gum (viscous, 1.25 g/10 g and 2.5 g/100 g) or alginate (gel forming, 2.5 g/100 g and 5 g/100 g). Physico-chemical properties of the test products were confirmed in simulated upper gastrointestinal conditions. In a cinema setting *ad libitum* intake of the test products was measured, concurrently with oral exposure time per cookie by video recording. In a separate study with 10 subjects, 4h gastric emptying rate of a fixed amount of test products was assessed by ^{13}C breath tests. *Ad libitum* energy intake was 22% lower for the product with 5 g/100 g alginate (3.1 (SD 1.6) MJ) compared to control (4.0 (SD 2.2) MJ, p <0.001). Intake of the other four products did not differ from control. Oral exposure time for the product with 5 g/100 g alginate (2.3 (SD 1.9) min) was 48% longer than for control (1.6 (SD 0.9) min, p =0.01). Gastric emptying of the 5 g/100 g alginate product was faster compared to control (p <0.05). We conclude that the addition of 5 g/100 g alginate (i.e. gel forming fibre) to a low fibre cookie results in earlier satiation. This effect might be due to an increased oral exposure time.

Introduction

The consumption of dietary fibre has been associated with increased satiety and reduced energy intake (1-5). Satiety and satiation are part of a complex system of appetite control, including cognitive factors, sensory sensations and post-ingestive feedback mechanisms (6). Satiety is defined as the inhibition of appetite and occurs as a consequence of eating. Satiation is defined as the satisfaction of appetite that develops during the course of a meal, and results in meal termination. Numerous studies have been done to clarify the effects of dietary fibre on satiety (4,5,7). Studies on the effects of fibre on satiation are, however, limited and show inconsistent results. For example Grimes and Gordon (8) found that the satiating capacity of wholemeal bread was higher than that for white bread. Opposing to this, Burley et al. (9) did not find differences in *ad libitum* intake between a meal containing a meat replacer with chitin and insoluble β-glucan, and a similar, low fibre meal. Odunsi et al. (10) also did not find differences in *ad libitum* intake after ingestion of capsules with cellulose and alginate compared to placebo capsules.

Dietary fibre is a term that reflects a heterogeneous group of compounds which differ in their chemical structure and physico-chemical properties. Dietary fibres may affect satiation via diverse related mechanisms (7,11). First, the metabolizable energy content of fibre is less than that for other nutrients (12), and as meal intake volume is relatively constant (13), the inclusion of fibre in foods decreases total energy intake. Second, adding fibre to a meal can increase chewing activity or oral exposure time to foods, which may result in earlier satiation (14-16). Third, the addition of fibre can increase viscosity and water holding capacity of digesta and induce formation of gels in the stomach (11,17). These properties can slow down gastric emptying and concurrently increase stomach distension. Stomach distension, or fullness, is seen as a causal factor in the chain of events leading to satiation (18,19). In response to the mechanical and physico-chemical properties of the ingested foods, a series of neural and humoral signals develop from the gut, which can result in satiation (20).

The aim of this research was to determine the effects of three distinctive dietary fibres with different physico-chemical properties on satiation. Hence we selected cellulose, a bulking fibre; guar gum, a viscous fibre; and alginate, a gel forming fibre, and we added the selected fibres to test products. Two dosages of guar gum and alginate were included to be able to study effects of high fibre, but less palatable products. Physico-chemical properties of the test products were characterized in simulated upper gastrointestinal conditions. Satiation was determined by measuring *ad libitum* intake of the test products in a real life setting. Furthermore, oral exposure time and gastric emptying rate were measured.

Subjects and methods

Two short-term intervention studies were conducted. Satiation and oral exposure time were determined in study one, and gastric emptying rate was assessed in study two. In both studies the subjects participated in six test sessions with six different test products.

Subjects

For both studies men and women, aged 18 to 50 year were recruited in Wageningen and Ede, The Netherlands. Subjects had to have a normal BMI (18.5 - 25.0 kg/m^2), and had to be healthy. Subjects were excluded if they were restrained eaters according to the Dutch Eating Behaviour Questionnaire (DEBQ) (score: men >2.89; women >3.39) (21). They were also excluded if they used an energy restricted diet or lost or gained more than 5 kg body weight during the last two months, if they had a lack of appetite, had diabetes, gastrointestinal problems, or were hypersensitive for any ingredient in the test products. This study was conducted according to the guidelines laid down in the Declaration of Helsinki and all procedures involving human subjects were approved by the Medical Ethics Committee of Wageningen University (registration number NL 26703.081.09). Written informed consent was obtained from all subjects. The study was registered in the National Institutes of Health clinical trial database (ClinicalTrials.gov no NCT00904124).

Out of the 124 subjects in study one, three dropped out due to reasons unrelated to the intervention. We included 121 subjects in data analysis, of which 112 participated in six sessions, seven in five sessions and two in four sessions. The missed sessions were due to illness or problems with planning. The study population for study one consisted of 45 men and 76 women, aged 25 $\pm$ 7 years, with a BMI of 22.0 $\pm$ 1.9 kg/m^2 and a DEBQ score of 2.1 $\pm$ 0.6. The number of women in the menstrual phase did not differ (p =0.79) between treatments.

Ten subjects, six men and four women, participated in study two. All subjects were included in data analysis, of which nine participated in six sessions and one in five sessions. The missed session was due to problems with planning. Mean age of the participants was 21 $\pm$ 3 y, mean BMI 21.8 $\pm$ 1.9 kg/m^2, and mean DEBQ score 1.8 $\pm$ 0.7.

Test products

The six test products were one-bite sized (6.8 $\pm$ 0.3 g) chocolate cookies. The basic recipe of the cookies contained 36% white flour, 27% butter, 18% sugar, 14% chocolate chips, 4% egg, 2% cacao powder and 0.1% salt. Flour was exchanged for dietary fibre. Cellulose (Vitacel L 00, Rettenmaier & Söhne) was given in a dose of 5%; guar gum (Viscogum^{TM} MP 41230, Cargill; molecular weight (MW) 60 - 1,000 kDa) in doses of 1.25% and 2.5%, and alginate (Protanal LF 5/60, FMC BioPolymer; MW 17 $\pm$ 710 kDa; guluronic acid:mannuronic acid (G:M) ratio of 1.9) in doses of 2.5% and 5%. A professional bakery manufactured the cookies freshly on each test day.

Duplicate portions of the products were collected on each test day and stored at -20 $^\circ$C pending measurements for macronutrients and physico-chemical properties. Before measurements, a homogenized mixture of cookies was ground until it passed a 2 mm sieve. Protein, total fat, total dietary fibre, moisture and ash were measured according to methods previously described (22). Available carbohydrate was estimated by subtracting moisture, ash, protein, fat and fibre from total weight. Atwater factors were used to calculate available energy: fat 37 kJ/g, protein and carbohydrate 17 kJ/g. For fibre 0 kJ/g was used because of uncertainty about the availability of energy

(12). This may have underestimated the available energy content. Macronutrient composition is shown in Table 3.1.

Physico-chemical properties were measured only for the high dose products and the control. These properties included viscosity and water holding capacity using three conditions to simulate the mouth, stomach and small intestine. Measurements were performed according to methods described by Turnbull et al. (23), with modifications for the amount of samples and types of reagents. Reagents used included α-amylase from porcine pancreas (1.16312.0001, Merck), pepsin from porcine gastric mucosa (P6887, Sigma-Aldrich), pancreatin from porcine pancreas (P1625, Sigma-Aldrich) and bile extract (B8631, Sigma-Aldrich). The amount of sample was increased fourfold, to compensate for lower fibre levels. Furthermore, the volume for each simulation was set to 30 mL, and amounts of sample and reagents were adjusted comparatively. In addition, amounts of enzymes were adjusted to obtain similar activity. Bile was increased fourfold to ensure good emulsification of fat. After each simulation, samples were centrifuged at 4250 g for 20 min. The supernatant was decanted and used for viscosity measurements. The tube with the remaining pellet was inverted to remove excess water. The pellet which contained insoluble material was weighed and dry matter was measured. Water holding capacity was expressed as the amount of water held after centrifugation by the insoluble material from 1 g of cookie.

Viscosity of the supernatant was measured at 37 °C, using a rheometer (MCR 501, Anton Paar) with double gap geometry. A shear sweep was performed at 1-1000/s in logarithmic scale during 5 min. Data obtained at shear rate 100/s were used to compare between samples.

Experimental procedure: study one

Ad libitum intake was measured in a randomized single blind crossover study with six test sessions, separated by at least two days. *Ad libitum* intake was calculated from the weight of the test products before and after consumption. Products were weighed in duplicate on a digital scale with a precision of 0.1 g. Subjects were not aware that the primary outcome was *ad libitum* intake, as this could affect the outcome of the study.

The study was performed in a cinema (Cinemec) to create a real-life setting aimed to distract subjects from visual and weight cues (24). During each test session subjects watched a movie in the genres romance or comedy. On each test day the subjects arrived at 18:00h. At 18:45h they were seated in the theatre. Just before entering the theatre, 400 g of test product was served in a white carton box and a bottle with 500 ml water was provided. The subjects were instructed to eat as little or as much of the test product as they wanted until they felt comfortably full. The movie was divided in two parts of 45 min, with a 15 min break. During the break, subjects left the theatre and handed in the box with test product. At the restart they received a new box with 400 g of test product. The participants were instructed to finish the bottle of water before the end of the movie.

Before and after *ad libitum* intake, subjects rated five appetite questions on 100 mm Visual Analogue Scales (VAS). Scales were anchored from 'not at all' to 'very much' and included feelings of hunger, fullness, desire to eat, prospective food consumption and thirst. Before *ad libitum* intake,

Table 3.1: Available energy and macronutrient composition of the test products (per 100 g).

Component	Control		Cellulose 5%		Guar gum 1.25%		Guar gum 2.5%		Alginate 2.5%		Alginate 5%	
	(g)	(En%)	(g)	(En%)	(g)	(En%)	(g)	(En%)	(g)	(En%)	(g)	(En%)
Available energy (kJ)[1]	2241		2087		2204		2171		2180		2122	
Fat	33.3	55	32.2	57	33.3	56	33.2	57	33.2	56	33.2	58
Protein	6.4	5	5.9	5	6.3	5	6.2	5	6.5	5	5.8	5
Available carbohydrates	53.1	40	46.7	38	51.0	39	49.3	39	49.6	39	46.8	38
Dietary fibre	3.6		10.6		5.6		6.9		6.0		9.0	

En%, percentage of energy, as derived from the specific nutrient compared to the total calculated energy content of the test product.

[1] Available energy was calculated based on chemical analysis of the macronutrient composition. Energy conversion factors used: Fat 37 kJ/g, protein and carbohydrate 17 kJ/g. Energy content of fibre was set at 0 kJ/g.

Table 3.2: Viscosity and water-holding capacity of the test products in simulated upper gastrointestinal conditions (Mean values and standard deviations).

Properties	Control		Cellulose 5%		Guar gum 2.5%		Alginate 5%		P[1]
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
Viscosity (mPa.s)[2]									
Mouth	1.4	0.2	1.3	0.3	34.5	9.4***	5.9	0.7	<0.001
Stomach	1.2	0.3	1	0.1	8.4	1.8***	1.7	0.4	<0.001
Small intestine	2.5	1.3	3.5	1.1	5.6	0.9***	4.1	0.8*	<0.001
Water holding capacity (g water/g cookie)[3]									
Mouth	0.41	0.02	0.47	0.06	0.70	0.02***	0.37	0.01	<0.001
Stomach	0.47	0.06	0.53	0.06	0.48	0.02	1.51	0.12***	<0.001
Small intestine	0.28	0.06	0.46	0.07	0.37	0.06	0.33	0.12	0.052

Mean values were significantly different from control: * P <0.05, *** P <0.001

[1] P-value from one-way ANOVA, subsequently all fibre treatments were compared to control with Dunnet's procedure.

[2] Viscosity in mPa.s at shear rate 100/s; mean of 6 measurements.

[3] The amount of water held by the insoluble material from 1 g of cookie; mean of four measurements.

the participants were also asked to rate palatability, expected satiation, and sensory attributes (sweetness, bitterness, chocolate taste, freshness, dryness, stickiness, difficulty to swallow) of the test product on 100 mm VAS.

To standardize the individual state of satiety, subjects were instructed to eat the same breakfast and lunch at all six test days and to record this in a diary. Individual state of satiety was further standardized by consuming a preload at 6:00pm. The preload provided approximately 18% of the daily energy requirements. This was chosen to correspond to half the energy content of a normal Dutch dinner (25). Individual energy requirements were calculated by the Schofield equation (26), and subjects were divided into one of three preload groups. Group one (estimated energy need $\leq$ 10 MJ, n=63) received 0.5 pizza, group two (10-14 MJ, n=56) received 0.75 pizza, and group three ($\geq$14 MJ, n=2) received 1.0 pizza.

Oral exposure time

Oral exposure time of the test products was measured by means of video recording a random subgroup of 11 men and 25 women. To record eating time, five video cameras were used (Sony Handycam DCR-HC51/DCR-SR55E; Sony). These were set at night shot mode and supported by two separate infrared lights. Video analysis on oral exposure time over the first 45 min of the movie was done through The Observer® XT9 (Noldus). Oral exposure time was measured in seconds and defined as time spent on chewing, swallowing, cleaning the mouth and teeth with tongue or fingers. Breaks were considered as not eating. Two researchers coded the video recordings.

Reliability analysis were carried out regularly, which resulted in an inter-observer agreement of κ = 0.75 (p <0.01). Due to varying reasons (e.g. view blocked, poor quality of light) videos of 21 to 27 subjects per test product were suitable for quantifying oral exposure time.

Experimental procedure: study two

In a second randomized single blind crossover trial, gastric emptying rate and appetite sensations were measured in six test sessions, separated by at least seven days. Subjects consumed a fixed amount of the test products, which corresponded to approximately 20% of daily energy requirements (25). This resulted in dosages varying from 80 to 100 g. Each portion was supplemented with 87.4 mg $[^{1-13}C]$octanoic acid (Campro Scientific GmbH). Breath samples were collected by breathing into a 10 ml Exetainer tube (Labco) via a drinking straw and then closing the tube with a cap. Samples were stored at room temperature and were analysed for ^{13}C enrichment in CO_2 on a Finnigan Delta C continuous-flow isotope ratio mass spectrometer (Finnigan MAT).

Subjects arrived at our research centre between 7:30 and 8:00am after a 10h overnight fast. They were asked to consume a low fibre meal on evenings before test sessions. In addition, they should avoid unusual vigorous physical activity and consuming products naturally enriched in ^{13}C (maize, millet, sorghum, cane sugar). Before ingestion of the test product, within 10 min together with 300 ml water, two baseline breath samples were taken. Subsequent breath samples were taken after exactly 15, 30, 45, 60, 75, 90, 105, 120, 150, 180, 210, and 240 min. Appetite sensations were rated on 100 mm VAS as described for study one, and measured at baseline and after 30, 60, 90, 120, 150, 180, 210, and 240 min. Subjects were seated at a desk and allowed to do light desk work during the session.

Statistical analysis

Data are presented as means and SD. Statistical analyses were performed with SAS (version 9.2; SAS institute Inc.). Significance was set at p <0.05. One-way ANOVA was used to analyse differences between physico-chemical properties of the cookies. For study one treatment effects on sensory ratings, palatability ratings, *ad libitum* intakes and eating time were analysed by means of a mixed model ANOVA (proc mixed). Treatment, day and treatment*day interaction (=order) were included as fixed factors and subject was included as random factor. For dose-response effects orthogonal contrasts between control, low and high dose fibres were calculated. If the treatment effect was statistically significant, Dunnet's procedure was used to compare the fibre treatments with the control treatment, to control for multiple testing. The appetite ratings were analysed according to a similar procedure, with the addition of time (before and after *ad libitum* intake) and treatment*time as fixed factors in the model. Additionally, to control for differences in appetite ratings at baseline, baseline values were added to the model as a covariate. For study two, treatment effects were analysed according to a similar procedure, after calculation of total areas under the curves for appetite ratings and gastric emptying rate (proc expand). Time to peak data were not normally distributed and were therefore log-transformed for analysis and presented as back-transformed geometric means (95% Confidence Intervals). Pearson's partial correlation coefficient, controlled

for subject, was calculated to assess relations between sensory properties, palatability and *ad libitum* intake for the treatments separately and together.

Results

Physico-chemical properties

Physico-chemical properties of the test products in simulated upper gastrointestinal conditions are presented in Table 3.2. Under mouth-like conditions, high dose guar gum increased viscosity up to 24-fold compared to control (p <0.001). The increased viscosity for high dose guar gum persisted under simulated conditions for stomach and small intestine (p <0.001). High dose alginate increased water holding capacity up to 3-fold in the stomach-like conditions compared to control (p <0.001).

Study one

Palatability and sensory ratings of test products

Mean palatability and sensory ratings of the test products are given in Table 3.3. Products with cellulose (p <0.001), high dose guar gum (p =0.001) and high dose alginate (p =0.023) were rated lower on palatability than control. Expected satiation was rated similar for all test products compared to control. All fibre-enriched products changed in texture ratings compared to the control product. The products with cellulose, high dose guar gum and both dosages of alginate were rated more sticky (p <0.001) than control.

Appetite ratings

After *ad libitum* intake, ratings for hunger, desire to eat and prospective consumption decreased (p <0.001) and ratings for fullness increased (p <0.001) for all test products compared to before *ad libitum* intake. The change in ratings compared to baseline did not differ between test products (data not shown).

Ad libitum intake

Figure 3.1 shows the total *ad libitum* intake of the test products. Before the break, at 45 min, *ad libitum* intake represented 67 to 70% of total intake for all test products. Intake of the products containing cellulose, both dosages of guar gum, and the low dose alginate did not change compared to the control product, regardless of the dimension used (i.e. gram or MJ). Compared to the control product, high dose alginate reduced *ad libitum* intake in gram by 17% (p <0.001), which corresponded to a reduction in MJ of 22% (p <0.001). In addition, a dose-response effect of alginate was found; increasing fibre dose reduced *ad libitum* intake (p <0.05).

Palatability scores were positively correlated with *ad libitum* intake (r =0.17; p <0.001). For the individual products this correlation was only found for test products containing cellulose (r =0.18; p =0.045), low dose guar gum (r =0.40; p <0.001), and high dose guar gum (r =0.19; p =0.041). Scores

Table 3.3: Palatability ratings, expected satiation and analytical attributes[1] by test product, before *Ad libitum* intake (Mean values and standard deviations)

Attribute	Control		Cellulose 5%		Guar gum 1.25%		Guar gum 2.5%		Alginate 2.5%		Alginate 5%		P[1]
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
Palatability	66	17	51	21***	62	17	59	17**	63	17	61	18*	<0.001
Expected satiation	52	19	53	18	49	18	51	17	52	18	55	16	0.022
Sweetness	58	18	50	20***	55	19	48	21***	52	19*	55	18	<0.001
Bitterness	30	20	29	21	32	21	31	21	30	21	28	20	0.082
Chocolate taste	64	17	57	18**	58	19*	53	20***	60	17	59	19*	<0.001
Freshness	68	20	41	22***	64	19	56	20***	64	20	63	19*	<0.001
Dryness	45	22	58	23***	50	21	52	22	50	23	53	23**	<0.001
Stickiness	40	23	49	23**	47	24	55	24***	57	23***	71	16***	<0.001
Difficulty to swallow	31	21	42	26***	37	22	41	24***	42	25***	51	25***	<0.001

Mean values were significantly different from control: * P <0.05, ** P <0.01, *** P <0.001

[1] Values were measured on a 100 mm Visual Analogue Scale anchored from 'not at all' to 'very much' (0 to 100). Measured in 121 subjects.

[2] P-value from mixed model ANOVA, subsequently all fibre treatments were compared to control with Dunnet's procedure.
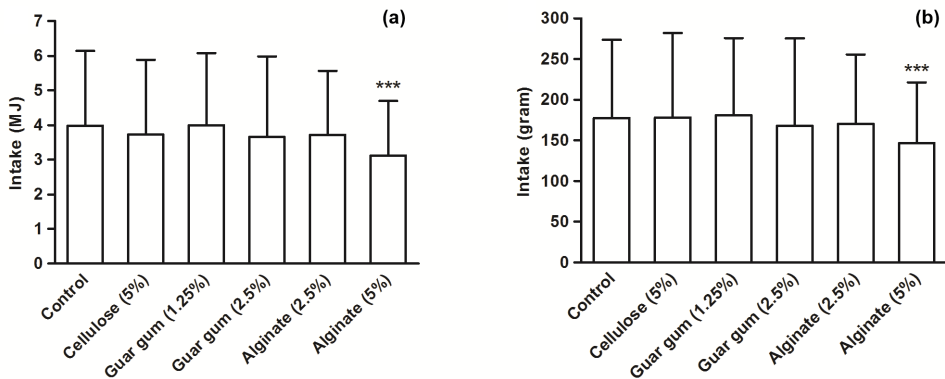
Figure 3.1: *Ad libitum* intake of the test products in a) MJ (SD) (n 121), and b) g (SD) (n 121). Analysis with mixed-model ANOVA resulted in p <0.001, subsequently all fibre treatments were compared to control with Dunnet's procedure. Orthogonal contrasts among control, low- and high-dose guar gum and alginate showed a dose-response effect of alginate (p <0.05). ***Values were significantly different from control (p <0.001).

for stickiness were inversely correlated with *ad libitum* intake (r = -0.10; p =0.008), but this was not found for the individual test products. Adjusting the results of *ad libitum* intake for palatability and stickiness of the test products, by including these variables as covariates in the model, did not change the findings.

Oral exposure time

In the subgroup for video analysis (n=36), *ad libitum* intake of test products did not differ from the intake in the complete group. Although there was an effect of treatment on total oral exposure time (p =0.045), this effect could not be localized to specific test products compared to control (Table 3.4). Oral exposure time per cookie was only longer for the high dose alginate, compared to control (p =0.01).

Study two

Table 3.5 shows the area under the curve (AUC) and time to peak for gastric emptying. Compared to control, AUC for gastric emptying was larger after consumption of the products with cellulose (p =0.048), low dose alginate (p =0.027), and high dose alginate (p =0.004). Additionally, time to reach the peak % dose recovery of ^{13}C per hour was 27% shorter for high dose alginate compared to control (p =0.03). AUC's for 4h ratings of hunger, fullness, desire to eat and prospective consumption did not differ between the test products and control (data not shown).

Table 3.4: Total oral exposure time and oral exposure time[1] of the test products measured by video observation (Mean values and standard deviations).

	Control (n=26)		Cellulose 5% (n=25)		Guar gum 1.25% (n=27)		Guar gum 2.5% (n=22)		Alginate 2.5% (n=24)		Alginate 5% (n=21)		P[1]
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
Total oral exposure time (min)[1]	20.2	8.9	20.2	10.6	24.9	11.7	24.1	14.0	22.3	9.5	22.9	12.5	0.045
Oral exposure time per cookie (min)	1.6	0.9	1.7	1.5	1.7	1.3	2.0	1.6	1.7	0.8	2.3	1.9**	0.043
Oral exposure time per MJ (min)	9.4	4.9	10.7	8.1	10.2	7.0	11.8	9.1	10.1	4.5	13.1	8.3**	0.031

Mean values were significantly different from control: ** P <0.01

[1] Total oral exposure time and oral exposure time per test product are reported in minutes over the first 45 min of a test day. Measured in a subgroup of thirty-six subjects.

[2] P-value from mixed model ANOVA, subsequently all fibre treatments were compared to control with Dunnet's procedure.

Table 3.5: Gastric emptying rate per test product expressed as area under the curve (AUC) and time to peak [1] (Mean values and 95% confidence intervals)

	Control (n=9)		Cellulose 5% (n=9)		Guar gum 1.25% (n=10)		Guar gum 2.5% (n=10)		Alginate 2.5% (n=10)		Alginate 5% (n=10)		P[2]
	Mean	95% CI	Mean	95% CI	Mean	95% CI	Mean	95% CI	Mean	95% CI	Mean	95% CI	
AUC	1780	1513 - 2047	2045	1769 - 2321*	1918	1650 - 2185	1864	1579 - 2149	2126	1860 - 2392*	2145	1877 - 2412**	0.007
Time to peak (min)	83	56 - 123	64	41 - 102	81	59 - 110	99	67 - 148	66	44 - 99	61	45 - 83*	0.006

Mean values were significantly different from control: * P <0.05, ** P <0.01.

[1] Gastric emptying was measured as percentage dose recovery of ^{13}C per h after ingestion of a fixed amount of test product. Total AUC over 240 min was calculated according to the trapezoid method. An increase in AUC reflects an increased amount of test product that is emptied into the duodenum over 240 min. Data on time to peak were log-transformed for analysis and are presented as back-transformed geometric means (95% CI).

[2] P-value from mixed model ANOVA, and subsequently all fibre treatments were compared to control with Dunnet's procedure.

3

Discussion

In this study we found that cookies supplemented with 5% alginate (i.e. gel forming fibre) reduced *ad libitum* intake in energy by 22%, compared to cookies without added fibre. Addition of guar gum (i.e. viscous fibre) and cellulose (i.e. bulking fibre) did not affect *ad libitum* intake. Cookies with 5% alginate increased oral exposure time with 48%, but also increased the rate of gastric emptying. This study was performed in a real life setting to distract subjects from visual and weight cues. We included two different dosages of guar gum and alginate to be able to study effects of high fibre, but less palatable products.

Selection of the types of fibre for this study was based on anticipated working mechanisms of bulking, viscous and gelling fibres on satiation. By definition, all fibres have bulking properties, as inclusion of dietary fibre in food products reduces energy density (12). In this study, *ad libitum* intake in weight remained unchanged after inclusion of cellulose compared to the control product without added fibre. The change in energy content after inclusion of cellulose was, however, not large enough to lead to significant decreases in energy intake.

In addition to weight or volume of foods, palatability is an important determinant of meal size (27). A very pleasant tasting meal may result in higher *ad libitum* intake. In our study, palatability ratings for the high dose fibre products were lower than that for the control product. However, adjusting for palatability did not explain the difference in *ad libitum* intake between high dose alginate and control product.

We hypothesized that addition of guar gum would reduce *ad libitum* intake (14,28) by increasing oral exposure time (16,29). The measurements of physico-chemical properties confirmed that guar gum was highly viscous in mouth conditions. However, in the satiation study we showed that guar gum neither reduced *ad libitum* intake nor increased oral exposure time. Although there were texture differences, we speculate that these were not large enough to prolong oral exposure time (30). Previous studies showing effects on oral exposure time, used liquid and semi-liquid test products with large differences in texture (14,28).

While no effect of guar gum was observed, oral exposure time increased after high dose alginate supplementation, although viscosity in the simulated mouth condition did not differ from control. Alginate forms a gel either at a low pH, or in the presence of divalent cations (e.g. Ca^{2+} or Mg^{2+}) (31). We postulate that alginate already started forming a gel in the oral cavity due to presence of water and divalent cations from saliva (32). This is also in agreement with the sensory ratings, as alginate was rated the most sticky and difficult to swallow.

We further hypothesized that increased viscosity of digesta as well as formation of gels would reduce gastric emptying rate, and as a result reduce *ad libitum* intake (11,17,19). The measurements of physico-chemical properties confirmed that guar gum increased viscosity in all three upper gastrointestinal conditions, and that alginate increased water holding capacity in stomach conditions. In the gastric emptying study we found, however, that none of the test products re-

duced gastric emptying rate. Gastric emptying rate even increased for alginate. Previous findings on the effects of viscous fibre (29,33,34) and gelling fibre (10,17) on gastric emptying have also been inconclusive. Despite this, increased viscosity as well as gel formation in digesta generally results in prolonged presence of nutrients in the small intestine, which in turn inhibits the absorption of glucose in blood and affects appetite regulating peptides (35). This process may have contributed to the reduced intake of high dose alginate cookies in the current study.

The initial hypotheses on oral exposure time, gastric emptying rate and *ad libitum* intake could not be confirmed. This may be explained by the rate of hydration. When mixed with liquids (e.g. saliva, gastric secretion), viscous and gelling fibres are expected to be hydrated and induce thickening or form a gel. The thickening of a fibre depends not only on factors such as structure, dose and molecular weight, but also on the rate of hydration (35-37). For gelling fibre, factors as dose, pH, presence of Ca^{2+}, and rate of hydration are crucial (31). In the simulation study, the test product was finely ground and the incubation time in mouth, stomach and small intestine conditions were relatively long, respectively 10, 60 and 180 min (23). In real life oro-gastric transit time may be faster, so fibres may not have been fully hydrated before arriving in the stomach and therefore not behave according to the anticipated working mechanisms.

In this study we showed that physico-chemical properties of fibres can affect food intake and satiation-related mechanisms in the upper gastrointestinal tract. Apart from the physico-chemical properties, as determined in simulated conditions, it should be realized that intraluminal conditions in the upper gastrointestinal tract, such as interactions with the digesta matrix, pH, hydration status and passage rate, impact fibre properties and post meal effects *in vivo*.

It is important to note that fibre properties associated with satiation (i.e. gel forming in this study) may not automatically be associated with a reduced energy intake or sustained satiety after repeated exposure. We previously showed that on a short term, viscous fibre increased satiety more than non-viscous fibre, whereas on a longer term effects on energy intake and body weight were independent of viscosity (7). Other mechanisms related to specific fibre properties, such as secretion of appetite regulating peptides, inhibited absorption of nutrients from the lumen, enhanced insulin sensitivity, and enhanced prebiotic activity may interplay, and affect energy intake or sustained satiety (38,39).

In conclusion, the addition of 5 g/100 g alginate (i.e. gel forming fibre) to a low fibre cookie resulted in earlier satiation in a real life setting. This effect may be mediated by an increased oral exposure time. Guar gum (i.e. viscous fibre) and cellulose (i.e. bulking fibre) did not affect *Ad libitum* intake. Fibre properties can change after interaction with the food matrix and the environment in the upper gastrointestinal tract, and as a result this can change the effect on satiation.

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4

Pectin is not pectin:

a randomized trial on the effect of different physicochemical properties of dietary fibre on appetite

Authors

Anne J. Wanders

Edith J.M. Feskens

Melliana C. Jonathan

Henk A. Schols

Cees de Graaf

Monica Mars

Abstract

An increased intake of dietary fibre has been associated with reduced appetite and reduced energy intake. Research on the effects of seemingly identical classes of dietary fibre on appetite has, however, resulted in conflicting findings. The present study investigated the effects of different physicochemical properties of fibre on appetite and underlying mechanisms. This was a randomized crossover study with 29 subjects (21 $\pm$ 2 y, BMI 21.9 $\pm$ 1.8 kg/m^2) consuming dairy based liquid test products (1.5MJ, 435 g) containing either: no pectin, bulking pectin (10 g), viscous pectin (10 g), or gelled pectin (10 g). The gelled pectin was also supplemented as capsules (10 g), and as liquid (10 g). Physicochemical properties of the test products were assessed. Appetite, glucose, insulin and ^{13}C recovery were measured before ingestion and after fixed time intervals. Preload viscosity was larger for gelled > viscous > bulking > no pectin, and was larger for gelled > liquid > capsules. Appetite reduced after gelled pectin compared to bulking (p <0.0001), viscous (p =0.005) and no pectin (p <0.0001). The ^{13}C recovery peak was delayed after gelled pectin (82 $\pm$ 18 min) compared to no pectin (70 $\pm$ 19 min, p =0.015). Furthermore, gelled (p =0.002) and viscous (p <0.0001) pectin lowered insulin responses compared to no pectin, with minor reductions in glucose response. Regarding methods of supplementation, appetite reduced after the gelled test product compared to after capsules (p <0.0001) and liquid (p <0.0001). Different methods of supplementation resulted in distinct metabolic parameters. Results suggest that different physicochemical properties of pectin, including methods of supplementation, impact appetite differently. Reduced appetite was probably mediated by increased preload viscosity, whereas inconsistent associations with metabolic parameters were found.

Introduction

An increased intake of dietary fibre has been associated with increased satiety and reduced energy intake (1-3). Satiety is defined as the inhibition of appetite and occurs as a consequence of eating (3). Dietary fibres may affect satiety via diverse mechanisms. These include: lowering the energy density of a food; increasing sensory exposure time to a food in the oral cavity; slowing down gastric emptying; modifying the postprandial glucose response; and changing neural and humoral signals in the gut (1-3).

Dietary fibre is a term that reflects a heterogeneous group of compounds which differ in their chemical structure and physicochemical properties (4). Recently, in a systematic review we showed that effects of dietary fibre on satiety can differ subject to both fibre properties and the interaction of fibre with the food matrix (5). At present, most intervention studies on the satiating effects of dietary fibre comprise effect studies of one specific fibre or fibre mixture. Moreover, many studies do not describe the physicochemical properties of the fibres in sufficient detail (5-7). Hence, the present study aims to verify the findings of the systematic review in an intervention study.

Variations in effects between seemingly identical classes of fibres may be explained by differences in molecular structure. A good example of a fibre which is naturally present in many different molecular structures is pectin. Pectin as present in fruit and vegetables is one of the major plant cell wall components, and depending on its molecular weight and degree of esterification, pectin can vary in its viscosity and gelling ability (8).

Apart from the molecular structure of the fibre, also the interaction of the fibre with foods or food components, processing procedure during food preparation, as well as its interaction with gastrointestinal content may differentially affect satiety (9, 10). When mixed with liquids, soluble fibres are expected to hydrate. Only when hydrated, viscous fibres induce thickening, and gel forming fibres may start forming a gel if the required conditions are fulfilled (e.g. presence of Ca^{2+} or H^+, temperature, etc) (11, 12). The thickening or gelling of a fibre depends therefore not only on factors such as molecular weight and degree of esterification, but also on the rate of hydration and gastrointestinal environment.

The present study aimed to investigate whether different physicochemical properties of one specific dietary fibre class affect appetite sensations differently. The secondary aim was to explore the underlying mechanisms for a potential difference in appetite. To accomplish this, pectins with different physicochemical properties were added to a dairy based liquid food matrix. The different types of pectin selected were: 1) no pectin (control), 2) non-viscous, non-gel forming pectin (hereafter referred to as bulking), 3) viscous pectin and 4) gel-forming pectin (gelled), which were all provided hydrated in the food matrix. Furthermore, the gel forming pectin was provided in two additional supplementation methods: 5) not hydrated, as capsules, and 6) hydrated-but not yet gelled, as two separate liquids (hereafter referred to as liquid). We hypothesized that the capsules delay appetite because they need to hydrate first and that the liquid product equally affects appetite because it starts thickening directly after arrival in the stomach.

Subjects and methods

Thirty healthy young men (aged 18 to 30 years), with a normal BMI (18.5 - 25.0 kg/m^2) were recruited from Wageningen, The Netherlands, and the surroundings. Exclusion criteria were as follows: scoring high on restrained eating (Dutch Eating Behavior Questionnaire (DEBQ), score >2.89) (13), lack of appetite, an energy restricted diet during the past two months, body weight change > 5 kg during the past two months, stomach or bowel diseases, hypersensitivity for the ingredients of foods under study, diabetes, thyroid disease or any other endocrine disorder, fasting glucose > 5.8 mmol/l, anemia (Hb <8.0 mmol/l), smokers and heavy alcohol users (>5 drinks a day). We also excluded subjects donating blood six weeks before or during the study. In total, 29 men with a mean age ($\pm$ SD) of 21 $\pm$ 2 y, a BMI of 21.9 $\pm$ 2.8 kg/m^2 and a DEBQ score of 1.8 $\pm$ 0.5 completed the study. One subject dropped out after 3 test days due to intestinal problems. Subjects were unaware of the exact aim of the study and were informed that we were interested in the effect of dietary fibre on metabolic parameters. They were informed about the other outcome measures after the study. To detect a difference in appetite ratings of 10% (14), (CV=12% (15), α=0.05, 1-β=0.8), a sample size of 30 subjects was calculated, given an anticipated dropout rate of 20%.

The present study was conducted according to the guidelines laid down in the Declaration of Helsinki and all procedures involving human subjects were approved by the Medical Ethics Committee of Wageningen University (registration number NL 33684.081.10). Written informed consent was obtained from all subjects. The study was registered in the NIH clinical trial database (ClinicalTrials.gov number NCT01257295).

Test products

In Table 4.1 the composition and physicochemical properties of the test products are given. The basic recipe of the test products consisted of a mixture of 100 g quark (Volle Franse kwark, Albert Heijn, the Netherlands), 100 g whole milk (Houdbare Volle Melk, Campina, the Netherlands), 200 g apple juice (Appelsientje Goudappel, FrieslandCampina, the Netherlands), and 25 g strawberry syrup (Karvan Cevitam, Heinz, Benelux). The test products were served with 150ml water. To the test products 10 g pectin was added, but the type of pectin and the method of supplementation differed. The six test products contained: 1) no fibre (control); 2) non-viscous, non-gel forming pectin (hereafter referred to as bulking) (Herbapekt SF 50-A-LV, HM-pectin, Degree of Esterification (DE)=62%, Molecular Weight (MW)=25kDa); 3) viscous pectin (Classic AU201USP, HM-pectin, DE=72%, MW=80kDa); 4,5 and 6) gel forming pectin (gelled) (Classic CU901, LM-pectin, DE=10%, MW= max 15kDa, all manufactured by Herbstreith & Fox, Germany). To hydrate the pectins, the apple juice and syrup were heated to 80 °C and then the pectin was mixed and dissolved. After cooling down, the quark and milk were added. Product 5 was identical to product 1, the control product, in addition 22 gelatin capsules containing the pectin were served separate. The capsules were manufactured specially for this study (Hospital de Gelderse Vallei, Ede, the Netherlands). Product 6 was composed slightly different and consisted of two liquid drinks (hereafter referred to as liquid), served with 200ml apple juice. The first liquid, which did not contain calcium, contained

the pectin, 150ml water and half of the syrup. The pectin was hydrated in the mixture at 80 °C. The second liquid contained the milk, quark and the other half of the syrup. The two liquids were consumed in this order. We hypothesized that the liquid product would start thickening directly after arrival in the stomach and that the capsules show a delayed effect on appetite because they need to hydrate first.

Table 4.1: Composition and physicochemical properties of the fibre containing test products in preloads and in simulated mouth and gastric conditions.

	Control	Bulking	Viscous	Gel forming	Capsules	Liquids[6]	
						1	2
Available energy (kJ)[1]	1544	1544	1544	1544	1544	159	1004
Added pectin (g)	0	10	10	10	10[5]	10	0
Volume test product (g)	425	435	435	435	425	172.5	212.5
Volume water (g)	150	150	150	150	150	200[6]	
Preload viscosity (mPa.s)[2]	17	79	1700	3900	17	111	118
Viscosity bolus (mPa.s)[3]							
Mouth	0.9	2.1	23.8	1.1			
Stomach	0.8	1.3	5.9	0.8	0.8	0.8	
Water holding capacity bolus (g water/100g test product)[4]							
Mouth	12.8	22.6	14.1	59.7			
Stomach	5.9	10.7	11.6	52.2	34.3	56.4	

[1]Available energy was calculated based on Dutch Food Composition tables. Energy conversion factors used: fat 37kJ/g, protein and carbohydrate 17 kJ/g, energy content of fibre was set at 0 kJ/g.

[2]Preload viscosity was the value at shear rate 90/s during a logarithmic shear sweep from 0.1-1000/s. For 'Liquids' viscosity is given for both pectin drink and dairy drink, respectively.

[3]Viscosity of the bolus was the value at shear rate 100/s during a logarithmic shear sweep from 0.1-1000/s of simulated mouth and gastric conditions.

[4]WHC: water holding capacity of the bolus is the amount of water held by the insoluble material from 100 g of test product after centrifugation under simulated mouth and gastric conditions.

[5]Gel forming pectin consumed as capsules was served separately. Total weight of the capsules was 12.4g.

[6]Gel forming pectin consumed as liquid consisted of two separate liquids consumed in a standardized order. The first liquid contained pectin, water and syrup, the second liquid contained milk, quark and syrup. Apple juice (380kJ) was served separately and consumed last.

The energy content of each test product corresponded to an estimated 13% of daily energy requirements in young male adults (16), which was 1544kJ (366kcal), excluding the available energy from fibre. Other macronutrients were 12 g protein (13 percent of energy (en%)), 49 g (54 en%) carbohydrates and 14 g (34 en%) fat. For gastric emptying measurements, 100 mg [1-13]C-sodiumacetate (99% enrichment; Campro Scientific GmbH, NL) was added to all test products, and for product 5 to the second liquid. The test products were prepared twice per week and stored for maximum two days at 7 °C.

Preload viscosity of the test products as consumed was measured at 20 °C using a rheometer (MCR 300, Anton Paar, Graz, Austria). A shear sweep was performed at 0.1-1000/s in logarithmic scale. Data obtained at shear rate 90/s were used to compare between samples. Viscosity and water holding capacity of the bolus were also measured under simulated mouth and gastric conditions according to methods described earlier (Wanders et al, BJN, in press), with adaptations for the high water content of the products, and adjustments for simulating the different methods of supplementation. In short, after simulation of mouth and gastric conditions with oral and gastric enzymes and reagents, samples were centrifuged. Viscosity was measured in the supernatant at 37 °C and data obtained at shear rate 100/s were reported. Water holding capacity was measured from the pellet containing the insoluble material. Water holding capacity was expressed as the amount of water held by the insoluble material from 100 g of test product.

Study design

The study was a randomized cross-over experiment, blinded for subjects, with six test sessions of approximately 4 hours. The study ran from January to June 2011. The six test products were randomized according to a Williams Latin Square. Thirty unique orders were produced by computer generated numbers and allocated by date entering the study. The washout period between test sessions was at least 12 days.

Experimental procedure

After following dietary instructions and after an overnight fast, subjects arrived at the research center between 8:00 and 8:30 am. The dietary instructions implied that during the two days before a test day, subjects were not allowed to eat fibre-rich foods. The evening before each test session subjects ate a standardized low fibre, ready-to-eat meal, which was provided by the researchers. From 9:00 pm onwards they were not allowed to eat and to drink energy-containing drinks. From 11:00 pm onwards, until the start of the test session, only water was permitted. In addition, they should avoid vigorous physical activity. To monitor compliance to these guidelines, the subjects were asked to record their intake and physical activity in a diary.

Table 4.2 gives an overview of the timing and procedures of a test session. After arrival a catheter was inserted in the antecubital vein, a baseline blood sample was taken, subjects gave two baseline breath samples, and they filled out a baseline appetite questionnaire and a baseline side effects questionnaire. Hereafter, subjects were instructed to consume the fixed amount of test product within 10 min. Directly after consumption, the subjects were asked to rate palatability, and the difficulty to consume the test product within the given time. The subjects were seated at a private desk in a quiet study room and allowed to do light desk work during the session, they were not allowed to eat or drink anything until 180 min. A toilet break was allowed at 120 min.

Breath samples and appetite questionnaires were taken after exactly 15, 30, 45, 60, 75, 90, 105, 120, 150 and 180 min after the first bite of the test product. Blood samples were taken at the same time points, excluding time points 75 and 105 min. After taking the last blood sample at 180min (between 11:00 and 11:30 am), the subjects were offered a buffet-style *ad libitum* lunch. Subjects

Table 4.2: Timing and procedures for each test session in which subjects consumed one of the six fibre containing test products.

Time[1]	Procedures[2]
-10	G, A, B, S
0	T
10	P
15	G, A, B, S
30	G, A, B
45	G, A, B
60	G, A, B
75	G, A
90	G, A, B
105	G, A
120	G, A, B
150	G, A, B
180	G, A, B, S
185	L
After lunch	A, S
3h after lunch	S

[1] Time from test product ingestion, t=0 is between 8:00 and 9:00 am.

[2] Abbreviations of procedures: G, breath sampling for gastric emptying; A, appetite questionnaire; B, blood sampling; S, side effects questionnaire; P, palatability questionnaire; T, test product; L, *ad libitum* lunch.

were instructed to consume as much of the lunch as they wanted, until pleasantly satiated. The lunch consisted of unusually large portion sizes of whole meal mini buns, low-fat margarine, four types of sandwich fillings, and water, coffee and tea with condensed milk and sugar. The sandwich fillings were: cheese, ham, fruit sprinkles and chocolate flakes. All the items were weighed before and after *ad libitum* consumption. Directly after lunch a final appetite questionnaire was taken. Side effects were measured by a questionnaire at 15 min, 180 min, after lunch and 3h after lunch.

Measurements

Appetite was measured by rating hunger, fullness, desire to eat, prospective food consumption and thirst on 100mm Visual Analogue Scales (VAS). The scales were anchored from 'not at all' to 'very much' (14). Subjects rated the side effects bloating, belching, flatulence, nausea, diarrhea on a 5-point scale from 'not at all' to 'very much'.

For glucose and insulin measurements, blood was collected into 2-mL EDTA-containing tubes. Tubes were centrifuged at 1000g/2216 rpm for 10 minutes at 4 °C, and kept on iced water before and after centrifugation. Plasma samples were stored at -80 °C until analysis. All blood samples of one subject were analyzed within the same run to eliminate inter-assay variation. Glucose was measured by the hexokinase method (Modular P800 analyzer, Roche, Switzerland). Detection limit was 0.11 mmol/L, and intra-assay and inter-assay coefficients of variation (CVs) at 3.66 mmol/L were 1.1%

and 1.9% respectively. Insulin was measured in duplo using commercially available human ELISA kits (Mercodia, Sweden). This assay had a detection limit of 0.1 mU/L. The intra-assay and inter-assay CVs at 11 mU/L were 3.4% and 3.6% respectively.

Gastric emptying rate was measured by the recovery of ^{13}C in breath. Breath samples were collected by breathing into a 10ml Exetainer tube (Labco, UK) via a drinking straw. Samples were stored at room temperature and analyzed for ^{13}C enrichment in CO_2 on a Finnigan Delta C continuous-flow isotope ratio mass spectrometer (Finnigan MAT, USA). The result is expressed as the percentage of the administered dose ^{13}C recovered in breath per hour (%dose/hr).

Statistical analysis

Data are presented as means and SD. Statistical analyses were performed with SAS (version 9.2; SAS institute Inc., Cary, NC, USA), separately for fibre types and supplementation methods. Significance was set at p <0.05. Product effects for palatability and difficulty to eat ratings, ad libitum intakes, were analyzed by means of a mixed model ANOVA (proc mixed, SAS). Treatment, day and treatment*day interaction (=order) were included as fixed factors and subject was included as random factor. If the treatment effect was statistically significant, pairwise differences were calculated and adjusted by Tukey's method to control for multiple testing. Peak concentrations and time to peak for ^{13}C recovery in breath, and glucose and insulin concentrations were analyzed according to a similar procedure, with the addition of baseline values as covariates to the model to control for differences at baseline. Repeated measurements for appetite ratings, ^{13}C recovery in breath, and glucose and insulin responses were also analyzed according to a similar procedure, with the addition of time and treatment*time as fixed factors. In addition, baseline values were added to the model as covariates. Due to the high number of pairs for treatment*time effects, significance levels were adjusted by a Bonferroni correction, which resulted in significance at p <0.008 for fibre types and at p <0.017 for supplementation methods. For side effects, data were regrouped in two categories: score 1 versus score 2-5 and were analyzed by the chi-square test.

Results

Test products

As expected, physicochemical properties of the test products differed (Table 4.1). For the different pectin types preload viscosity of the test products was lowest for control and increased from bulking to viscous and gelled pectin. For the different methods of supplementation preload viscosity of the test products was lowest for capsules, increased for liquid and was highest for the gelled product. Under simulated conditions, the viscous pectin increased bolus viscosity 10 to 24-fold in the mouth compared to the other pectin types, which, under stomach conditions, diminished 4 to 7-fold due to dilution. The gelled pectin increased water holding capacity of the bolus 2 to 8-fold in both mouth and stomach conditions compared to the other pectin types. Subjects rated the test product with gelled pectin lower on palatability and more difficult to eat compared to the other three pectin types (all p <0.0001). With respect to different methods of supplementation, the test product with

capsules was rated highest on palatability, whereas the gelled product was rated as most difficult to eat (Table 4.3a and 4.3b).

Table 4.3a: Palatability and difficulty to eat within the given time for a test product containing different fibre types, as rated by the subjects[1].

	Control		Bulking		Viscous		Gel forming		P[1]
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
Palatability	59	18[a]	59	16[a]	51	22[a]	29	22[b]	<0.001
Difficulty to eat in 10 minutes	11	13[a]	14	16[a]	24	28[a]	59	30[b]	<0.001

Table 4.3b: Palatability and difficulty to eat within the given time for a test product containing fibre supplemented by different methods, as rated by the subjects[1].

	Gel forming		Capsules		Liquids		P[1]
	Mean	SD	Mean	SD	Mean	SD	
Palatability	29	22[a]	52	21[b]	39	21[a]	0.002
Difficulty to eat in 10 minutes	59	30[b]	16	19[a]	18	20[a]	<0.001

[1]Values were measured on a 100mm Visual Analogue Scale anchored from 'not at all' to 'very much' (0 to 100). Measured in 29 subjects.

[2]P-value from mixed model ANOVA, subsequently all fibre treatments were compared with Tukey. Values in a row with different superscripts are significantly different.

Appetite

Appetite and thirst ratings are presented in Figure 4.1. Baseline ratings did not differ between the test products (all p >0.369). Regarding the products with different pectin types, the gelled pectin significantly reduced hunger, desire to eat and prospective intake and increased fullness ratings, compared to control (p <0.0001), bulking pectin (p <0.0001), and viscous pectin (p =0.005). Additionally, viscous pectin increased fullness ratings compared to control (p =0.023). Thirst was rated significantly higher after consuming the viscous pectin compared to the other three pectin types (p <0.0001). With respect to the different methods of supplementation, the gelled product significantly reduced hunger, desire to eat and prospective intake, and increased fullness ratings, compared to the capsules (p <0.0001) and the liquid product (p <0.0001). Additionally, capsules increased fullness ratings compared to the liquid product (p =0.036).

Energy intake

Ad libitum energy intake 3h after consuming the test products did not differ between the different pectin types (p =0.32), but did differ between the methods of supplementation (p =0.040) (Table 4.4a and 4.4b). Energy intake was 12.4% lower after consuming the test product with capsules compared to the liquid product (p =0.030), with no differences for the gelled product. The lower energy intake was reflected in significantly lower protein (12.0%, p =0.008), carbohydrate (13.7%, p =0.022) and fibre (14.8%, p =0.013) intake. Appetite ratings after ad libitum lunch were similar for all test products, which confirms that subjects ate until equal satiety.

Table 4.4a: Energy and macronutrient intake after a buffet-style ad libitum lunch in 29 subjects after consuming a test product with different fibre types.

	Control		Bulking		Viscous		Gel forming		P[1]
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
Energy (MJ)	4.72	1.11	4.48	1.45	4.49	1.21	4.34	1.44	0.32
Total fat (g)	44	12	39	15	39	12	39	15	0.07
Protein (g)	48	12	45	14	45	12	45	15	0.21
Carbohydrates (g)	134	46	134	54	134	47	125	49	0.39
Fibre (g)	14	5	14	6	14	5	13	5	0.41
Coffee/tea/water (g)	342	152	374	189	367	177	354	165	0.17

Table 4.4b: Energy and macronutrient intake after a buffet-style ad libitum lunch in 29 subjects after consuming a test product containing fibre supplemented by different methods.

	Gel forming		Capsules		Liquids		P[1]
	Mean	SD	Mean	SD	Mean	SD	
Energy (MJ)	4.34	1.44 [a,b]	4.07	1.32 [a]	4.65	1.39 [b]	0.04
Total fat (g)	39	15	37	14	41	14	0.22
Protein (g)	45	15 [a,b]	42	14 [a]	48	15 [b]	0.01
Carbohydrates (g)	125	49 [a,b]	117	46 [a]	136	52 [b]	0.03
Fibre (g)	13	5 [a,b]	12	5 [a]	14	6 [b]	0.02
Coffee/tea/water (g)	354	165	336	140	364	157	0.20

[1]P-value from mixed model ANOVA, subsequently all fibre treatments were compared with Tukey. Values in a row with different superscripts are significantly different.

Gastric emptying

As a proxy for gastric emptying rate, ^{13}C recovery was measured in breath (Figure 4.2 and Table 4.5a and 4.5b). Regarding the different pectin types, after the test product with gelled pectin the ^{13}C recovery peak concentration was reached on average 12 min later than control (p =0.015). With respect to

the different methods of supplementation, after consuming the capsules the ^{13}C recovery peak concentration was reached the fastest (64.1 ± 21.9 min), followed by the gelled product (82.2 ± 17.8 min), and the liquid product (98.3 ± 21.1 min).

Glucose, Insulin

Glucose and insulin dynamics, peak concentrations and time to peak are presented in Figure 4.2 and Table 4.5a and 4.5b. Compared to the control test product, overall insulin responses were smaller after the products with viscous pectin (p =0.002) and gelled pectin (p =0.0001). For gelled pectin this was reflected in somewhat lower glucose concentrations after 15 min (p =0.004) and higher concentrations after 45 min (p =0.003) compared to control. For viscous pectin this was reflected in a somewhat lowered peak glucose concentration compared to control (p =0.024). Regarding the different methods of supplementation, for the gelled and liquid products insulin responses were smaller compared to the capsules (both p <0.0001). For the gelled product this was reflected in lower glucose concentrations after 15 min (p =0.0004) and higher concentrations after 45 min (p =0.0012) compared to capsules. Whereas for the liquid product glucose concentrations were higher after 30, 45 and 60 min (all p <0.007) compared to capsules.

Side effects

In each test session, subjects rated side effects on five different time points. Directly after consumption of the test products the number of subjects reporting a 2 or higher on the 5-point scale increased for bloating from 17% to 45%, for belching from 7% to 24% and for nausea from 10% to 18%. These changes, however, did not differ between the test products. There were no differences between the test products at any time points for any of the side effects asked (data not shown).
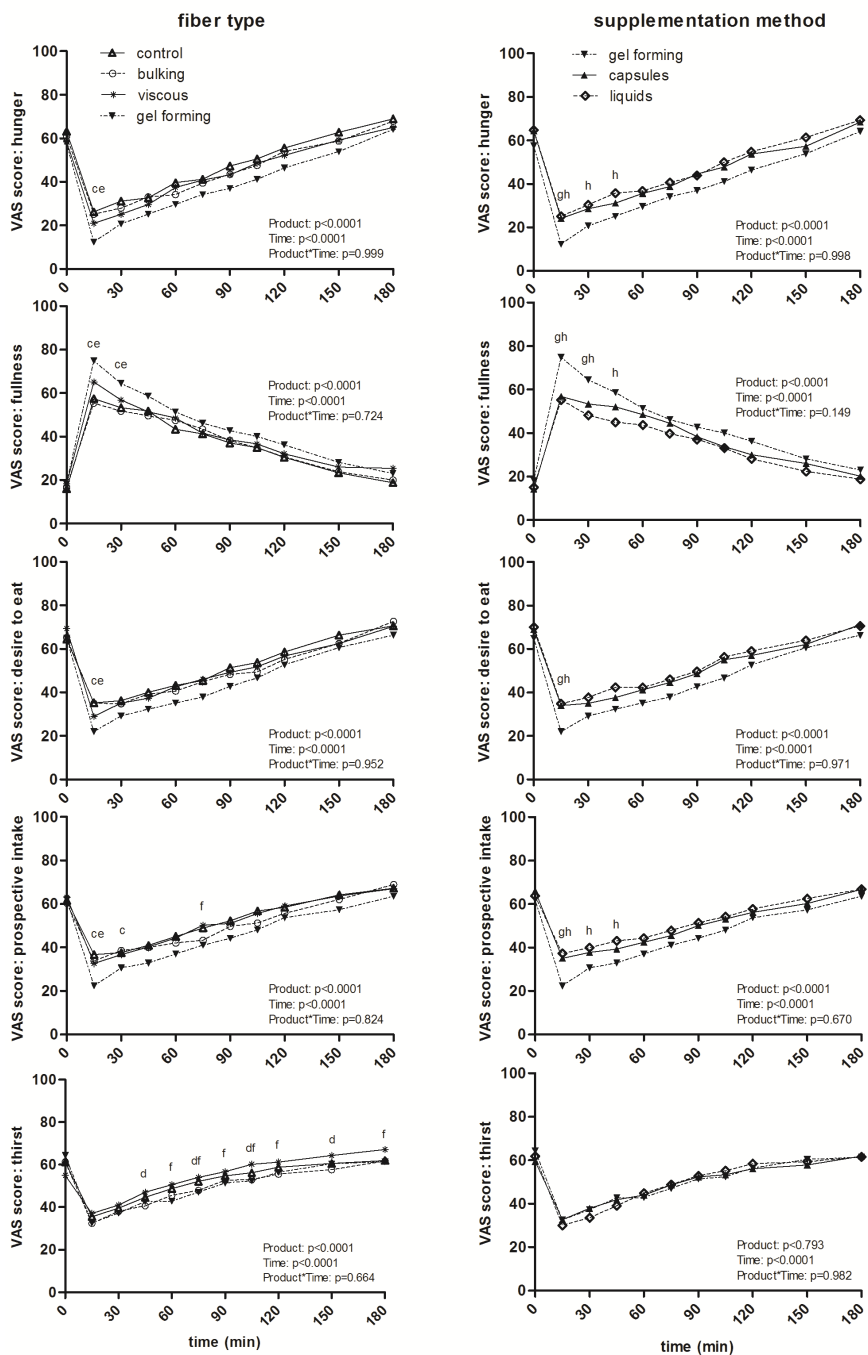
Figure 4.1: Mean appetite ratings, measured on 100mm VAS scales on set time points up to 180 minutes, in 29 subjects after consuming a test product with different fibre types and after consuming a test product supplemented by different methods. a: control different from bulking; b: control different from viscous; c: control different from gelled; d: bulking different from viscous; e: bulking different from gelled; f: viscous different from gelled; g: gelled different from capsules; h: gelled different from liquids; i: capsules different from liquids.
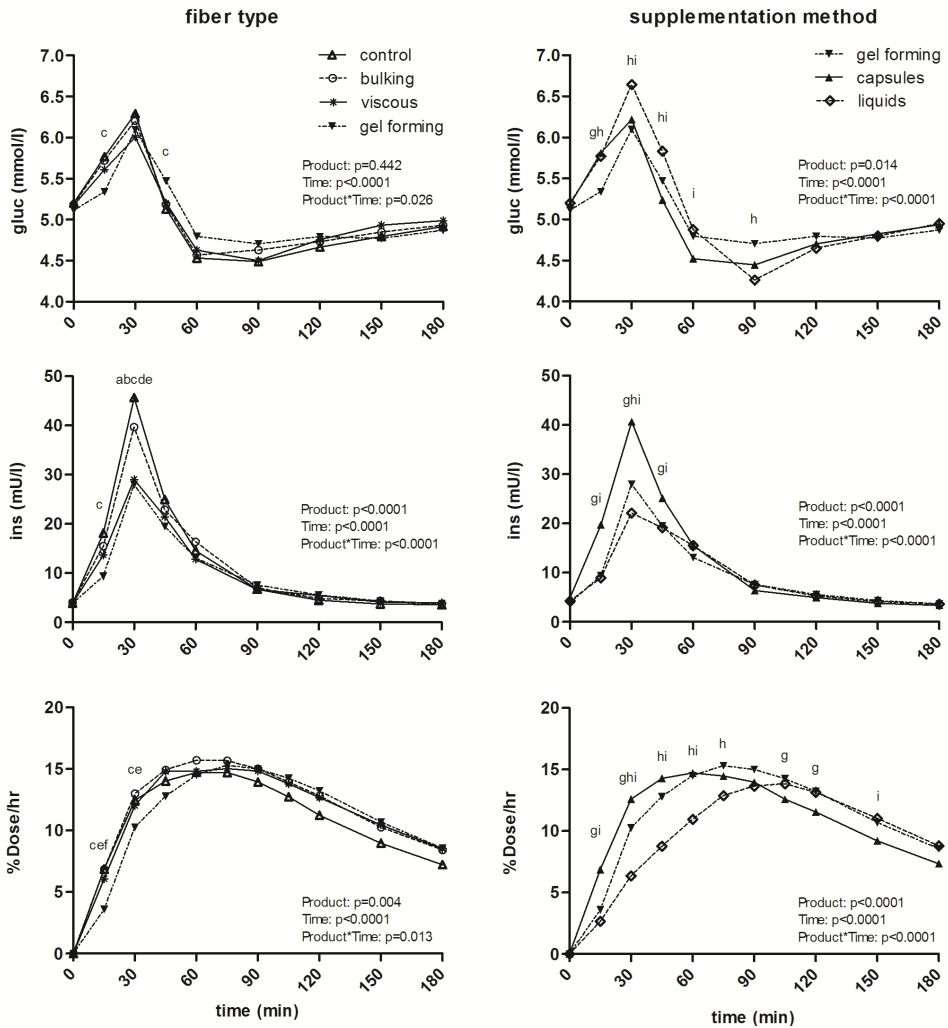
Figure 4.2: Mean glucose, insulin and ^{13}C excretion on set time points up to 180 minutes, in 29 subjects after consuming a test product with different fibre types and after consuming a test product supplemented by different methods. a: control different from bulking; b: control different from viscous; c: control different from gelled; d: bulking different from viscous; e: bulking different from gelled; f: viscous different from gelled; g: gelled different from capsules; h: gelled different from liquids; i: capsules different from liquids.

Table 4.5a: Peak concentrations and time to peak for glucose, insulin and ^{13}C recovery in 29 subjects after consuming a test product with different fibre types.

		Control		Bulking		Viscous		Gel forming		P^1
		Mean	SD	Mean	SD	Mean	SD	Mean	SD	
^{13}C recovery	Peak (% dose recovery per hour)	15.3	2.7	16.4	6.1	16.3	6.0	15.8	4.3	0.78
	time to peak (min)	70.3	18.8 ^{a}	74.0	20.4 ^{a,b}	75.5	21.0 ^{a,b}	82.2	17.8 ^{b}	0.03
Glucose	Peak (mmol/l)	6.5	0.7^a	6.3	0.7^{a,b}	6.1	0.7^b	6.2	0.7^{a,b}	0.03
	time to peak (min)	26.4	8.6	26.9	6.2	27.9	6.6	31.0	9.8	0.12
Insulin	peak (mU/l)	47.0	26.2^a	40.5	21.1 ^{a,b}	30.7	18.3^b	30.1	15.4^b	< 0.0001
	time to peak (min)	30.5	6.3	33.1	6.2	33.6	8.6	34.7	8.1	0.11

Table 4.5b: Peak concentrations and time to peak for glucose, insulin and ^{13}C recovery in 29 subjects after consuming a test product containing fibre supplemented by different methods.

		Gel forming		Capsules		Liquids		P^1
		Mean	SD	Mean	SD	Mean	SD	
^{13}C recovery	Peak (% dose recovery per hour)	15.8	4.3	15.4	3.4	14.6	3.3	0.37
	time to peak (min)	82.2	17.8 ^{b}	64.1	21.9 ^{a}	98.3	21.1 ^{c}	< 0.0001
Glucose	Peak (mmol/l)	6.2	0.7^{a,b}	6.4	0.6^a	6.7	0.6^b	0.0006
	time to peak (min)	31.0	9.8 ^{a}	24.3	9.3^b	31.0	5.6^a	0.008
Insulin	peak (mU/l)	30.1	15.4^a	44.3	21.6^b	26.6	14.9^a	< 0.0001
	time to peak (min)	34.7	8.1 ^{a}	30.5	9.4^a	40.9	13.2^b	0.0004

^{1} P-value from mixed model ANOVA, subsequently all fibre treatments were compared with Tukey. Values in a row with different superscripts are significantly different.

Discussion

This study verified the hypothesis that effects of dietary fibre on appetite differ subject to both fibre properties and the interaction of fibre with the food matrix. We found that a gelled pectin reduced appetite ratings significantly compared to a viscous pectin and a bulking pectin. Additionally, the same gelled pectin reduced appetite more when it was consumed as a gel, compared to when it was consumed in the form of capsules or in a liquid form.

Earlier research on seemingly identical classes of dietary fibre on appetite have resulted in inconsistent findings. Moreover, most studies on the satiating effects of dietary fibre were effect studies of one specific fibre or fibre mixture (5). Hence, in the present study three distinct types of pectin were selected and consumed hydrated in a liquid food matrix. Furthermore, one of these pectin types was consumed in two additional supplementation methods. In this study pectin was used as a model for different fibres with different physicochemical properties. By selecting solely pectins, effects of highly variable molecular structures and fibre dosages could be excluded, and a justified comparison between different physicochemical properties could be made. The physicochemical properties of the test products were confirmed in simulated mouth and gastric conditions. Our results confirm that fibre physicochemical properties, which include the methods by which fibres are supplemented, are of prime importance when studying their satiating properties.

For both the different pectin types and supplementation methods, the test product with the highest preload viscosity reduced appetite the most. Previous studies, using different types (7, 17, 18) or one type (18-20) of dietary fibre, also showed that higher preload viscosity reduced appetite ratings or *ad libitum* energy intake. Some studies have found a graded reduction of appetite with increasing preload viscosity (18, 20), but not all (7, 19). Interestingly, another study showed that viscosity of the preload at the moment of ingestion reduced *ad libitum* energy intake more than preloads that increased viscosity after ingestion (17). In our study preload viscosity was relatively low compared to other studies (17, 21), which may explain the relatively small effect sizes on appetite. Our findings, however, confirm an important contribution of preload viscosity to appetite. Preload viscosity may affect appetite via an increased oro-sensory exposure time (22). In the present study oro-sensory exposure time was measured indirectly by asking the subjects to rate the difficulty to eat the test product within the given time.

It was postulated that viscous and gel forming dietary fibres are able to reduce appetite ratings (11) by delaying gastric emptying (18, 20) or physically inhibiting the absorption of nutrients in the lumen of the small intestine (17, 23). In the present study this mechanism was confirmed by the gelled pectin, the only pectin type that slowed down the ^{13}C recovery in breath and the only pectin type that reduced appetite ratings. One earlier study assessed both gastric emptying rate and appetite ratings after pectin supplementation, and also found a positive relation (24). Other studies found reduced gastric emptying rates after pectin supplementation (25-28), but not all (29-31). In these studies appetite sensations were not measured. Possible explanations for not finding a reduced gastric emptying rate after pectin supplementation are a small pectin dosage (25), or

a small contrast in preload or bolus viscosity (29). These results and the results from the present study suggest that gastric emptying may be an underlying mechanism for appetite reduction after consumption of viscous or gel forming dietary fibres.

Interestingly, the different methods of supplementing the gel forming pectin completely changed the findings on appetite, gastric emptying and glucose and insulin response. Actually, the concept of different findings after different methods of supplementation is not new, it was already presented in a classic intervention study done in 1977 by Haber et al. (32). In this study appetite, glucose and insulin responses were compared after eating 500g apples either raw, as puree or as juice. It was found that juice was less satisfying than puree, and puree less than raw apples. These graded differences were also seen for glucose and insulin responses. The differences in effects were considered to be related to the disruption of the food texture. For isolated fibres supplemented to foods, earlier studies already showed that different methods of fibre supplementation differently affect glucose and insulin response. It was found that viscous fibre incorporated in a liquid food reduced glucose and insulin responses more than viscous fibre incorporated in a solid food (10). Also, when incorporated or sprinkled on top of foods, viscous fibres reduced glucose and insulin responses more compared to ingesting the fibres with a glass of water right before the food (9, 33). Appetite ratings were measured in one study, which did not reveal differences in appetite between the different methods of supplementation (33). The present study confirms that the method of supplementation of viscous or gel forming dietary fibre may change findings on glucose and insulin response and it points out that the method of supplementation also may affect appetite ratings.

The findings for gastric emptying and glucose and insulin response after the liquid test product deviated considerably from the expected outcome. The liquid test product with gel forming pectin was consumed as two separate liquids, served with 200ml apple juice. First a mixture of water, syrup and pectin was consumed, then a mixture of quark, milk and syrup. Based on *in-vitro* tests we hypothesized that the liquid test product would start thickening directly after arrival in the stomach, due to the interaction of pectin with the Ca^{2+} from the dairy. However, the strong and quick rise in the glucose response suggests that the first drink, containing only carbohydrates and pectin, started to empty from the stomach rapidly after consumption. The second drink, containing fat, protein, carbohydrates and the ^{13}C isotope, was emptied slower, likely due to the presence of more nutrients (21), and possibly due to the suggested thickening. We assume that consuming the two liquids in the reversed order, or bite by bite, would result in different findings for gastric emptying and glucose and insulin response. This warrants further research.

The gel forming pectin as capsules reduced *ad libitum* energy intake compared to the same pectin as a liquid. After visually inspecting the appetite ratings at 180 min, it is not that surprising that there were no differences between other test products for *ad libitum* energy intake. After 180 min the appetite ratings appear to be back to baseline levels and to be very similar. Previous studies measuring *ad libitum* energy intake after consuming pectins, or other types of soluble or viscous fibres, have resulted in inconsistent outcomes, with on average a very small reduction in

energy intake (5). The inconsistent outcomes may be explained by variations in study designs, e.g. nature of test product, timing of the *ad libitum* test meal, nature of the *ad libitum* test meal, etc. (14). Despite the similar appetite ratings, the capsules and the liquid test product differed in subsequent *ad libitum* energy intake. This finding may be a chance finding, but may also be explained independently from appetite ratings. The pectin in the capsules was physically entrapped in the food matrix, and needed to be hydrated first to become physically active (11, 12). The pectin can therefore have aided to processes affecting energy intake later in the gastro-intestinal tract, for example by retaining water and increasing small bowel transit time (3, 4).

In the present study each test product with pectin was administered once. There is an ongoing debate whether a product with a higher satiety value after a single exposure leads to sustained satiety after repeated exposure (14, 34). With respect to gel forming pectins, on top of increased satiety after a single exposure, other metabolic factors may add towards sustained satiety or reduced longer term energy intake. These potential metabolic factors include secretion of appetite regulating peptides, inhibited absorption of nutrients, reduced postprandial lipid concentrations, altered adipocyte metabolism, and biologic actions in the large intestine (1-3). These longer term effects are, however, not studied frequently and show inconsistent findings (35-38). Additional research on the effects of repeated exposure of viscous or gel forming dietary fibres on appetite and related outcomes as energy intake and body weight is necessary.

To conclude, the results of the present study demonstrate that physicochemical properties of dietary fibre are of prime importance when studying their effects on satiety. With pectins as a model for different fibres with different physicochemical properties, we showed different effects on satiety for different fibre types hydrated in a liquid food matrix. In addition, we also showed different effects on satiety when one type of pectin was consumed according to different supplementation methods. The effects on satiety were most likely mediated by increased preload viscosity, whereas no consistent associations with gastric emptying were found. Future studies should describe physicochemical properties of dietary fibre and the food matrix under study in detail.

Acknowledgements

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Satiety and energy intake after single and repeated exposure to gel forming dietary fibre:

post ingestive effects

Authors

Anne J. Wanders
Monica Mars
Karin J. Borgonjen-van den Berg
Cees de Graaf
Edith J.M. Feskens

Abstract

Background: Viscous or gel-forming dietary fibres can increase satiety by an increase in oral exposure. Effects of viscous or gel-forming fibres on satiety by post ingestive mechanisms such as gastric emptying, hormonal signals, nutrient absorption or fermentation are unclear. Moreover, it is unclear whether effects persist after repeated exposure.

Objective: To investigate satiety and energy intake after single and repeated exposure to gelled fibre via post ingestive mechanisms.

Design: In a two-arm crossover design, 32 subjects (24 females, 21 $\pm$ 2 y, BMI 21.8 $\pm$ 1.9 kg/m^2) consumed an isocaloric (0.5MJ, 200g) test food with either 10 g gel forming pectin or 3 g gelatin and 2 g starch, matched for texture and eating time, once daily for 16 consecutive days. Hourly satiety ratings were measured on days 2 and 16. Energy intake was assessed by *ad libitum* diets on days 1 (run in), 2, 14, 15 and 16 of both intervention periods. Body weight was measured before the start of the intervention and on days 15, 16 and 17.

Results: Subjects rated hunger, desire to eat and prospective intake about 2% lower (p <0.015) and fullness higher (+1.4%; p =0.041) when they received pectin compared to control. This difference was similar after single and repeated exposure (p > 0.64). Energy intake after receiving pectin was lower after single exposure (-5.6%, p =0.012) compared to control, but not after repeated exposure (p =0.62). Body weight did not change during both interventions.

Conclusions: Gelled pectin can increase satiety and reduce energy intake by other means than texture and eating time. The effects on satiety persisted over time whereas the energy intake reduction did not.

Introduction

Observational studies have shown that the intake of dietary fibre is inversely associated with body weight and waist circumference (1, 2). A reduction in body weight is likely mediated by a reduced appetite and energy intake. Dietary fibre, however, is a term that reflects a heterogeneous group of compounds which differ in their chemical structure and physicochemical properties (3). As a result, different types of dietary fibre may have different effects on appetite and energy intake (4-6).

Earlier research showed that viscous or gel-forming dietary fibres, such as pectin and guar gum, can increase satiety and reduce subsequent energy intake (7-9). Viscous or gel-forming dietary fibres may affect satiety by various mechanisms, such as an increased oral exposure; a delayed gastric emptying; modified neural and hormonal signals in the gut; slowed down or diminished absorption of nutrients; or an altered fermentation pattern in the large intestine (4-6).

In many studies on viscous or gel-forming dietary fibres the control treatments were liquids (7). The subsequent effect on satiety may therefore be explained by an increased oral exposure (Wanders BJN 2012; Wanders et al., submitted). Increased eating time and a subsequent increase in oral exposure have been repeatedly shown to increase satiety (10, 11), and can also occur after consuming non-fibre thickeners. In contrast to non-fibre thickeners, such as starch and gelatin, which are broken down by digestive enzymes, viscous or gel-forming dietary fibres stay intact and may affect additional satiety related mechanisms in the gastro-intestinal tract. Yet, it is unclear what the effects of viscous or gel-forming dietary fibres are beyond oral exposure. To our knowledge, one earlier study compared the effect on satiety between a gelled dietary fibre and an equal gelled non-fibre control (12). It was found that appetite for a meal reduced with around 5% over 3.5h after consumption of the gelled fibre, without changes in subsequent energy intake.

The first aim of the present study was to assess satiety and energy intake after consuming gelled fibre via post ingestive mechanisms. The approach with a fibre and control test food matched for texture and eating time enabled studying satiety mechanisms in the gastro-intestinal tract. The second aim of the study was to explore whether the effects after single exposure would persist after repeated exposure. There is an ongoing debate whether a food that increases satiety and lowers subsequent energy intake after single exposure leads to sustained increased satiety and a reduced energy intake after repeated exposure (13, 14). At present, only a limited number of studies on repeated exposure is available on viscous or gel-forming dietary fibres (15-17), however, none of these studies was designed to compare single and repeated exposure. The present study comprises a two-arm crossover design, in which subjects consumed each test foods for 16 consecutive days. We selected a 10 g dose of gelling pectin with demonstrated satiety increasing effects compared to a non-gelling control (Wanders et al, submitted).

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Subjects and methods

Subjects

Thirty-five healthy, normal weight (BMI 18.5 - 25.0 kg/m^2) subjects aged 18 to 30y were recruited in the Wageningen area, the Netherlands. Subjects were excluded if they scored high on restrained eating (DEBQ: score men > 2.89, women > 3.39) (18). They were also excluded if they used an energy restricted diet, lost or gained more than 5 kg body weight in the last two months, had a lack of appetite, had stomach or bowel diseases or disorders, used antibiotics or dietary fibre supplements in the last two months, were hypersensitive for any ingredient in the test foods or were vegetarian. They were furthermore excluded if they had diabetes or any other endocrine disorder, had fasting glucose concentrations >5.8 mmol/l, or if they were smokers or heavy alcohol users (>5 drinks a day). In a screening session weight, height and fasting glucose concentrations (finger prick) were measured and subjects were instructed in detail about the procedures. Thirty-two subjects, of which 24 women, completed the study. They had a mean age of 21.1 ± 2.4 y, a mean BMI of 21.8 ± 1.9 kg/m^2, a mean DEBQ score of 1.7 ± 0.5 for men and 2.2 ± 0.5 for women. One subject dropped out at day 1 (run in) due to disliking the test food, 1 dropped out at day 13 (control) due to problems with the *ad libitum* diet, and 1 dropped out at day 14 (control) due to scheduling difficulties.

This study was conducted according to the guidelines laid down in the Declaration of Helsinki and all procedures involving human subjects were approved by the Medical Ethics Committee of Wageningen University (registration number NL38515.081.11). Written informed consent was obtained from all subjects. The study was registered in the National Institutes of Health clinical trial database (ClinicalTrials.gov number NCT01526759).

Study design

In a double-blind, two-arm randomized crossover design subjects consumed test foods for 16 consecutive days, with two weeks washout. Table 5.1 gives an overview of the procedures of each intervention period. The test food was consumed daily between 10:30 and 11:00 hours, and contained either gel forming pectin or a gelatin-starch blend as a control with similar consistency. On day 1 (run in) all subjects consumed the control test food, and on days 2 to 16, subjects were randomly assigned to receive either the pectin or the control test food. Subjects collected their test foods twice per week at the research center. To assess total energy intake, during the first two days and the last three days of both intervention periods the subjects consumed *ad libitum* diets provided by us. During the other days of the intervention periods, and the washout, subjects were instructed to consume their habitual diet. Satiety ratings and breath hydrogen, as an indicator for colonic fermentation, were assessed over two 14h periods on days 2 and 16. Blood samples were taken after days 1 (run in), 2 and 16 to assess fasting glucose, insulin, leptin, and short chain fatty acid concentrations. Furthermore, illness, medicine use and adverse events were recorded daily and body weight and step counts were assessed each morning when subjects visited the research center to consume *ad libitum* breakfast.

Table 5.1: Procedures for both intervention periods in which subjects consumed one of two test foods.

Day	Procedures[1]
1	R, D, E, W
2	T, D, E, W, F, A, B
3	T, D, Eb, W, F
4	T, D
5	T, D
6	T, D
7	T, D
8	T, D
9	T, D
10	T, D
12	T, D
13	T, D
14	T, D, E, W
15	T, D, E, W
16	T, D, E, W, A, B
17	Eb, W, F

[1]Abbreviations of procedures: R, run-in test food; D, diary; T, test food; E, *ad libitum* energy intake; Eb, *ad libitum* energy intake (only breakfast); W, body weight and step count; F, fasting blood sample; A, 14-h appetite ratings; B, 14-h breath samples.

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Test foods

The test foods were isocaloric dietary supplements (58kcal/100g) equal in consistency and eating time (Table 5.2) and were especially developed for this study (NIZO food research BV, Ede, the Netherlands). The test foods were served in portions of 200 g in non-transparent plastic cups with spoons. The pectin test food contained (g/100 g): 5 g pectin (Classic CU901, LM-pectin, DE=10%, molecular weight = max 15kDa; Herbstreith & Fox, Neuenbürg/Württ, Germany), 1.5 g starch, 10.4 g sugar, 0.12 g calcium, 0.4 g citric acid, 0.1 g vanilla aroma. The control test food contained (g/100 g): 1.5 g gelatin, 3.5 g starch, 10.4 g sugar, 0.12 g calcium, 0.5 g citric acid, 0.1 g vanilla aroma. To calculate available energy, Atwater factors were used for protein and carbohydrate (17 kJ/g) and fibre was estimated as 8.5 kJ/g (19). The pectin dose of 10 g/day was based on our previous study (Wanders et al., submitted), in which 10 g of this type of pectin significantly increased satiety ratings after single exposure. Table 5.3 provides the sensory properties of the test foods obtained from an independent panel.

Stiffness of the test foods as consumed and viscosity and water holding capacity in simulated mouth and stomach conditions were measured (Table 5.2). Viscosity of the test foods could only be measured in simulated mouth and stomach conditions because they were proper gels. Stiffness was measured as the slope of the penetration curve at a speed of 0.3mm/s 7 °C and at 18 °C in g/mm

Table 5.2: Composition and characteristics of the test foods in preloads and in simulated upper gastrointestinal conditions.

	Control	Pectin
Protein (g/100g)(en%)	1.5 (10)	-
Carbohydrates (g/100g)(en%)	13.0 (90)	12.0 (84)
Dietary fibre (g/100g)(en%)	-	5.0 (16)
Available energy (kJ/100g)[1]	246	246
Volume test food (g)	200	200
Eating time[2] (min)(SD)	5.0 (2.4)	4.5 (2.4)
Preload stiffness[3] at 7 °C (g/mm)	69	66
Preload stiffness[3] at 18 °C (g/mm)	26	37
Viscosity (mPa/s)		
Mouth	0.8	3.7
Stomach	0.8	0.8
Water holding capacity (g water/100g test food)[4]		
Mouth	4.8	40.2
Stomach	7.5	77.3

[1] To calculate available energy, for protein and carbohydrate Atwater factors were used (17kJ/g), and fibre was estimated as 8.5kJ/g (20). The test foods did not contain fat.

[2] Eating time of the control and pectin test food was assessed by 18 subjects different from the subjects in the present study. These subjects consumed 200g of each test food randomized over two occasions, and recorded consumption time. Eating time did not differ between the two test foods (p =0.315).

[3] Measured as the slope of the penetration curve with a speed of 0.3mm/s (Texture Analyser, type TA-XT2, Stable Micro Systems Ltd. Godalming, UK).

[4] WHC: water holding capacity is the amount of water held by the insoluble material from 100g of test food.

(Texture Analyzer, type TA-XT2, Stable Micro Systems Ltd. Godalming, UK). Viscosity and water holding capacity in simulated mouth and stomach conditions were measured according to methods described earlier (Wanders et al, BJN, in press)(20), with adaptations for the high water content of the products. In short, after simulation of mouth and gastric conditions with oral and gastric enzymes and reagents, samples were centrifuged. Viscosity was measured in the supernatant at 37 °C and data obtained at shear rate 100/s (MCR 300, Anton Paar, Graz, Austria) were reported. Water holding capacity was measured from the pellet containing the insoluble material. Water holding capacity was expressed as the amount of water held by the insoluble material from 100 g of test food.

Table 5.3: Ratings on sensory properties[1] and palatability[2] for the two test foods.

	Control		Pectin		P[1]
	Mean	SD	Mean	SD	
Thickness	6.3	1.9	5.9	1.6	0.27
Melting	5.7	1.9	5.0	2.0	0.22
Smell intensity	4.4	1.9	4.6	2.2	0.60
Sweetness	5.0	1.8	5.0	1.8	0.95
Sourness	2.8	1.9	4.7	2.2	< 0.001
Bitterness	1.7	1.0	3.2	2.2	0.001
Smoothness	7.3	1.4	6.2	1.8	< 0.001
Stickiness	4.3	2.2	5.7	1.6	0.005
Mouth filling	5.2	1.7	6.3	1.5	0.008
Aftertaste intensity	4.0	2.1	5.7	1.7	< 0.001
Palatability	6.1	1.7	4.0	1.7	< 0.001

[1]Sensory properties were rated by 23 subjects different from the subjects in the present study. These subjects received 25g samples of each test food on one occasion, in randomized order, and rated the properties on a 9-point Likert scale anchored from 'not at all' to 'very much'.

[2]Palatabilty was rated by subjects in the present study, immediately after each intervention period on an 11-point Likert scale anchored from 'not at all' to 'very much'.

[3]P-value from paired t-test.

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Energy intake

To assess total energy intake, all the subjects' meals were served *ad libitum* at the research center at days 1 (run in), 2 and 14 to 16 of both intervention periods, including breakfast at days 3 and 17. In the morning (between 7:30 and 8:30 hours) and evening (between 17:30 and 18:30 hours) bread meals were served *ad libitum* in buffet style. Hot meals at lunch (between 12:30 and 13:30 hours) were individually served in portions corresponding to 200% of the energy content of a normal Dutch hot meal (21). A package with snacks could be taken out for the afternoon and evening. Subjects were not allowed to eat other foods than provided. The variety of foods served was limited to everyday foods to prevent subjects from overeating. The buffet at breakfast and evening consisted of whole meal mini-buns, crackers, low-fat margarine, two types of cheese, two types of meat slices (ham and chicken), four types of sweet fillings (jam, chocolate spread, apple spread and peanut butter) and three types of fruit (apple, pear, orange). The hot lunch was a mixed meal consisting of pasta or rice, meat and cooked vegetables, served with a raw vegetable salad with dressing as a side-dish, and a fruit salad as a dessert. To prevent boredom, three different dishes were served balanced throughout the study design; each dish was served on a fixed week day. As afternoon and evening snacks we provided the subjects with three apples, five slices of gingerbread and five mini currant buns. During the *ad libitum* days it was only allowed to drink water, tea and coffee (with condensed milk and sugar). Other liquid and semi-solid foods containing calories were not included

in the menu, as liquid calories have low satiating value (11, 22). From all the foods provided subjects could serve themselves and eat until comfortably satiated. To prevent the subjects from consuming foods in amounts similar to amounts consumed habitually, unusually large plates were used and unusual portion sizes were provided (23). Food intake was measured by weighing and counting the remaining foods. Energy intake was calculated using the Dutch Food Composition Database (24). Energy intake was calculated per meal time: lunch, dinner, snacks and next day breakfast, and total per day. Total and meal time energy intake was then calculated for day 1 (run in), day 2 and day 16 (mean day 14 to 16).

Satiety ratings

On days 2 and 16, each subject completed hourly satiety ratings over a 14h period using a Personal Digital Assistant (PDA, HP IPAQ) with software (EyeQuestion version 3.8.3., Logic8 BV, Elst, the Netherlands). Upon arrival at the research center in the morning subjects received the PDA and they rated hunger, fullness, desire to eat, prospective food consumption and thirst on 11-point Likert scales anchored from 'not at all' to 'very much'. Satiety ratings were completed before and after the three meals and furthermore every hour from breakfast until 22:15 hour in the evening. An hourly alarm was programmed to remind subjects. Satiety ratings were analyzed for the total day and separately for morning (before breakfast to before lunch), afternoon (after lunch to before dinner) and evening (after dinner to end of day). Moreover, ratings over the two hours after test food intake (11:15 hour to before lunch) were also analyzed.

Other measurements

Parallel to the satiety ratings on days 2 and 16, each subject collected hourly alveolar breath samples over a 14h period using reusable 250 ml sample holding bags (Quintron, Milwaukee, USA). Breath samples were taken before breakfast, after lunch, after dinner and furthermore every hour from breakfast until 21:15 hours in the evening. Breath samples were analyzed for hydrogen content with a Quintron Microanalyzer (Quintron Instruments, Milwaukee, USA) within one week after collecting. Measurements of day 16 in intervention period 1 and day 2 in intervention period 2 were discarded from the dataset, due to wrongly stored sample holding bags (stopcock closed instead of open).

To assess fasting glucose, insulin, leptin and short chain fatty acid concentrations, after days 1 (run in), 2 and 16, blood samples were collected into 6-mL EDTA-containing tubes. Instructions for fasting were that from 21:00 hours eating was not allowed, and from 23:00 hours onwards only water was allowed. Tubes were centrifuged at 1000 g/2216rpm for 10 minutes at 4 °C, and kept on iced water before and after centrifugation. Plasma samples were stored at -80 °C until analysis. Glucose was measured by the hexokinase method (Modular P800 analyzer, Roche, Basel, Switzerland). Insulin and leptin were measured using commercially available human ELISA kits (Mercodia, Uppsala, Sweden). Concentrations of the short chain fatty acids acetate, butyrate and proprionate, were assessed by ^{1}H-NMR spectroscopy according methods as described by Souza da Silva et al. (25).

Body weight was assessed each morning when subjects visited the research center before the *ad libitum* breakfast, without wearing shoes or heavy clothing. Subjects were instructed not to change their physical activity, this was monitored on each *ad libitum* day by the number of steps measured with a pedometer (Yamax Digi-walker, SW-200, Tokyo, Japan). Baseline body weight was calculated as the mean of the measurements at day 1 and 2. End body weight (day 16) was calculated as the mean of day 15 to 17. The similar procedure was followed for the number of steps.

During both intervention periods, subjects were asked to keep a diary to register the exact time of intake of the test foods, adverse events (bloating, belching, flatulence, nausea, diarrhea, other), illness and use of medication. Directly after both intervention periods evaluation questionnaires were given, in which the subjects were asked to rate the test foods for palatability on 11-point Likert scales anchored from 'not at all' to 'very much'.

Statistical analysis

Data are presented as means with standard deviations unless reported otherwise. Statistical analyses were performed with SAS (version 9.2; SAS institute Inc., Cary, NC, USA). Significance was set at $p < 0.05$. Test food effects per study day were analyzed by means of ANOVA (proc mixed, SAS). For the variables total daily energy intake, fasting glucose, insulin, leptin and short chain fatty acid concentration, body weight and step count, test food, intervention period, day, test food*day and test food*intervention period (=order) were included as fixed factors and subject was included as random factor. After confirming that effects on run-in days were similar, these data for energy intake, fasting glucose, insulin and leptin were removed from the dataset. Repeated measurements for satiety ratings were analyzed according to a similar procedure, with the addition of time and test food*day*time as fixed factor in the model. Sensory and palatability ratings were analyzed according to a similar procedure. Hydrogen excretion data were not normally distributed and were therefore log-transformed for analysis and presented as back-transformed geometric means. As a result of the removal of hydrogen data from day 16 in period 1 and day 2 in period 2, subject was included as a covariate instead of as a random factor. Adverse events were reported by the number of subjects reporting an event at least once and analyzed by the chi-square test.

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Results

Subjects complied well with the instructions to consume the test foods each day between 10:30 and 11:00 hours. From daily records it was shown that 86% was consumed in time, 11% within 30 minutes of the instructed time and 3% more than 30min late or early. Reasons to deviate from the instructed time were in general meetings or sport events which did not allow food intake.

The two test foods were comparable regarding energy content, stiffness and eating rate (Table 5.2), and for the sensory ratings thickness and melting behavior (Table 5.3). There were differences in some of the sensory properties, i.e. the pectin test food was rated as more sour and bitter, more sticky and more mouth filling than the control. Moreover, palatability of the pectin test food was significantly lower than the control ($p < 0.001$). As hypothesized, physicochemical properties of the
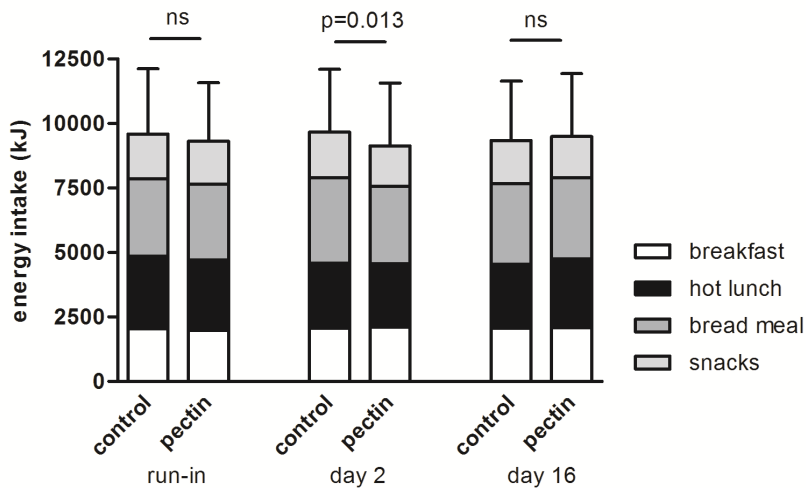
Figure 5.1: Mean energy intake (kJ) per day and per meal time on day 1 (run in), day 2 and day 16 by subjects who consumed either control or pectin test food (n=32). Results after mixed model ANOVA: test food (p =0.137), test food*test day (p =0.034).

two test foods in simulated upper gastrointestinal conditions were different (Table 5.2). The pectin test food had a 4-fold higher viscosity in mouth conditions, an 8-fold higher water binding capacity in mouth conditions, and 10-fold higher water binding capacity in stomach conditions.

Energy intake

During the run-in day, total energy intake was similar for the two groups (p =0.34) (Figure 5.1). After single exposure to the pectin test food (day 2), total daily energy intake was significantly lower (9.13 ± 2.45 MJ) than after the control (9.67 ± 2.43 MJ) (-5.6%, p =0.013). On day 16, energy intake was similar when the subjects received the pectin test food (9.49 ± 2.44 MJ) compared to when they received the control (9.32 ± 2.30 MJ) (p =0.62). There were no differences between the two test foods in energy intake at the different meal times (breakfast, hot lunch, evening bread meal and snacks) (test food*day*meal time interaction: p =0.59). Post-hoc tests, however, revealed a borderline significant difference for the bread meal on day 2, energy intake was 3.01 ± 0.86 MJ after the pectin test food and 3.31 ± 1.01 MJ after the control (-9.1%, p =0.065).

Satiety

Satiety ratings reflected the cycle of 3 meals a day clearly (time-effect: all p <0.0001) (Figure 5.2). Overall, subjects rated hunger lower (-1.7%; test food-effect: p =0.007), fullness higher (+1.4%; p =0.041), desire to eat lower (-1.7%; p =0.014) and prospective intake lower (-1.8%; p =0.003) when they received the pectin test food compared to when they received the control. This difference in satiety rating was comparable after single and repeated exposure to the test foods (test food*day interaction: all p >0.65). Over the total mornings satiety ratings were not different between the

two test foods, whereas right after consumption, from 11:15 hours until lunchtime, there were differences. In this period, subjects rated hunger lower (-3.3%; test food-effect: p =0.029), desire to eat lower (-3.5%; p =0.020) and prospective intake lower (-3.5%; p =0.010) when they received the pectin test food compared to when they received the control. This difference was comparable after single and repeated exposure (test food*day interaction: all p >0.54). Over the afternoon, subjects consuming the pectin test food rated hunger lower (-2.2%; p =0.033), prospective intake lower (-2.0%; p =0.037), and only on day 1 they rated desire to eat lower (-3.3%; p =0.036) then after control. In the evening subjects rated fullness higher (+2.9%; p =0.017), desire to eat lower (-3.7%; p =0.006) and prospective intake lower (-2.2%; p =0.029) after receiving the pectin test food compared to control, which was comparable after single and repeated exposure (test food*day interaction: all p >0.31). The two test foods had no different effects on thirst ratings.

Other measurements

Baseline body weight was similar for the two groups (p =0.99). Body weight did not change over the two week period when the subjects received the pectin test food (day 16: 66.5 ± 9.7 kg) compared to when they received the control (day 16: 66.5 ± 9.7 kg) (test food*day interaction: p =0.60). Step counts did also not differ between the two groups at baseline (p =0.266) and were similar at the end of the two week period after the pectin test food (day 16: 9888 ± 3367 steps) and control (day 16: 10038 ± 2981 steps) (test food*day interaction: p =0.56).

After single exposure to the pectin test food breath hydrogen was elevated compared to the control (p =0.0075) (Figure 5.3). On day 16, breath hydrogen excretion was not different between the pectin test food and control (p =0.13). When the subjects received the pectin test food, fasting glucose concentrations were higher (test food-effect: 5.1 ± 0.4 mmol/l p =0.019), than when they received control (5.0 ± 0.4 mmol/l). The difference did not change after single or repeated exposure to the test foods (test food*day interaction: p =0.66). No differences were seen in fasting insulin and leptin concentrations (Table 5.4), and in fasting short chain fatty acids (data not shown).

Adverse events and other illnesses possibly related to the test food intake were registered in the daily records. During the period in which the control and pectin test foods were consumed, bloating was reported respectively by 8 vs. 13 subjects (p =0.18); belching by 3 vs. 2 subjects (p =0.64); flatulence by 9 vs. 12 subjects (p =0.42); nausea by 5 vs. 3 subjects (p =0.45); and diarrhea by 4 vs. 5 subjects (p =0.72). These complaints were generally mentioned to be mild.
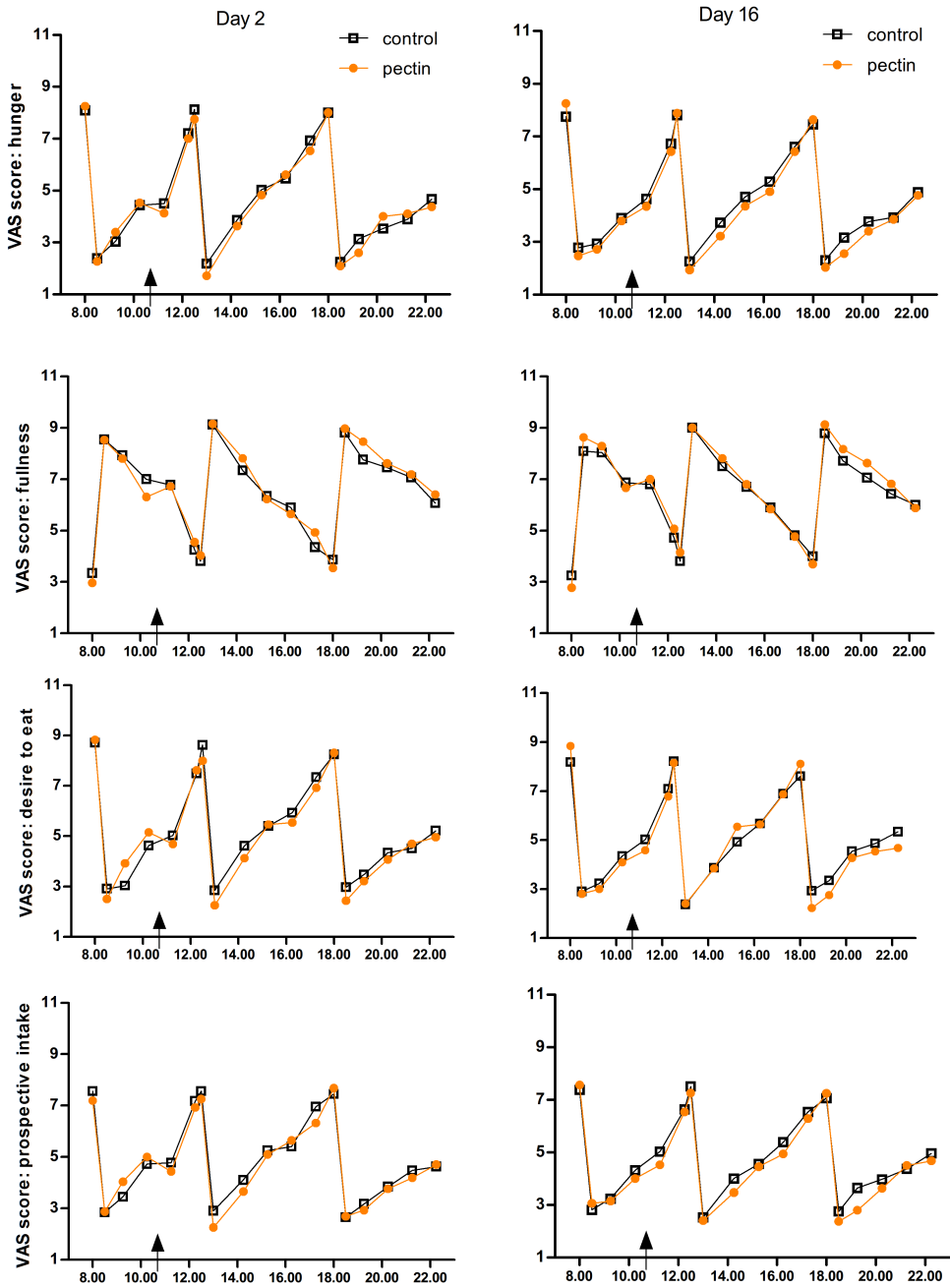
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Figure 5.2: Mean ratings for hunger, fullness, desire to eat and prospective intake, measured on a 11 point Likert scale (from not at all to very) hourly from 8:00 until 22:00 on days 2 and 16. At 10:30h (see arrow) the control or pectin test food was consumed (n=32). Results after mixed model ANOVA for test food (all appetite ratings $p < 0.05$), time (all appetite ratings $p < 0.0001$), test food *test day (all appetite ratings $p > 0.65$).
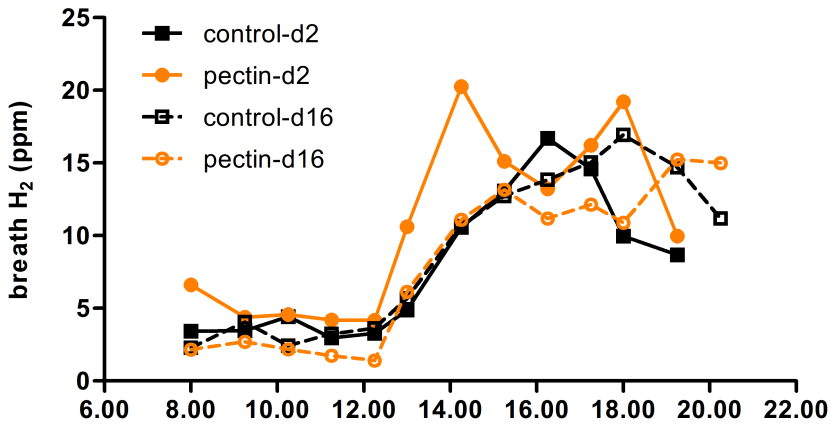
Figure 5.3: Mean breath hydrogen excretion (ppm), measured hourly from 8:00 until 20:00 on days 2 and 16. Data were log-transformed for analysis and are presented as back-transformed geometric means. At 10:30 h the control or pectin test food was consumed (n=32). Results after mixed model ANOVA test food (p =0.362), test food*test day (p =0.003).

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Table 5.4: Fasting glucose, insulin and leptin concentrations in subjects who consumed either control or pectin test food (n=32).

		Day 1 (run in)		Day 2		Day 16		Test food	Test food * test day
		Mean	SD	Mean	SD	Mean	SD	P[1]	P[1]
Glucose (mmol/l)	Control	5.1	0.4	5.0	0.4	5.0	0.5	0.019	0.66
	Pectin	5.1	0.5	5.1	0.4	5.2	0.4		
Insulin (mU/l)	Control	7.0	2.6	5.6	1.9	6.7	2.1	0.29	0.24
	Pectin	7.1	3.0	6.2	2.2	6.6	2.6		
Leptin	Control	7.2	4.3	7.2	4.3	6.6	4.0	0.99	0.15
	Pectin	6.9	4.0	6.6	4.1	7.1	5.2		

[1] P-value from mixed model ANOVA.

Discussion

The present study investigated satiety and energy intake after single and repeated exposure to a gelled fibre. To gain insight in the post ingestive satiety mechanisms, the test foods were matched for texture and eating time. We found that after single exposure to a 10g dose of gelled pectin, satiety ratings were higher and subsequent energy intake was lower compared to the control. Over the 16 day study period the increased satiety ratings persisted, whereas the energy intake reduction did not. The results of the present study show that gelled pectin can increase satiety by other means than a change in texture and eating time alone. Moreover, the study shows that, even though the effects are small, the increased satiety persists over time.

State of the art methods were used to measure satiety and energy intake under free living conditions (26). Satiety ratings were measured with PDAs hourly over a full day, and energy intake was measured with an *ad libitum* diet over multiple days according to standardized methods. Moreover, it was not allowed to consume liquid foods containing calories, as these have low satiating value (11, 22). The design of our test foods was restraint by structural differences between gelled pectin and gelled non-fibres. Therefore, not all sensory properties could be made identical and some differences were observed in palatability. Palatability has been associated with later satiation (27), and sensory properties as taste intensity have been associated with earlier satiation (28). However, effects of palatability and taste intensity on subsequent satiety are unlikely (29). We therefore believe that test food properties affecting oral exposure, other than texture and eating time, may not have affected our findings.

Our findings show that both on day 2 and on day 16, the pectin test food increased satiety ratings with about 3.5% over the two hours after consumption, and with about 2% over the whole day, compared to the control test food that was equal in texture and eating time. In an earlier study in which the same gelled pectin was compared to a liquid control, 3h satiety ratings increased with about 7% (Wanders et al, submitted). The present findings therefore suggest that the satiety effects of gelled pectin can not only be attributed to increased oral exposure, but can also be attributed to post-ingestive effects such as: delayed gastric emptying; changed appetite regulating neural and hormonal signals in the gut; slowed down absorption of nutrients; and altered fermentation in the large intestine (4-6).

The primary difference between the two test foods was the consistency right after ingestion. In simulated mouth and stomach conditions, the control test food had a lower viscosity and water holding capacity than the pectin test food. This difference can be explained by both the presence of salivary amylase and the increase of temperature towards body temperature. Whereas starch is broken down by enzymes and gelatin starts to melt in the mouth, pectin is unaffected by enzymes and melts in the mouth to a lesser extent. This difference in texture after ingestion may result in a change in gastric emptying rate. In an earlier study we showed that a single dose of the same gelling pectin resulted in a reduced gastric emptying rate (Wanders et al, submitted). Moreover, Schwartz et al., showed that sustained pectin consumption persistently delayed gastric emptying, which may

be due to adaptive changes (30). A delay in gastric emptying may enhance gastric mechanoreceptor stimulation and as a result prolong fullness feelings (31).

Both a delay in gastric emptying, and the increased water holding capacity of the intestinal content may slow down nutrient absorption in the small intestine. As a result, the release of neural and hormonal signals in the gut may be prolonged and lead to longer satiety (32). In the present study we did not measure postprandial release of signals in the gut, but we did measure fasting glucose, insulin and leptin. We did, however, not find reductions in fasting glucose levels after repeated exposure, which is in agreement to earlier studies (33, 34).

A third process that may explain the satiety increasing effect of the pectin is fermentation in the large intestine. Three hours after consuming a single dose of pectin, breath hydrogen excretion showed a clear peak, which suggests an increase in colonic fermentation (35). Whereas hydrogen on itself is probably not directly associated with appetite (35), altered activity of gut microbiota may promote the production of short chain fatty acids (36, 37), which has been related to an increased satiety and a reduced body weight (38, 39). In the present study the increase in hydrogen production did not persist over time, which was confirmed by the absence of differences in fasting concentrations of short chain fatty acids. In contrast to findings in the present study, in other studies fermentable fibres have resulted in sustained changes in hydrogen excretion (38, 40). The inconsistency may be explained by dissimilar fermentation patterns in the large intestine after different types of fermentable fibre (41-43). After sustained pectin consumption adaptation of bacterial metabolism towards efficient fermentation pathways not producing hydrogen or short chain fatty acids may have taken place (44).

After single exposure to the pectin test food, energy intake lowered with about 6%, which was not observed at the end of the study period, neither was this reflected in a reduction of body weight. This finding did not match with the persistent increase in satiety that was observed throughout the 16 days of intervention. We hypothesize that to affect actual eating behavior, larger changes in satiety ratings may be needed. It was suggested that an 8-10% change in satiety ratings is a relevant effect size (26, 45), which may also be a relevant effect size to influence energy intake. A recent study with a fermentable, but not viscous or gel forming wheat dextrin supports this suggestion (46). Over two weeks of supplementation with dosages of 8, 14, 18 and 24 g/day, all dosages increased satiety ratings compared to 0 g/day. Interestingly, only the dosages of 14g and higher significantly lowered body weight (47). These results suggest that to achieve a persistent reduction in energy intake, larger increases in satiety should be aimed for, which may be achieved by a higher dosage of dietary fibre.

In a previous paper we suggested that after repeated exposure, other metabolic processes may add towards sustained satiety or reduced longer term energy intake (Wanders et al., submitted). In the present study, however, no further changes were found after repeated exposure. Based on an array of studies (e.g. as reviewed in (7)) we postulate that dietary fibres can have both 'mechanical' effects and 'colonic' effects on appetite. The mechanical effects can for example be oral exposure, gastric emptying rate and nutrient absorption. These effects are mediated by food matrix or

intestinal content characteristics, such as viscosity and accessibility of nutrients in the lumen, and can generally be provoked by relatively small dosages of fibre. In contrast, colonic effects may depend highly on fibre specific properties such as prebiotic activity, composition of gut-microbiota, and fermentation end products. The effective dosage of fibre that may induce a change in colonic effects depends largely on the specific fibre type characteristics. This may explain why a gelled and highly fermentable pectin does not change energy intake after repeated exposure, whereas wheat dextrin, a fibre that is not viscous and does not form gels, but is fermentable, has large effects on energy intake (46). This suggestion, however, is preliminary and should be verified with additional research.

We conclude that a relatively small dosage of gelled pectin can increase satiety and reduce energy intake by other means than oral exposure. The small effects may have been mediated by a delayed gastric emptying, a prolonged release of hormonal signals, a slowed down nutrient absorption or an altered fermentation pattern. The effects on satiety persisted over time whereas the energy intake reduction did not.

Acknowledgements

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Intake of dietary fibre types and associations with change in BMI and waist circumference:

results from a population-based prospective cohort study

Authors

Johanna Rienks
Anne J. Wanders
Truus G.J. Van Woudenbergh
Frank J. Van Rooij
Albert Hofman
Anneleen Kuijsten
Jacqueline C. Witteman
Oscar H. Franco
Edith J.M. Feskens

Abstract

Background: A high intake of dietary fibre has been associated with smaller weight gain. However, when dietary fibres from different food sources are studied, associations with weight are inconsistent. This might be due to the difference in dietary fibre type content. Our objective was to examine the associations between intake of different dietary fibre types and changes in BMI, weight and waist in a population-based prospective study.

Methods: Our analysis included 1,859 participants of the Rotterdam study with measured weight, height and waist circumference at baseline and after on average 6.4 years follow-up. Potential under-reporters of energy intake, based on the ratio of energy intake and estimated basal metabolic rate, were excluded. Habitual diet, including dietary fibre, was assessed using a validated two-step 170-item semi-quantitative food frequency questionnaire. A new food composition table on fibre types was compiled using literature-based values. Multiple linear regression analysis on annual change in BMI, body weight and waist was performed including baseline anthropometric, demographic, lifestyle, and dietary variables as potential confounders.

Results: Intake of total dietary fibre, main fibre sources (i.e. cereal, fruit, vegetables and potatoes) and fibre types (i.e. cellulose, lignin, pectin, soluble and insoluble fibre) were not associated with subsequent change in BMI, body weight, and waist circumference. The inverse association between total dietary fibre intake and annual BMI change was borderline significant (beta $_{high\ vs\ low}$ = -0.020 (95%CI: -0.050 to 0.011).

Conclusion: High intakes of total dietary fibre, fibre sources and fibre types were not associated with annual change in BMI, body weight, and waist circumference. This finding may be partly due to the older age of the study population.

Introduction

In 2009, the prevalence of overweight and obesity (BMI >25 kg/m^2) in adults across Europe varied between 37% and 69% (1). Being overweight or obese puts people at a higher risk of coronary heart disease, type 2 diabetes, hypertension, and certain cancers (1). Measures that contribute to the prevention of obesity are physical activity and dietary factors, among others dietary fibre (2).

Several prospective (3-7) and cross-sectional observational studies (8-13) have shown that a higher intake of dietary fibre is associated with lower body weight, lower BMI, and smaller waist circumference. Dietary fibre is defined as all polysaccharides that are not digested in the human small intestine, such as pectin, hemicellulose, and cellulose (14). To account for these different fibre types, in a number of the observational studies fibre intake was classified by food source, such as fibre from cereals, fibre from fruits, fibre from vegetables, and fibre from legumes. Two large prospective studies (3, 4), and several cross-sectional studies (11, 12, 15, 16) showed that cereal fibre is consistently inversely associated with a lower body weight, whereas for other fibre sources, such as fruit and vegetables, either inverse, no, or positive associations were observed. These inconsistent findings may be caused by the heterogeneous composition of types of dietary fibre within food sources. For example, of the total fibre content in fruits, pectin concentrations range from 5% in pineapple to more than 40% in oranges and cantaloupe. In vegetables, of the total fibre content cellulose concentration ranges from 25% in green beans to more than 50% in mushrooms and pumpkin (17).

Different types of dietary fibre may facilitate body weight control through different physiologic mechanisms, which are related to a reduced appetite and energy intake (18). Randomized controlled trials have shown indeed that specific types of dietary fibre may have different effects (19). Foods rich in viscous fibres, such as pectin, may slow down gastric emptying and lead to a more gradual nutrient absorption, which can enhance satiety; foods rich in fermentable fibres, such as soluble fibre, can increase short chain fatty acid concentrations which can also enhance satiety.

Even though randomized controlled trials are generally believed to provide the highest level of evidence, examining long term weight change is limited due to the relative short duration of many trials. Prospective cohort studies, however, could not investigate whether specific types of dietary fibre are associated with obesity, because food composition tables do not contain information on types of dietary fibre. The aim of this study was therefore to examine the associations between intake of total dietary fibre, dietary fibre from different food sources, dietary fibre types, and body mass index, body weight and waist circumference in a cohort of Dutch elderly men and women. To achieve this, a new food composition table on types of dietary fibre was compiled using values from available literature.

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Methods

Rotterdam study

The Rotterdam Study is a prospective population-based cohort study, which aims to target cardiovascular, endocrine, hepatic, neurological, ophthalmic, psychiatric, and respiratory diseases in the elderly. All residents of the Ommoord suburb in Rotterdam aged 55 years and over were invited for participation (n=10,275). Between 1990 and 1993 baseline measurements were performed on 7,983 participants (78% of the eligible population). Follow-up is carried out at 2 to 3 year intervals and is currently in its fifth cycle. The Medical Ethics Committee of Erasmus University approved the study, and all participants signed an informed consent form before participation. The study design has been described in detail elsewhere (20, 21).

Population for analysis

Of the 7,983 participants 5,435 had food intake data (22). Participants with missing data on change in body weight and waist circumference were excluded (n=2269), as well as participants without data on covariates (n=214). Under-reporting of energy intake (EI) was estimated by the ratio of EI to basal metabolic rate (BMR), EI:BMR <1.2 (23), where BMR was estimated by the WHO equation (24). Of the population 1,093 participants (37%) were identified as potential energy under-reporters and excluded. This proportion amounted to 26% of the normal weight participants, 40% of the overweight, and 60% of the obese. The remaining sample for the present analysis was 1,859 participants.

Assessment of dietary intake

A two-step 170-item semi-quantitative food frequency questionnaire (SFFQ) was administered at baseline to assess habitual dietary intake (22). First, the participant self-administered foods consumed at least twice a month over the last year at home. Then they were interviewed by a trained dietician who further quantified the amount and frequency of reported foods. The relative validity of the SFFQ was assessed among 80 participants who completed 15 days of food records in six periods within one year. Relative validity obtained by Pearson's correlation coefficient, adjusted for age, sex, and energy and corrected for within-person variation in food records, was 0.62 for dietary fibre intake. To estimate reproducibility, a second SFFQ was filled out 2 years after the first. This resulted in an intra-class correlation coefficient of 0.67 (25).

Intake of total dietary fibre, fibre from food sources and fibre types

Energy intake and intake of nutrients other than dietary fibre were calculated by using Dutch food composition table version 1993 (26). Total dietary fibre was calculated by using version 1996, as the method for fibre estimation improved (27). In addition, dietary fibre intake from food sources was separately calculated for cereals, potatoes, vegetables, and fruits (26). As Dutch food composition tables do not contain information on types of dietary fibre, values for the following five types were obtained from other sources: cellulose, pectin, lignin, soluble non-cellulosic polysaccharide (NCP), and insoluble NCP according to a modification of the five criteria as defined by Greenfield

and Southgate (28). In short, first it was presumed that foods that do not contain total dietary fibre, do also not contain fibre types. Second, analytical values on dietary fibre types were searched in original publications (17, 29-36). Third, values that are still missing after the second step were obtained from foreign food composition tables (37-44). Fourth, values that are still missing after the third step were imputed from similar foods, or from other forms of the same foods (e.g. boiled versus steamed). Last, if needed values on dietary fibre types were recalculated as a proportion of total dietary fibre as given in the Dutch food composition table. Publications providing dietary fibre types as measured by the Association of Analytical Communities (AOAC) 985.29 and AOAC 991.43 methods were prioritized, as these have been most used for food composition databases (45). These methods resulted in original analytical values for the fibre types cellulose, pectin, and lignin for the major quantity of the foods in our study. The remaining values and the values for soluble NCP and insoluble NCP had to be obtained from Englyst or Southgate type methods (45). Soluble NCP were considered the same as soluble fibre, and the total amount of insoluble fibre was calculated as the sum of insoluble NCP, lignin, and cellulose.

Assessment of outcome measures

Data from anthropometric measurements at baseline and after 6-7 years of follow-up were used (20). Measurements were performed by trained personnel at the research centre at baseline and follow-up. Weight (kg) and height (cm) were measured with the participant standing in the upright position wearing no shoes and light clothing. BMI was calculated by dividing weight by height squared (kg/m^2). Waist circumference (cm) was measured between the lower rib and the top of the iliac crest using a tape measure. Change in the outcome measures BMI, weight, and waist circumference were calculated by subtracting the baseline measure from the follow-up measure.

Statistical analysis

Baseline characteristics for demographic, lifestyle, and dietary factors were computed for each tertile of total dietary fibre intake. Intake of total dietary fibre, dietary fibre sources, dietary fibre types, and all other nutrients were adjusted for energy using the residual method (46). Nutrient intakes were reported as the sum of the residual and the mean predicted nutrient intake at the mean energy intake (8,272 kJ/d). To calculate the top 10 of foods contributing most to the intake of each fibre type, per food the absolute intake of each fibre type was calculated for the whole population. Pearson's correlation coefficients were calculated between energy adjusted total dietary fibre, dietary fibre sources and dietary fibre types.

Multiple linear regression models were used to estimate associations of baseline total dietary fibre, dietary fibre sources, and dietary fibre types with subsequent annual change in BMI, body weight, and waist circumference. Covariates included age (years), sex, smoking status (current, former, or never smoker), educational level (low, intermediate, or high), alcohol intake (non-drinker, $0.1 \geq 4.9$g/d, $4.9 \geq 15$g/d, $15 \geq 30$g/d, $30 \geq 60$g/d, or >60g/d), intake of protein (g/d), total fat (g/d), carbohydrates (g/d), energy (kJ/d), baseline outcome measure (e.g. BMI change is adjusted

for baseline BMI) (47), and fibre sources were also adjusted for fibre from other sources. Tests for trend were performed by assigning the median intake value of each tertile to each participant and modelling this variable as a continuous variable. Effect modification by sex or BMI was investigated by including a product term of dietary fibre types with sex or BMI to the model, and by stratified analysis by sex and by BMI categories at baseline (normal weight <25, overweight 25 ≤30, obese ≥30 kg/m^2). Two-tailed p-values <0.05 were considered statically significant. All analyses were conducted using STATA 11.0.

Results

The mean intake of dietary fibre in this population was 17.2 ± 4.6 gram per day. Cereals contributed 35% to total fibre intake, vegetables 23%, fruit 19%, and potatoes 16%. Regarding the types of fibre, cellulose contributed 26% to total fibre intake, pectin 18%, lignin 9%, soluble fibre 35%, and insoluble fibre 58%. To all dietary fibre types wholemeal and wheat bread, potatoes, oranges, and apples were the major contributors, except for pectins to which, instead of breads, vegetables contributed most, and for lignin to which banana's and chocolate bread fillings contributed (Table 6.1). Pearson's correlation coefficients showed that fibre types were highly correlated to each other (varying from 0.44 to 0.94), whereas the fibre from different food sources were not (varying from -0.13 to 0.08) (Table 6.2).

Baseline characteristics and dietary intakes of the study population across tertiles of total fibre intake are shown in Table 6.3. Over 6.4 ± 0.3 years, average BMI change in the population was +0.47 ± 1.62 kg/m^2; weight change was -0.11 ± 4.40 kg; height change was -1.66 ± 1.43 cm; and waist change was +3.5 ± 8.23 cm. The median intake of total fibre was 62% higher in the highest tertile than in the lowest tertile (21.0 versus 13.0 g/day). Compared with participants in the lowest tertile, participants in the highest tertile were younger and were less often current smokers. Furthermore, they had a lower energy intake from fat and a higher energy intake from carbohydrates and protein. For all fibre sources and fibre types, dietary intakes increased over the tertiles.

Multiple linear regression showed that total dietary fibre intake across tertiles was not associated with annual change in BMI, body weight, or waist circumference (Table 6.4). The inverse association between total dietary fibre and annual BMI change was borderline significant; comparing a median intake of total fibre of 21.0 versus 13.0 g/d, BMI was 0.020 kg/m^2 lower per year of the study (95%CI: -0.050 to 0.011). For fibres from the different food sources no significant associations with changes in BMI, body weight, or waist circumference were observed. However, for fibre from cereals an inverse association with waist circumference change reached borderline significance (beta$_{high vs low}$ = -0.098 cm/y (95%CI: -0.242 to 0.045). Regarding the different fibre types, intakes of pectin and insoluble fibre tended towards inverse associations with annual BMI change, and intake of insoluble NCP tended towards an inverse association with annual waist change, but no significant linear trends were found across the tertiles (pectin p$_{linear trend}$ = 0.14; insoluble fibre p$_{linear trend}$ = 0.16; insoluble NCP p$_{linear trend}$ = 0.14).

Table 6.1: Top 10 of foods contributing to the intake of total dietary fibre and dietary fibre types in the Rotterdam study [1] (n=1,859).

	Total dietary fibre	Cellulose	Lignin	Pectin	Soluble fibre	Insoluble NCP	Insoluble fibre
1	wholemeal bread	potatoes	wholemeal bread	potatoes	potatoes	wholemeal bread	wholemeal bread
2	potatoes	wholemeal bread	potatoes	orange	wholemeal bread	wheat bread	potatoes
3	wheat bread	apple	banana	apple	orange	potatoes	wheat bread
4	apple	wheat bread	chocolate flakes	endive	apple	apple	apple
5	orange	orange	wheat bread	garden peas	wheat bread	orange	orange
6	endive	broad beans	apple	broad beans	endive	wheat bran	broad beans
7	banana	garden peas	orange	plums	plums	crispbread	banana
8	French beans	French beans	endive	spinach	French beans	spiced honey cake	garden peas
9	white bread	carrots	kiwi	banana	carrots	French beans	French beans
10	runner beans	tomatoes	crispbread	wholemeal bread	vegetable soup	endive	chocolate flakes

[1]To calculate the top 10, the absolute intake of each fibre type was calculated per food for the whole population.

Table 6.2: Pearson's correlation coefficients among total energy-adjusted dietary fibre, dietary fibre sources, and dietary fibre types in the Rotterdam study (n=1,859).

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		(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)	(11)
Total dietary fibre	(1)	1										
Fibre sources												
Fibre from cereals	(2)	0.66	1									
Fibre from fruit	(3)	0.50	0.08	1								
Fibre from vegetables	(4)	0.42	0.00	0.06	1							
Fibre from potatoes	(5)	0.05	-0.04	-0.13	0.10	1						
Fibre types												
Cellulose	(6)	0.84	0.43	0.46	0.63	0.40	1					
Lignin	(7)	0.71	0.41	0.53	0.24	0.04	0.62	1				
Pectin	(8)	0.71	0.12	0.73	0.65	0.16	0.86	0.60	1			
Soluble fibre	(9)	0.80	0.38	0.59	0.55	0.37	0.94	0.67	0.90	1		
Insoluble NCP	(10)	0.85	0.86	0.29	0.20	-0.01	0.68	0.63	0.44	0.64	1	
Insoluble fibre	(11)	0.93	0.70	0.45	0.42	0.18	0.89	0.77	0.71	0.86	0.92	1

Abbreviation: NCP: non-cellulosic polysaccharides.

Table 6.3: Baseline characteristics by tertiles of total dietary fibre intake in the Rotterdam study (n=1,859).

	Tertiles of total dietary fibre intake (g/d)[1]		
	Tertile 1	Tertile 2	Tertile 3
	n = 620	n = 620	n = 619
	13.0 (11.4-14.4)[2]	17.0 (16.1-18.0)[2]	21.0 (19.8-22.9)[2]
Age (y)[3]	66.2±6.5	65.8±6.6	65.0±6.4
Sex (% women)	49.8	59.0	54.1
Current smokers (%)	30.8	20.3	16.6
Education (% high)	11.8	12.9	13.2
Overweight (%)	45.2	49.5	42.3
Obesity (%)	8.7	9.5	6.6
BMI (kg/m^2)	25.5±3.3	25.8±3.1	25.3±3.0
BMI change per year (kg/m^2) [4]	0.07±0.27	0.08±0.26	0.08±0.23
Body weight (kg)	72.6±11.5	72.6±11.3	71.8±10.4
Body weight change per year (kg) [4]	-0.04±0.73	−0.004±0.72	−0.002±0.62
Waist circumference (cm)	89.0±10.7	88.4±10.8	87.1±10.5
Waist circumference change per year (cm) [4]	0.54±1.32	0.53±1.25	0.56±1.30
Dietary intake[5]			
Energy (MJ/day)	9.4±1.9	9.0±1.7	9.4±2.0
Carbohydrate (% of energy)	41.8±6.8	42.9±6.3	45.4±6.0
Protein (% of energy)	15.3±2.4	16.3±2.5	16.8±2.6
Fat (% of energy)	38.6±5.8	37.6±5.6	35.6±5.6
Alcohol (g/d)	15.1±19.3	11.2±13.8	8.9±11.3
Alcohol n (% non-drinker)	17.0	15.0	18.7
Fibre sources [5]			
Fibre from cereals (g/d)	6.1±2.5	8.8±2.5	11.7±3.5
Fibre from fruit (g/d)	3.5±2.2	5.0±2.6	6.5±3.9
Fibre from vegetables (g/d)	5.0±1.8	5.8±1.9	7.1±4.2
Fibre from potatoes (g/d)	3.8±1.9	4.0±2.1	4.1±2.2
Fibre types [5]			
Cellulose (g/d)	5.2±1.1	6.6±1.0	8.2±1.7
Pectin (g/d)	3.7±1.0	4.7±1.0	5.8±1.8
Lignin (g/d)	1.8±0.5	2.3±0.5	2.9±0.7
Soluble fibre (g/d)	7.1±1.4	8.7±1.4	10.7±2.1
Insoluble NCP (g/d)	3.8±1.2	5.6±1.1	7.6±1.7
Insoluble fibre (g/d)	10.8±2.1	14.5±1.7	18.8±3.2

Abbreviations: BMI, body mass index; NCP, non-cellulosic polysaccharides.

[1] Tertiles of energy adjusted residuals of total dietary fibre intake.

[2] Tertile values are medians; 25 th-75th percentiles in parenthesis.

[3] Mean ± SD (all such values).

[4] Change from baseline to follow up.

[5] Reported dietary intakes were adjusted for energy using the residual method, except for alcohol.

Table 6.4: Change in BMI, body weight and waist circumference per year according to tertiles of intake of total energy-adjusted dietary fibre, dietary fibre sources, and dietary fibre types in the Rotterdam study (n=1,859).

	Tertile 1	Tertile 2		Tertile 3		p for trend
		beta[1]	95% CI	beta[1]	95% CI	
BMI change (kg/m^2/y)						
Total dietary fibre	ref	-0.010	-0.039 to 0.019	-0.020	-0.050 to 0.011	0.11
Fibre sources[2]						
Fibre from cereals	ref	-0.026	-0.055 to 0.002	-0.011	-0.041 to 0.019	0.52
Fibre from fruit	ref	-0.010	-0.039 to 0.019	-0.006	-0.037 to 0.024	0.76
Fibre from vegetables	ref	-0.012	-0.040 to 0.016	-0.015	-0.045 to 0.014	0.26
Fibre from potatoes	ref	0.022	-0.006 to 0.051	-0.000	-0.029 to 0.029	0.86
Fibre types						
Cellulose	ref	-0.002	-0.031 to 0.026	-0.015	-0.044 to 0.014	0.38
Lignin	ref	-0.020	-0.049 to 0.009	-0.007	-0.037 to 0.024	0.84
Pectin	ref	-0.016	-0.045 to 0.012	-0.025	-0.055 to 0.005	0.14
Soluble fibre	ref	-0.027	-0.055 to 0.002	-0.017	-0.047 to 0.012	0.36
Insoluble NCP	ref	-0.016	-0.045 to 0.012	-0.005	-0.035 to 0.025	0.52
Insoluble fibre	ref	-0.024	-0.053 to 0.004	-0.020	-0.051 to 0.010	0.16
Body weight change (kg/y)						
Total dietary fibre	ref	0.002	-0.076 to 0.080	-0.037	-0.119 to 0.045	0.21
Fibre sources[2]						
Fibre from cereals	ref	-0.064	-0.142 to 0.013	-0.013	-0.094 to 0.067	0.83
Fibre from fruit	ref	-0.027	-0.105 to 0.052	-0.017	-0.101 to 0.066	0.76
Fibre from vegetables	ref	-0.026	-0.103 to 0.051	-0.017	-0.097 to 0.063	0.66
Fibre from potatoes	ref	0.078	0.001 to 0.155	0.008	-0.071 to 0.087	0.83
Fibre types						
Cellulose	ref	0.013	-0.064 to 0.090	-0.029	-0.108 to 0.051	0.64
Lignin	ref	-0.045	-0.124 to 0.033	-0.030	-0.113 to 0.054	0.61
Pectin	ref	-0.028	-0.105 to 0.049	-0.056	-0.137 to 0.025	0.24
Soluble fibre	ref	-0.040	-0.117 to 0.037	-0.025	-0.106 to 0.056	0.66
Insoluble NCP	ref	-0.033	-0.110 to 0.045	0.000	-0.081 to 0.081	0.79
Insoluble fibre	ref	-0.043	-0.120 to 0.035	-0.038	-0.120 to 0.043	0.34
Waist change (cm/y)						
Total dietary fibre	ref	-0.007	-0.145 to 0.131	-0.061	-0.207 to 0.085	0.39
Fibre sources[2]						
Fibre from cereals	ref	-0.114	-0.252 to 0.023	-0.098	-0.242 to 0.045	0.14
Fibre from fruit	ref	-0.050	-0.189 to 0.090	0.077	-0.071 to 0.225	0.28
Fibre from vegetables	ref	-0.102	-0.239 to 0.035	-0.095	-0.237 to 0.047	0.25
Fibre from potatoes	ref	0.053	-0.083 to 0.189	-0.014	-0.155 to 0.127	0.96
Fibre types						
Cellulose	ref	0.034	-0.102 to 0.171	-0.053	-0.194 to 0.089	0.54
Lignin	ref	-0.098	-0.238 to 0.042	-0.042	-0.190 to 0.106	0.54
Pectin	ref	-0.087	-0.224 to 0.051	-0.002	-0.146 to 0.142	0.98
Soluble fibre	ref	-0.110	-0.247 to 0.027	-0.013	-0.156 to 0.131	0.88
Insoluble NCP	ref	-0.099	-0.236 to 0.039	-0.100	-0.244 to 0.044	0.14
Insoluble fibre	ref	-0.097	-0.235 to 0.041	-0.053	-0.198 to 0.093	0.46

Abbreviations: 95% CI: 95% confidence interval; ref, reference group; NCP, non-cellulosic polysaccharides.

[1]Model was adjusted for baseline age, sex, smoking (current, former, or never smoker), education (primary, low/intermediate, high education), alcohol (six categories: non-drinker, $0.1 \geq 4.9$, $4.9 \geq 15$, $15 \geq 30$, $30 \geq 60$, or >60g/d), carbohydrate, protein, fat, energy, and baseline BMI, body weight or waist circumference.

[2]The models for fibre sources were also adjusted for fibre from other sources.

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Discussion

In this prospective cohort study in an elderly Dutch population, the intake of total dietary fibre, dietary fibre from different food sources, and dietary fibre types were not associated with annual changes in BMI, body weight, and waist circumference. The inverse association between total dietary fibre and annual change in BMI was borderline significant.

The main strength of this study was the use of a new food composition table containing data on dietary fibre types. This will give ample opportunities in future research to study associations between dietary fibre types and disease outcomes in observational studies. Up until now, studies have been limited to the intake of total dietary fibre and fibre sources. Studying fibre types instead, as done in the present study, is of interest as fibre food sources comprise mixtures of different fibre types. In randomised controlled trials, different fibre types have been shown to differently affect body weight (18, 19), yet, these trials are limited due to their relative short duration. The new food composition table enabled us to examine associations between fibre types and changes in measures of obesity in a population-based prospective cohort study with detailed information on potential confounders.

However, there were also limitations. Measurement errors may have occurred for energy intake. Energy intake under-reporting is a common phenomenon, and usually it is greater among participants with higher BMI, among women, and among participants who are weight conscious (48). In the present study, participants were excluded if the ratio of energy intake and estimated BMR was <1.2, which is the energy intake minimally required to live (23). With increasing baseline BMI, participants tended to under-report their energy intake more frequently. Although BMR was estimated, as data on energy expenditure were not complete, the exclusion of energy under-reporters resulted in more reliable findings. Further, interpretation errors may occur when comparing our results from an older study population with results in other studies. Weight gain is a chronic process that occurs mostly during early adulthood. During the later years of life (60+ y) height declines and weight gain tends to level off and even decline, whereas the amount of body fat increases and is redistributed towards visceral fat (49). In an elderly population body weight change and BMI change may underestimate adiposity, and waist change may be a more important predictor of adverse health risks (49, 50). Before definite conclusions about the association between fibre types and BMI can be drawn, the associations should be studied in younger populations as well.

The modest inverse association between total dietary fibre intake and BMI change are comparable to observations in larger populations. In a large prospective cohort study, a 10.0 g/d higher total fibre intake was significantly associated with an annual weight change of -39 gram, and an annual waist circumference change of -0.08 cm/y (3). Although not significant, the findings from our study were comparable; we found that an 8.0 g/d higher total fibre intake was associated with an annual waist change of -0.06 cm/y, and an annual weight change of -37 g/y in a population with an unstable height. Moreover, two other large prospective studies showed that for a 20 g/d higher total dietary fibre intake, weight gain was 1.18 kg lower over 8 y of follow-up (4), and for a 12.3 g/d higher total

dietary fibre intake, weight gain was 1.52 kg lower over 12 years of follow up (5). These findings suggest that a higher fibre intake may result in modest, though relevant changes in BMI, body weight and waist circumference.

In contrast to our hypothesis, none of the fibre food sources and fibre types were significantly associated with a change in BMI, body weight, or waist circumference in our study. Different associations were hypothesized, as within a fibre food source (e.g. apple vs. banana) dietary fibre comprises of a heterogeneous range of fibre types (29), and randomized clinical trials showed different effects of fibre types on body weight (19). There are at least few reasons why no associations were found between fibre types and BMI, body weight, or waist circumference.

First, the fibre types we studied differed from the fibre types having body weight lowering effects in randomized clinical trials. A systematic review indicated that specifically the fibre types dextrins, marine polysaccharides, chitosan, and fructans were able to decrease body weight (19). However, in the intervention studies as reviewed, these fibre types were not consumed as natural foods, but as isolated fibre in dosages that do not occur in a normal dietary pattern. Plausible mechanisms of action of viscous fibres, such as marine polysaccharides, are entrapping or binding nutrients in the intestinal content, and slowing down nutrient uptake or lower energy digestibility (51, 52). Fermentable fibres, such as dextrins and fructans, may affect body weight regulation via fermentation products as short chain fatty acids, that have been related to a reduced appetite and a reduced body weight (53, 54). As pectin is generally considered to be viscous; soluble fibre is generally considered to be fermentable; and cellulose is generally considered not viscous and not fermentable, the different fibre types in our study were hypothesized to have different effects.

Second, the new food composition table with fibre types may be limited by the use of a range of references using different analytical methods for measuring fibre types. Systematic differences between the analytical methods may have led to overestimations of the fibre types measured with Englyst or Southgate type methods. However, until there is an agreed and validated AOAC method that can be used to generate food composition data (45), we believe that our food composition table with fibre types is as accurate as is currently possible.

Last, although the values for fibre types in the food composition table were estimated as accurate as possible, even within dietary fibre types different properties may occur. A good example is pectin. Pectins comprise heterogeneous molecules that can vary with the food source and extraction conditions. Variation in molecular weight and degree of esterification can, as a result, lead to differences in solubility, viscosity, and fermentability within the fibre type (55). If the properties of dietary fibres are underlying to the associations with BMI, body weight, and waist circumference, then the possible variability of properties within fibre types may explain why we did not find associations.

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In conclusion, this study in a cohort of elderly Dutch participants indicates that intake of total fibre, fibre sources, and fibre types is not associated with change in BMI, body weight, or waist circumference. As these observed associations may be limited due to the older age of the study population, more prospective studies on younger populations are needed before definite conclusions can be drawn.

Funding

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7

General Discussion

The objective of this thesis was to explore the effects of different dietary fibre classes on appetite, and its underlying mechanisms. Acute and long term effects of dietary fibre classes were investigated by diverse study designs comprising a systematic review, three intervention studies and an observational study. In this chapter, first a short overview of the main findings of the research will be given. This is followed by a discussion of the results in the view of the used methodology and in perspective to other studies. This chapter will conclude with implications and suggestions for further research.

Overview of the main findings

The literature review of studies in acute settings showed that dietary fibres with viscous properties increased satiety and lowered subsequent energy intake more frequent than fibres without viscous properties. Furthermore, fibre consumed in a liquid food matrix increased satiety and lowered subsequent energy intake more than fibre in a solid food matrix **(chapter 2)**. In an intervention study we showed that solid foods containing a high-dose of gel forming fibre induced earlier satiation, but did not affect satiety **(chapter 3)**. We showed that the earlier satiation was probably mediated by the increased time that was needed to consume the product and not by a slowed down gastric emptying rate. In the same study solid foods containing bulking, viscous, and low-dose gel forming fibre did not affect satiation or satiety. In a successive study we observed that foods with gel forming fibre increased satiety compared to a control food **(chapter 4, 5)**, whereas foods with bulking and viscous fibre did not affect satiety **(chapter 4)**. The study also showed an increase in satiety when gel forming fibre was consumed hydrated as a gel, compared to when the same fibre was consumed as capsules or hydrated as a liquid. Processes that may explain these differences in satiety are a higher test food viscosity and slowed down gastric emptying rate **(chapter 4)**.

In acute settings, our findings indicate that fibres with viscous and gel-forming properties induce earlier satiation and increased satiety. The findings also suggest that fibres with viscous and gel-forming properties are more effective when they are present in liquid food matrices. The effects on satiation and satiety may be mediated by increased oro-sensory exposure and a slowed down gastric emptying rate.

With respect to longer term effects, the literature review showed that in general dietary fibre reduced energy intake and body weight. However, not all fibre types seemed to be equally effective. The changes in long term energy intake and body weight could not be associated with viscosity, solubility or fermentability of the fibre, nor with food matrix properties **(chapter 2)**. In an intervention study we found that consuming a gelled fibre for two weeks persistently increased satiety compared to a gelled non-fibre control, but did not reduce energy intake nor body weight **(chapter 5)**. In a cohort of elderly Dutch men and women the intake of total dietary fibre, dietary fibre from food sources and dietary fibre types were not significantly associated with a reduction in body weight or waist circumference. Although, in general inverse associations where observed **(chapter 6)**.

Methodological considerations

Before interpreting the main findings and discussing them in perspective to other studies, it is important to reflect on the methodology that was used in this thesis. This section will discuss the different study designs and outcome measures.

Study design

The research described in this thesis comprises a broad range of study designs. We performed a systematic review (chapter 2), three intervention studies (chapters 3,4,5) and one observational study (chapter 6). Moreover, the outcome measures varied per study; we studied satiation (chapter 3), satiety (chapter 2,4,5), energy intake (chapter 2,5) and body weight (chapter 2,6). To our knowledge, the extensive literature review was the first review that systematically and quantitatively summarized all available intervention studies relevant to the effects of dietary fibre classes on satiety, energy intake and body weight. The review generated new hypothesis which were tested in the subsequent intervention studies. For the observational study a new food composition table comprising dietary fibre types was compiled. This allowed us to study the long term effects of different dietary fibre classes on body weight.

The primary purpose of the three intervention studies was to study the effects of dietary fibre classes on appetite and underlying mechanisms, while holding all other factors constant (1-3). The studies had randomized crossover designs and included homogeneous populations of lean (BMI 18.5-25 kg/m^2), healthy young men or women who were unrestrained eaters and in energy balance (4, 5). The study in chapter 4 was strictly controlled: the subjects had to follow dietary guidelines starting two days before a test day, they had to consume a standardized meal on the evening before the test day, and they had to stay at the laboratory on the test day itself. On the test days subjects followed a strictly controlled test protocol. The studies in chapters 3 and 5 were done in semi-real life settings. These studies also followed controlled protocols, but the complex nature of eating behaviour was let free. This was done by distracting the subjects from visual and weight cues (6), by watching a movie (chapter 3), and by allowing to consume the test foods at home (chapter 5). Despite measuring energy intake at the laboratory, subjects could make their own spontaneous choices. The population based observational study in chapter 6 was not controlled. This study may be limited by measurement errors and uncontrolled confounding. However, a major strength of a study like this is that the results can be easily extrapolated to the general population, as the cohort represents the real-life situation.

Outcome measures

Three main behavioural outcomes were studied in this thesis: satiation, satiety and energy intake. As defined throughout the thesis, satiation is the process that brings an eating occasion to an end, and defines meal size. In real life, most eating occasions are terminated through environmental and cognitive factors such as portion size (7), variety of available foods (8), and time to the next meal (9). Similar to other studies (10-12), we measured satiation through the measurement of

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ad libitum intake from an unusually large portion of test foods under standardized conditions in a cinema. We standardized for personal factors such as satiety state, and for environmental factors such as presence of others, level of distraction and time to eat (13). Zijlstra et al. showed that, when replicating a free-living study in a laboratory setting, absolute intakes were different, but the changes in intake were very similar (11). Based on this research, it is likely that with different test foods and under different conditions absolute intakes may have been different. We, however, believe that our semi-real life setting was appropriate to study the satiating effects of test foods different in fibre content.

Throughout this thesis appetite was measured by satiety ratings (i.e. hunger, fullness, desire to eat and prospective intake) and by subsequent energy intake. These measures are considered the golden standards for measuring effects on appetite (13). Despite that subjective satiety and food intake are related, food intake does not always reflect satiety. This deviation depends on environmental and cognitive factors, that include study design factors such as the time interval between preload and test meal. In chapter 4, energy intake was measured 3h after the preload. At that time, for each test condition hunger ratings were high and approximately back at baseline level, leaving no differences between the test conditions. The action of the preload may have been decayed before the test meal was presented, which may have resulted in a failure to detect a difference in energy intake (1).

In acute studies, energy intake is generally measured by providing ad libitum test meals. Longer term studies, however, typically use methods varying from food records (e.g. weighed food record, estimated food record) to food recalls (e.g. 24h food recall, food frequency questionnaire). These methods are prone to under-recording and under-eating (14, 15). Under-recording can be due to failure to record all food items consumed, or due to underestimating the amounts consumed. Under-eating occurs when respondents eat less than required to maintain a stable body weight. In our longer term intervention study (chapter 5), we therefore chose to measure energy intake by *ad libitum* meals consumed for three consecutive days. This method appeared to be successful in measuring energy intake, as the subjects' energy intake agreed with known habitual intakes in a comparable Dutch population (16). In the observational study (chapter 6), energy and dietary fibre intakes were measured with a semi-quantitative Food Frequency Questionnaire. Validation of the semi-quantitative Food Frequency Questionnaire showed that it was an appropriate tool to rank the participants according to their energy and total fibre intake (17). This property makes the data applicable for epidemiologic studies. However, the energy and fibre intakes may not be directly comparable to intakes as measured by *ad libitum* test meals.

In contrast to energy intake, body weight is a cheap and easy measure and has a high internal validity when measured according to a standardized protocol (18). Assuming that a sustained reduction of energy intake is causally related to a reduction in body weight, an important limitation of measuring body weight as an outcome in intervention studies is the required study duration. As the study in chapter 5 was limited to 16 days, which is too short to expect differences in body weight (19), it was focused on satiety and energy intake. We think that, at present, available studies on body weight

better reflect long term effects of fibre intake than available studies on energy intake. This is due to a greater number of studies and the high internal validity of measuring body weight.

Markers for underlying mechanisms

Different markers were used to investigate the role of sensory signals. Apart from assessing sensory signals such as taste, odour, texture, and palatability with questionnaires, actual eating time per test food unit was measured by video recording (chapter 3), difficulty to eat was rated after test food intake (chapter 4), and actual eating time of the test food was assessed by an independent consumer panel (chapter 5). We believe that the present markers are valid and according to state of the art methodology. However, to further elucidate how and which sensory signals affect satiety, additional research is warranted.

As a marker for gastric signals we measured gastric emptying rate by non-invasive ^{13}C-breath tests. Research has shown that gastric emptying measured by ^{13}C-breath tests correlates very well with radioscintigraphy, the golden standard (20, 21). A limitation, however, of adding ^{13}C-isotopes to test foods, is that the ^{13}C-breath test is not fully validated for intragastric influences as ^{13}C-marker distribution (22). Fibre properties and phase separation could therefore lead to inhomogeneous emptying of the ^{13}C-marker and result in misinterpretation of gastric emptying measurements. An example is the surprising finding for the fibre test foods consisting of two liquids (chapter 4). The combination of the slow gastric emptying rate and the quick rise in plasma glucose concentrations suggests that inhomogeneous emptying took place. As suggested by Delzenne et al., (23) it would be of high interest to study the effects of dietary fibre in the stomach by means of advanced non-invasive techniques. For example, magnetic resonance imaging (MRI) can be used as a non-invasive method which has been validated for measurement of gastric volumes, gastric emptying, and gastric contractile activity for liquid and solid meals (24, 25).

The nutrient signals that were measured as markers for underlying mechanisms were postprandial glucose and insulin responses and fasting glucose and insulin concentrations. Gastro-intestinal peptides, such as ghrelin, GLP-1 and CCK were not included in the study designs in this thesis. To date, concentrations and changes in gastrointestinal peptides could not be related to satiety in a way that they can explain satiety sensations (26-28). However, gastrointestinal peptides may help understanding the mechanisms by which different dietary fibre classes act on satiety.

Dietary fibres and acute effects on appetite

Dietary fibres and satiation

Cereals, vegetables, fruits and other foods naturally rich in dietary fibre contain, by definition, a mixture of different dietary fibres. In general, fibre rich foods have a high water content, a low energy density (29) and have a more rough texture than foods low in fibre (30). Earlier studies have shown that dietary fibre content in natural foods is inversely associated to eating rate (10), and that dietary fibre content in natural foods is positively associated with earlier satiation (31).

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Moreover, independent of dietary fibre content, earlier studies showed that lower palatability, increased meal volume, and increased time to eat foods are also associated with earlier satiation (10, 29, 31, 32).

Complementary to the available research on foods naturally rich in dietary fibre mixtures, the study in chapter 3 was the first to explore the effects of dietary fibres with different physico-chemical properties on satiation. The results showed that fibres with different properties may have different effects on satiation. Dietary fibre with gel forming properties induced earlier satiation, whereas fibres with bulking or viscous properties did not induce earlier satiation. The effect of gel forming fibre on satiation was mediated by both increased eating time and reduced palatability, and probably not by gastric emptying time. The effect of the increased eating time was independent of palatability.

The effect of increased eating time on earlier satiation is a phenomenon that has been described before, e.g.(10, 11, 33, 34). As few studies were done on solid foods, this effect has been primarily related to beverages. For solid foods it was hypothesized that within food categories texture differences are generally very subtle, and therefore result in only small changes in oral processing time and eating rate (10, 12). In our study the gel-forming fibre significantly increased eating time. The alginate may already have started thickening while chewing due to presence of water and divalent cations from saliva (35). In this study we showed that solid foods with added dietary fibre induced earlier satiation, which may have been mediated by increased eating time.

What should be pointed out as well is that none of the dietary fibres induced later satiation than the low-fibre control food. This finding confirms that meal volume has a larger effect on meal termination than energy content (36, 37). Adding fibre to a meal lowers energy content and by ingesting a constant meal volume, total energy intake may be reduced. These results suggest that fibre types that are easily processed in foods and do not affect texture or palatability, may reduce energy density and therefore affect total energy intake.

Dietary fibres and satiety

Foods naturally rich in dietary fibre mixtures have been found to increase satiety by increased meal volume, and increased time to eat foods (29, 31). However, for single types of dietary fibre, such as alginate or guar gum, intervention studies have resulted in conflicting findings (38-41). To better understand these conflicting findings, we performed a literature review on fibres with different properties (chapter 4). This systematic exploration showed that both the chemical properties of the fibre, as well as the food matrix in which the fibre is provided may affect satiety. Few other studies also systematically assessed effects of fibre properties on satiety. Lyly et al. showed that post-meal satiety was enhanced by the addition of a high viscous beta-glucan to a beverage when compared to a low viscous beta-glucan. The effect did not change by changing the fibre dosage or the energy content of the beverage (42). Hoad et al. demonstrated a graded increase of satiety with increasing preload beverage viscosity by guar gum and different types of alginate (43).

Together with the literature review, these findings suggest that dietary fibres with thickening properties increase satiety. This hypothesis, however, could not be confirmed in our intervention study (chapter 4). We demonstrated that the fibre with viscous properties did not affect satiety, whereas the fibre with gelled properties did increase satiety. These results may be explained by the viscosity of the test food. Studies that found effects of viscous fibre on satiety generally provided test foods with viscosities ranging from 1.5 Pa.s to 56 Pa.s (42-48). In our study, test food viscosity was 1.7 Pa.s for the viscous fibre, and 3.9 Pa.s for the gelled fibre. Thus, our viscous test food had a viscosity at the lower end of the effective range. It may be that minimum levels of viscosity in the test food are required to affect satiety.

Moreover, the findings from the literature review also suggest that different types of food matrices differently affect satiety. It was suggested that fibre in a liquid food matrix increased satiety more than fibre in a solid food matrix. However, in the intervention study (chapter 4) we demonstrated an interaction between the liquid food matrix and thickening of the fibre. A gel forming fibre was provided in three different conditions: 1) unhydrated, 2) hydrated and not thickened, and 3) hydrated and thickened. In the first two conditions satiety did not increase, whereas satiety increased when the fibre was hydrated and thickened. This suggests that to increase satiety, fibres with thickening properties should be hydrated and thickened.

This new hypothesis was tested by re-analysing the data from the review (chapter 2). Because many studies did not explicitly characterize their fibre intervention, we made the following assumptions. Hydrated fibre was defined as a soluble fibre mixed with a drink and stirred or heated before ingestion. Unhydrated fibre was defined as soluble fibre consumed as capsules or included in foods with low water content. Studies with unclear fibre hydration levels were excluded, this were for example studies that provided fibre in sausages (49) or vegetable patties (50). After re-analysis, all soluble fibres that were hydrated before consumption (n=26) reduced hunger with about 7.6% over 4 h, and fibres that were unhydrated (n=12) resulted in no change in hunger. Subsequently, the findings were narrowed down to all soluble fibres with viscous properties. When these viscous fibres were hydrated (n=19), hunger was reduced with about 9.4% over 4 h, whereas unhydrated viscous fibres (n=10) resulted in no change in hunger. These new findings, in combination with the results from chapter 4, confirm that hydration in combination with thickening properties are essential properties for satiety increasing effects in an acute setting. The new analysis also revealed that soluble but not viscous fibres lowered hunger with about 0.8% over 4 h, and insoluble fibres lowered hunger with about 2.4% over 4 h.

Underlying mechanisms

Our studies showed that dietary fibre types that were hydrated and thickened in the food matrix or during oral processing induced earlier satiation and increased satiety. The thickening may be induced by either gel forming or viscous properties. Thickening likely affects sensory signals, but may also affect gastric and other signals further down in the gastrointestinal tract, as we showed that a reduced gastric emptying rate was associated to increased satiety (chapter 4).

Sensory signals

An increase in sensory signals after an increased test food viscosity may have mediated earlier satiation (chapter 3) and increased satiety (chapter 4). Earlier research showed that increasing sensory signals by increasing oral exposure time may lead to earlier satiation and a increased satiety response (32, 51). For example, Zijlstra et al. showed that a higher eating rate resulted in a higher total food intake, whereas standardizing eating rate resulted in a similar total food intake for a viscous and liquid test food (11).

Another sensory signal that may have affected our findings is palatability. Generally, foods high in dietary fibre are lower in energy density, and foods lower in energy density are associated with a lower palatability (29, 31). In accordance with earlier research (9, 52), we found that palatability was partly responsible for the earlier satiation (chapter 3). Still, after statistically adjusting for palatability, the association between gel forming fibre and earlier satiation persisted. This indicates that there likely is an independent effect. In our studies on satiety (chapter 4 and 5), palatability could not be separated from other sensory signals such as difficulty to eat. However, earlier research has shown that effects of palatability on subsequent satiety are unlikely (9, 52). We therefore believe that it is unlikely that the difference in palatability affected our findings.

Cognition may have also played a role in the stronger increase in satiety after consuming foods with increased viscosity. Humans may associate foods that provide more sensory signals as foods that are higher in nutrient density. In case of a high nutrient dense food, consumption can be less while still achieving an appropriate ingestion of nutrients. Therefore, foods providing more sensory signals may lead to earlier satiation (53, 54).

Gastric signals

In agreement with earlier research (43, 48), we demonstrated that gel forming fibre that is hydrated in a liquid food matrix may increase satiety by decreasing gastric emptying rate (chapter 4). Whereas non-dietary fibre thickening agents are generally broken down by the presence of salivary amylase and digestive enzymes, dietary fibres remain mostly intact at arrival in the stomach (55). A slower gastric emptying rate enhances gastric mechanoreceptor stimulation and gastric satiety signals, which can affect satiety. The processes that lead toward a reduced emptying rate are not yet clear, but may be due to the more difficult movement of the meal through the stomach, due to the presence of other nutrients (56, 57), or due to the 'ileal brake'. The ileal brake is a negative feedback mechanism which inhibits gastric emptying and small intestinal transit when undigested nutrients reach the ileum (58).

Interestingly, we found that gel forming fibre in solid foods induced earlier satiation, but accelerated gastric emptying rate. Earlier research on gastric emptying of high-fibre solid foods reported contrasting findings. After adding dietary fibre some studies observed delayed emptying (59, 60), but also accelerated gastric emptying was reported (61). The differences may be due to the different mechanisms by which liquid and solid foods are emptied. The emptying of foods from the stomach usually starts immediately with liquids, whereas solids are emptied when they have been processed

into sufficiently small particles (62, 63). A study in dogs observed that the size of solid food particles that emptied from the stomach increased after adding fibre. This led towards a reduced nutrient absorption in the intestine (64). An increased particle size may explain an increased emptying rate for fibre supplemented solid foods, but how this occurs remains to be elucidated.

Meal viscosity has relatively small effects on gastric emptying rate. Marciani et al. showed that a 1000-fold increase in viscosity caused reductions in emptying rate by a factor of 1.3 (48). At arrival in the stomach, high viscous meals are rapidly diluted to minimize delay in gastric emptying (65). A second process by which dietary fibres may slow down gastric emptying is by forming gels in the stomach. Gel forming fibres, such as pectins and alginates, may form gel lumps in the stomach under specific circumstances. For example by acid secretion in the stomach or by the presence of multivalent ions, such as calcium from foods (43). Earlier studies showed that alginates that formed gel lumps in the stomach increased satiety in a dose-responsive manner (66, 67). These studies suggest that gastric processes may affect satiety independently of oro-sensory exposure. In our studies (chapter 3 and 4) we were not able to demonstrate consistent effects on gastric emptying after the interventions that were expected to form gels in the stomach. We therefore also suggest that the change in thickening may not have been large enough to slow down gastric emptying rate.

Nutrient and hormonal signals
Postprandial glucose responses, but more clearly postprandial insulin responses differed after consumption of the different fibre types. Earlier studies showed that to elicit an effect on glucose and insulin responses after consuming dietary fibre, a sufficiently high viscosity should be exerted (68-70). For example, compared to non-viscous hydrolysed guar gum, high-viscous guar gum blunted glucose and insulin responses (70). An explanation may be that postprandial blood glucose and subsequent insulin concentrations are largely determined by the rate at which nutrients are delivered to the proximal small intestine (71). A slower delivery may be due to a slowed down gastric emptying, but may also be due to entrapment of nutrients in the small intestine by the gel. Compared to non-gelled meals, nutrients that are entrapped in a gel lump will be available further along the intestinal tract (43), and may blunt the glucose and insulin responses.

It is, however, unclear whether these effects are also present in different food matrices. Recently, Juvonen et al. studied postprandial signals after ingestion of proteins (72) with a study design comparable to ours (chapter 4). They studied proteins in three different conditions: liquid, viscous and as a rigid gel. Comparable to our findings, the rigid gel increased satiety, and insulin response was blunted compared to the liquid and the viscous proteins. They also showed that after consuming the rigid gel postprandial GLP-1 and CCK responses were blunted (72). These results suggest that it may be the firmness of the food that modulates the postprandial hormonal signals. This was confirmed by a subsequent study that provided the same proteins to a more complex test food that resulted in smaller texture differences. Compared to the first study all findings were blunted or diminished, and were therefore associated to the texture differences (72, 73). Findings for

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dietary fibre may be different due to their resistance to digestive enzymes, but this remains to be elucidated.

Although dietary fibres may affect glucose and insulin response, it is unclear whether these metabolic responses are causally related to satiety. Earlier work showed that satiety could, to a certain level, be correlated to differences in insulin dynamics (27, 28, 74), but not to glucose (27, 74). For gastrointestinal peptides as ghrelin, GLP-1, CCK, PYY, research has not been able to correlate them to satiety in a way that they can explain satiety sensations (23, 28, 75).

In conclusion, dietary fibre types that are hydrated and thickened in a food matrix or during oral processing induce earlier satiation and increased satiety. The thickening may be induced by either gel forming or viscous properties and it may be that minimum levels of thickening are required to affect satiety. Under specific circumstances, gastric processes can affect satiety independently of oro-sensory exposure.

Dietary fibres and long term effects on appetite

For acute settings it was shown that dietary fibres with thickening properties and hydrated in a liquid food matrix can induce earlier satiation and increase satiety. These findings cannot be extrapolated to long term settings as such (76, 77). Dietary fibres may elicit physiological effects other than discussed so far and adaptation through compensatory mechanisms may occur (19). In the following section the effects of different dietary fibre classes after repeated exposure will be discussed.

Dietary fibres, energy intake and body weight

Although it was not confirmed by our observational study in an elderly population-based cohort (chapter 6), other prospective (78-82) and cross-sectional cohort studies (83-88) have shown that a higher intake of total dietary fibre is associated with lower body weight and waist circumference. To account for different fibre types, in a number of these cohort studies fibre intake was classified by food source, such as fibre from cereals, fruits, vegetables or legumes. Two large prospective studies (78, 79), and several cross-sectional studies (86, 87, 89, 90) showed that fibre from cereals is consistently associated with body weight changes, whereas other fibre sources, such as fibre from fruit and vegetables result in inconsistent associations. An explanation for the inconsistent associations may be the heterogeneous composition of dietary fibre types in the different food sources. For example, of the total fibre content in fruits, pectin concentrations range from 5% in pineapple to >40% in oranges and cantaloupe, and of the total fibre content in vegetables, cellulose concentrations range from 25% in green beans to >50% in mushrooms and pumpkin (91).

To study the effects of different dietary fibre classes in an observational study, we compiled a new food composition table that specifies for types of dietary fibre (chapter 6). This table allowed us to examine the associations between the intake of both dietary fibre from different food sources and dietary fibre types, and changes in body weight, BMI and waist circumference in a cohort of elderly

Dutch men and women. We found that intakes of fibre from food sources and fibre types were not significantly associated with BMI and body weight. Although, the inverse association between total dietary fibre and annual change in BMI was borderline significant. The lack of significant findings may have been limited by the older age of the study population.

Underlying mechanisms

Sensory signals

Whereas in acute settings fibres with thickening properties increase satiety, it is unclear whether the effects of thickening fibres persist after repeated exposure. None of the available studies on thickening fibres was designed to compare satiety after single and repeated exposure (92-94). With respect to energy intake and body weight, fibres with viscous properties were not found to affect energy intake or body weight (chapter 2). We showed that for viscous fibres energy intake was lowered in 50% of the studies (n=12), and body weight was lowered in 53% of the studies (n=45). These percentages do not confirm an effect on energy intake or body weight. However, as was shown for acute effects, the method of consumption may alter the findings. Therefore, for energy intake and body weight we also re-analysed the review data. The methods were similar to the methods described for satiety. The new results show that the viscous fibres were hydrated in a liquid matrix in three studies (92-94), of which in two studies energy intake was lowered (93, 94). Body weight was lowered in 43% of studies with hydrated, viscous fibre (n=21). These findings do not suggest additional effects of viscous fibres when they are hydrated in a liquid matrix. It should, however, be noted that in 18 studies on body weight the fibre was provided as powder to be ingested with water. A short time interval between mixing with water and ingestion may have led to insufficient increases in viscosity or gel strength, which is required to lead to an increased oro-sensory exposure, a reduced gastric emptying rate or a reduced nutrient absorption.

Other studies have shown that an increased oro-sensory exposure time may have persistent effects on satiety and energy intake over time (33, 95, 96). The studies showing this were, however, unrelated to dietary fibre. Hogenkamp et al. created an increased oro-sensory exposure time by thickening with starch (95) and by altering the mode of consumption (33). Increased oro-sensory exposure led to a constant earlier satiation over periods of 5 (95) and 10 days (33). DiMeglio et al. examined energy intake compensation after consuming matched solid or liquid foods for four weeks. They clearly showed that energy intake compensation took place only after consuming the solid food, which is likely mediated by a higher oro-sensory exposure time (96). Although these studies suggest that effects of increased oro-sensory exposure may persist over time after repeated exposure, research is warranted to study the effects of consuming fibres with thickened properties over longer time periods.

Gastric and nutrient signals

Compensatory mechanisms may have occurred in our study on the persistence of effects on satiety and energy intake after repeated ingestion of a gelled fibre (chapter 5). The small increase in satiety persisted after repeated ingestion, whereas the reduction in energy intake did not. Possible compensatory mechanisms after repeated ingestion of dietary fibre comprise unconscious

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learning processes and physiological adaptation related to gastric emptying, nutrient absorption or fermentation. After repeated ingestion of a food, the central nervous system may associate the sensory attributes of a food with its post-ingestive metabolic effects and its energy content (97). When tasting a food again, the individual may link the sensory signals to the satiety perception and adjust the amount consumed during the meal (98). This unconscious learning may explain why the gel forming fibre increased satiety, but not reduced long term energy intake.

Although limited research is available, it was suggested that a reduction in gastric emptying time may persist over time (99). A few well-designed studies on alginate, a gel forming fibre, confirm that the effects may persist. So far, studies on alginate concluded that the effect on satiety is strongly dependent on conditions that include alginate type and the food matrix, i.e. to increase satiety, hydrated, strong gelling fibre with added calcium is required (100, 101). A few studies were done with alginate under the right conditions. These studies observed a 7% (102), and a 10% (103) reduction in energy intake after 1 week of daily alginate supplementation. The only study on body weight change observed a greater weight loss after 12 weeks of daily alginate supplementation compared to control (104). Based on these studies on alginates, it can be speculated that a reduced gastric emptying rate or nutrient absorption persists over time. However, due to the very limited number of studies, and possible interaction with fermentation effects (100), additional research is necessary.

Colonic and metabolic signals
It is not yet fully understood how fermentation of dietary fibre can affect satiety, energy intake and body weight (105). Generally, fermentation of dietary fibres in the large intestine may alter the growth of specific gut microbiota and promote short chain fatty acid production (106, 107). Short chain fatty acids have been related to increased satiety and reduced body weight (108, 109). In the literature review we observed that among fermentable fibre types, effects of fermentation may be different on energy intake and body weight. We showed that in 67% of the studies with fermentable fibre (n=22) energy intake was lowered and in 56% of the studies with fermentable fibre (n=36) body weight was lowered. Contrarily, in our own intervention study (chapter 5), we found that the increase in hydrogen production did not persist over time. Several explanations can be given for different effects among different fermentable fibres on energy intake and body weight. First, different fibre types may result in different fermentation patterns, for example in fermentation speed and fermentation products (110, 111). Second, adaptation of bacterial metabolism towards efficient fermentation pathways may occur over time (112). Furthermore, a minimal fibre dosage may be necessary to induce subsequent changes in energy intake or body weight (113). To our knowledge, no studies are available that systematically compare the effects of different types of fermentable fibre. To understand the effects different fermentable fibre types have on energy intake and body weight, additional studies are warranted.

In addition to thickening and fermentable properties, dietary fibres that do not have these properties may also affect energy intake and body weight. This is supported by a re-analysis of the review data (chapter 2) for poorly soluble and poorly fermentable fibre, which comprised mainly studies on

wheat bran and chitosan. Energy intake was lowered in 5 out of 7 studies (71%) and body weight in 12 out of 14 studies (86%). These observations suggest that poorly soluble and poorly fermentable fibres may be effective in lowering long term energy intake and body weight. Besides its typical bulkiness, that increases the volume throughout the gastrointestinal tract without providing energy (114, 115), there may be several other processes by which poorly soluble and poorly fermentable fibres act. Poorly fermentable fibres may promote laxation, reduce transit time and increase stool weight (116-118). The fibres have a relatively low water holding capacity, but since they are very limitedly fermented they have an important role in retaining water in the stool (116). Additionally, this fibre class may also reduce the energy digestibility, for example by entrapping fat in the intestine, which is an often mentioned mechanism of action of chitosan (119). As poorly soluble and poorly fermentable dietary fibres comprise a large part of the fibre intake in a general population (chapter 6) (91, 120), this may be an explanation for the consistent inverse associations found for fibre from cereals and body weight (78, 79, 86, 87, 89, 90).

In conclusion, dietary fibres may decrease long term satiety, energy intake and body weight. The decreases could not be associated with viscosity, solubility, fermentability or with food matrix properties. It is still unclear whether oro-sensory exposure, gastric emptying time and fermentation properties elicited by dietary fibre affect long term appetite.

Implications and suggestions for further research

For local governments, a reason to set recommendations for dietary fibre intake was that higher intakes of dietary fibre have been associated with beneficial effects on health outcomes, such as obesity, heart disease and type 2 diabetes mellitus (121-123). Though, over the past number of years, nutrition scientists more and more acknowledge that the unique characteristics of each type of dietary fibre may determine its effects on health outcomes, such as the control of body weight (42, 122, 124).

In this thesis we explored the effect of different dietary fibre classes on appetite and its underlying mechanisms. Identification of fibre characteristics that determine the physiological effects is highly valuable as there are many types of dietary fibre, and new types of dietary fibre are continuously developed. From a scientist's point of view it is of high interest to understand the processes by which dietary fibre can affect appetite. From a food industry point of view it is valuable as this iden-tification may lead to development of new fibre ingredients and to solid substantiation of health claims. Up until now, the EFSA panel on dietetic products, nutrition and allergies, evaluated only one health claim on dietary fibre (i.e. glucomannan) and body weight as sufficiently established (125). Identification of the characteristics of dietary fibre that determine its physiological effects, aids to the substantiation and would save significant amounts of time and financial resources. As a consequence, this development is also highly valuable from a consumer point of view.

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This thesis is one of the first research projects that systematically studied the effects of dietary fibres on appetite, and its underlying mechanisms. Hence, many of the observations and suggestions need to be confirmed. In this section we will describe several suggestions for further research.

The different dietary fibre classes, as reviewed and explored in this thesis, were mainly based on physico-chemical properties that have been regularly assessed and published, such as viscosity, solubility and fermentability. An important constraint of many already published studies was that physico-chemical properties of the fibres were not, or limited reported, and therefore had to be estimated by us. For all future research on dietary fibre and appetite a thorough characterization of the fibres in terms of food properties and physico-chemical properties is recommended. Physico-chemical properties that may also be used to classify dietary fibres are water holding capacity, fermentation pattern and energy digestibility.

Although classification by physico-chemical properties seems promising, it should be kept in mind that physico-chemical properties are hardly ever static. For example as shown earlier in this thesis, viscosity of the fibre highly depends on the food matrix, but it may also depend on hydration rate, acidification in the stomach and intestinal conditions (126, 127). Another example is the characterisation of chitosan, which was defined by us as an insoluble fibre. However, under certain conditions (e.g. acidic environments) chitosan is soluble and should be classified as a soluble fibre. The methodology by which fibre characteristics are determined should agree with the hypothesised underlying mechanisms. Ideally, when tested in *in vitro* systems, physico-chemical properties should be measured mimicking different sites in the human body with human digestive enzymes, as the physico-chemical properties may differ depending on the site (116, 128).

Acute effects

We showed that in acute settings dietary fibre types that are hydrated and thickened in the food matrix or during oral processing induced earlier satiation and increased satiety. The thickening could be induced by either gel forming or viscous properties. In our study on satiation the fibres were provided in solid foods. The conclusions of this thesis, however, suggest that if the fibres would have been provided hydrated in a beverage (124), the subsequently larger contrasts in oro-sensory exposure would result in larger effects on satiation. It may even be that these test foods would then slow down gastric emptying rate and contribute to an earlier satiation. This hypothesis could be tested in further research.

Moreover, to elucidate the effects of fibres with thickening properties on processes related to both satiation and satiety, but other than oro-sensory exposure, a study design in which thickened non-fibres are compared with thickened fibres could be of high interest. Such study designs eliminate differences caused by oro-sensory exposure, which is a well-known process leading towards earlier satiation and a higher satiety response (32, 51). Such studies can reveal which physiological effects these fibres with thickening properties have on processes such as gastric emptying rate and nutrient uptake.

Although our results suggest that the acute effects of dietary fibre on satiety may be primary induced by the thickening of the food, there may be a possible threshold effect. It would be relevant to study whether there are minimum levels of viscosity affecting subsequent satiety. Moreover, some studies found that the composition and complexity of the food matrix may affect the outcomes (56, 57, 72, 73). To understand the effect of the food matrix of the dietary fibre on satiety, additional systematic studies are warranted.

Long term effects

Our research confirmed that repeated ingestion of dietary fibre may reduce long term energy intake and body weight. The changes could, however, not be associated with viscosity, solubility, fermentability or with food matrix properties.

Whereas in acute settings the effects of dietary fibre on satiety was likely induced by contrasts in oro-sensory exposure, in long term studies evidence for this phenomenon is scarce. Studies on repeated exposure to foods thickened with dietary fibre are therefore warranted.

After repeated ingestion of dietary fibre compensatory mechanisms may occur. The wide range of dietary fibre types may affect a range of physiological processes in the human body. To get a better view on the different mechanisms by which dietary fibres affect these processes, and to which extent these processes are related to appetite, more studies with a systematic approach are warranted. In the view of chapter 5, we suggest to systematically study isolated types of fibres with diverse properties in several study designs depending on the underlying mechanisms of interest. For example, to study the effects in the upper gastro-intestinal tract, a very interesting fibre type is methylcellulose. It is a fibre that is not fermented by microbiota, and it is available in viscous and non-viscous forms of which specific types can form a rigid gel at body temperature. On the other hand, to study the effects of fermentation, fibre types without viscous or gel forming properties but with large differences in fermentation patterns could be selected. These studies may include different study durations to assess whether and when compensatory mechanisms may take place.

Apart from internal signals, the regulation of food intake involves a range of external signals, such as the availability of foods, the presence of others, being dietary restraint, and prior beliefs about foods. Human studies measuring underlying mechanisms of appetite may be confounded by such external signals (129). Moreover, human studies may have restrictions in the experimental setup, such as dosage of the intervention products, study duration, and compliance of subjects to the study protocol. Currently, pigs are increasingly used as a model for human digestive function, as they are, like humans, omnivorous colonic fermenters (130, 131). Because of their resemblance in digestive function, pig models are of high interest to use for systematic assessment of the impact of dietary fibres on underlying mechanisms of appetite.

Whereas many observational studies found associations between total dietary fibre and fibre from cereal and body weight, we could not reproduce these findings in our observational study. As these associations may be limited due to the older age of the study population, more prospective

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studies on younger populations are needed before definite conclusions can be drawn. In addition, up until now observational studies have been limited to studying intake of total dietary fibre and fibre sources. Our new food composition table gives ample opportunities to study associations between dietary fibre types and other disease outcomes in observational studies.

Ultimately, much of the research on dietary fibre and appetite is targeted to contribute in weight management and to prevent overweight and obesity. There may be physiological and behavioural differences that affect satiation and satiety in lean and obese people. Gastric capacity (132) and gastrointestinal peptides (133) were suggested to differ between lean and obese people, but also eating rate (134) and hedonic responses to foods (135). It is therefore necessary that the effects of fibre supplementation are verified in groups representative for the target population.

Main conclusions

To explore the effect of different dietary fibre classes on appetite and its underlying mechanisms, the research described in this thesis focussed on both acute and long term effects.

In acute settings, we conclude that dietary fibre classes that are hydrated and thickened in a food matrix or during oral processing induce earlier satiation and increased satiety. The thickening may be induced by either gel forming or viscous properties and it may be that minimum levels of thickening are required to affect satiety. Under specific circumstances, gastric processes may affect satiety independently of oro-sensory exposure.

Regarding long term effects, we conclude that dietary fibre can decrease long term appetite, energy intake and body weight. The decreases could not be associated with the fibre classes viscosity, solubility, fermentability or with food matrix properties. Yet, it is unclear whether oro-sensory exposure, gastric emptying rate and specific fermentation properties elicited by dietary fibre affect long term appetite. The research indicates that after repeated intake of dietary fibre multiple underlying mechanisms play a role.

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7

Summary in Dutch (Samenvatting)

De term 'voedingsvezels' is een verzamelnaam voor diverse bestanddelen in plantaardig voedsel. Voedingsvezels zijn veelal koolhydraten die niet door verteringsenzymen in de dunne darm kunnen worden afgebroken. Voorbeelden van soorten voedingsvezels zijn: cellulose, pectine, guar gum en inuline. Onderzoek heeft laten zien dat het eten van meer voedingsvezels positieve effecten op de gezondheid kan hebben. Bijvoorbeeld een verbetering van de stoelgang, een verlaging van het cholesterolgehalte en kleinere schommelingen in de bloedsuiker- en insulinespiegel. Voedingsvezels lijken daarnaast een belangrijke bijdrage te kunnen leveren bij het voorkómen van overgewicht en obesitas, door een rol in de regulatie van de eetlust en voedselinneming. Diverse groepen voedingsvezels lijken verschillende effecten te hebben in de regulatie van eetlust, voedselinneming en lichaamsgewicht. Het doel van dit proefschrift was om te onderzoeken wat de effecten zijn van verschillende groepen voedingsvezels op de eetlust en de daarbij horende onderliggende processen. Hiervoor zijn directe effecten (één dosis voedingsvezel) en lange-termijn effecten (2 weken of langer dagelijks een dosis voedingsvezel) van verschillende groepen voedingsvezels onderzocht. Dit werd gedaan door middel van een literatuuronderzoek, drie experimenten en een observationele studie.

Hoofdstuk 2 beschrijft het literatuuronderzoek waarin 104 bestaande publicaties over het eten van voedingsvezels en de effecten daarvan op eetlust, energie-inneming en lichaamsgewicht op een systematische wijze met elkaar zijn vergeleken. De voedingsvezels werden gegroepeerd naar de soort voedingsvezel (b.v. cellulose, pectine en guar gum), de fysisch-chemische eigenschappen (viscositeit, oplosbaarheid en fermenteerbaarheid) en naar de vorm van consumptie (vast, vloeibaar of als supplement). De resultaten lieten zien dat een éénmalige dosis voedingsvezel de eetlust kan verlagen wanneer de vezels meer visceus zijn of wanneer de vezels in een vloeibare voedselmatrix worden geconsumeerd. Lange-termijn consumptie van voedingsvezels leverde gemiddeld een verlaging op van energie-inneming en lichaamsgewicht, waarbij enkele specifieke soorten voedingsvezels een sterker verband lieten zien. Tussen de fysisch-chemische eigenschappen van voedingsvezels, de vorm van consumptie van voedingsvezels en energie-inneming of lichaamsgewicht konden in het literatuuronderzoek geen verbanden worden aangetoond.

Vervolgens is in twee experimenten onderzocht of voedingsvezels met verschillende fysisch-chemische eigenschappen in voedsel (vergroten van volume, viscositeit verhogen en geleren) in verband konden worden gebracht met de eetlust tijdens de maaltijd (hoofdstuk 3) of na een maaltijd (hoofdstuk 4). **Hoofdstuk 3** liet zien dat de 121 proefpersonen 22% minder aten van koekjes met een hoge dosis gelvormende voedingsvezels, dan van de koekjes zonder toegevoegde voedingsvezels. Deze bevinding kon niet worden verklaard door een langzamere maaglediging. Wel hadden de proefpersonen significant meer tijd nodig om één koekje te eten. De inname van alle andere soorten koekjes (volume vergrotend, viscositeit verhogend, en een lage dosis gelvormend) verschilde niet van de koekjes zonder toegevoegde voedingsvezels. **Hoofdstuk 4** beschrijft het effect op de eetlust bij 29 proefpersonen na consumptie van een milkshake waaraan de verschillende soorten voedingsvezels waren toegevoegd. De resultaten lieten zien dat de milkshake met gelvormende vezels de eetlust significant verlaagde gedurende 3 uur na consumptie, vergeleken met de milkshake zonder toegevoegde vezels. Bij de milkshakes met volume vergrotende en viscositeit verhogende voedingsvezels

was dit niet het geval. De milkshake met gelvormende vezels was het 'dikste' product en werd door de proefpersonen beoordeeld als het moeilijkst om te eten. Daarnaast hadden de proefpersonen na consumptie van de milkshake met gelvormende vezels een langzamere maaglediging en een lagere bloedsuiker- en insulinespiegel. Hoofdstuk 4 laat ook het effect zien van verschillende vormen van consumptie van vezel op de eetlust. De eetlust van de proefpersonen was lager nadat de voedingsvezel werd geconsumeerd als een gel, vergeleken met wanneer de vezel werd ingenomen als capsules, of wanneer de vezel werd geconsumeerd nadat het was opgelost in een drank. De vezel geconsumeerd als een gel was het dikste product en werd door de proefpersonen beoordeeld als het 'moeilijkst' om te eten. Daarnaast hadden de proefpersonen nadat de vezel werd geconsumeerd als een gel een langzamere maaglediging.

Gebaseerd op het onderzoek zoals beschreven in hoofdstukken 2,3 en 4 concluderen we dat voedingsvezels de eetlust verlagen wanneer ze een voedingsmiddel dikker maken. De lagere eetlust komt waarschijnlijk door de dikte van het voedingsmiddel en de daardoor lagere snelheid waarmee het voedingsmiddel gegeten wordt. Daarnaast heeft de langzamere maaglediging mogelijk ook een rol.

Om beter te begrijpen wat de effecten van voedingsvezels zijn onafhankelijk van het effect van de dikte van het voedingsmiddel en de eetsnelheid, is een derde experiment uitgevoerd. Dit onderzoek wordt in **hoofdstuk 5** beschreven. Bij 32 proefpersonen werd onderzocht wat de effecten van gelvormende voedingsvezels op de eetlust waren, waarbij de dikte en de eetsnelheid van het vezelrijke voedingsmiddel en het controle voedingsmiddel zo veel mogelijk gelijk werden gehouden. Dit werd gedaan met een appelmoesachtig product. De proefpersonen aten de vezelrijke of controle voedingsmiddelen 16 dagen op rij. Na 1 dag bleek dat het vezelrijke voedingsmiddel de eetlust gemiddeld met 2% verlaagde en de energie-inneming gemiddeld met 5%. Na 16 dagen was de eetlust nog steeds 2% lager, maar de energie-inneming was weer gelijk. Er werden daarnaast geen duidelijke effecten gevonden op het bloedsuiker- en insulinespiegel en ook geen duidelijke effecten van fermenteerbaarheid van vezels in de dikke darm. Dit onderzoek liet zien dat buiten effecten van dikte van het voedingsmiddel en de eetsnelheid om, gelvormende voedingsvezels de eetlust en de energie-inneming kunnen verlagen, al zijn deze effecten klein. Het onderzoek liet ook zien dat de effecten niet blijvend hoeven te zijn: effecten op korte termijn kunnen op lange termijn verdwijnen.

Hoofdstuk 6 beschrijft een observationeel onderzoek naar de samenhang tussen de gebruikelijke consumptie van verschillende soorten voedingsvezels en een verandering in lichaamsgewicht. Dit werd gedaan door middel van een grote bestaande steekproef uit de Rotterdamse bevolking (de Rotterdam studie) bestaande uit 1.859 personen ouder dan 55 jaar. Bij deze groep mensen is de gebruikelijke voedingsvezel-inname (nagevraagd met een vragenlijst) vergeleken met de verandering in lichaamsgewicht over een periode van 6,4 jaar. Deze verandering in lichaamsgewicht werd weergegeven als body mass index (BMI). De vezelinname is daarnaast uitgesplitst in bronnen van voedingsvezels (granen, fruit, groenten en aardappelen) en soorten voedingsvezels (cellulose, lignine, pectine, oplosbare en onoplosbare vezels). Om de soorten voedingsvezels uit te rekenen

werd een nieuwe voedingsmiddelentabel ontwikkeld. De resultaten van het onderzoek lieten zien dat het verband tussen het meer consumeren van voedingsvezel en een kleinere stijging in BMI net niet significant was. Er werden geen significante verbanden gevonden tussen de consumptie van de verschillende bronnen van voedingsvezels (granen, fruit, groenten en aardappelen) en BMI, en tussen de consumptie van de verschillende soorten vezels (cellulose, lignine, pectine, oplosbare en onoplosbare vezels) en BMI.

Ten slotte geeft **Hoofdstuk 7** een samenvatting van de belangrijkste bevindingen, methodologische aspecten en de interpretatie van de bevindingen van de studies in dit proefschrift. Dit proefschrift is één van de eerste onderzoeksprojecten waarin op een systematische wijze werd gekeken naar de effecten van verschillende groepen voedingsvezels op de eetlust, en de daarbij horende onderliggende processen. De conclusie van dit proefschrift is dat op de korte termijn vooral voedingsvezels die een voedingsmiddel dikker maken de eetlust lijken te verlagen. Dit komt waarschijnlijk door de lagere snelheid waarmee een dergelijk voedingsmiddel gegeten wordt. Daarnaast spelen waarschijnlijk ook nog andere processen in het maag- en darmkanaal een rol. Op de lange termijn levert consumptie van voedingsvezels gemiddeld een verlaging op in energie-inname en lichaamsgewicht. Er werden geen specifieke verbanden gevonden met de door ons onderzochte groepen voedingsvezels. Verder onderzoek zal moeten uitwijzen welke processen onderliggend zijn aan de lange-termijn effecten.

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<div align="right">Anne</div>

About the author

Curriculum vitae

Anne Wanders was born on the 23rd of January 1981 in Didam, the Netherlands. After completing secondary school at Andreas Scholengemeenschap in Zevenaar, she started her studies in Nutrition and Health at Wageningen University. She obtained her Master's degree with a major in Dietary Behaviour and Disease Prevention and a minor in Epidemiology and Public Health. As part of her studies she conducted her internship on development of food preference, and increasing children's fruit and vegetable intake at the Department of Nutrition, University of Oslo, Norway. After obtaining her Master's degree in November 2005, Anne was appointed as a junior consultant at Foodstep, Wageningen. She performed quantitative and qualitative research within the food service area. In July 2007 she started as a junior researcher in a collaboration between VU University Amsterdam and Wageningen University. She coordinated a dietary intervention study on the effects of Conjugated Linoleic Acid, a trans fatty acid of animal origin, on lipid and lipoprotein levels. This work resulted in several high impact papers. In September 2008, she started her PhD research on dietary fibres and appetite, of which the results are described in this thesis. This PhD project was part of the strategic research programme 'Satiety and Satisfaction' of Wageningen University and Research Centre, with the aim to combat obesity in an integrated way by a collaboration between nutritional, food technological, communication and consumer sciences. Anne joined the educational programme of the Graduate School VLAG and she was involved in teaching and supervising students at the BSc and MSc level. She attended several (international) courses and conferences. At the Wageningen Nutritional Sciences Forum in 2009 she won the poster award, at the 2011 annual meeting of NWO nutrition she was nominated for the Foppe ten Hoor Award, and at the 2012 annual symposium VoedingNederland, she won her own session together with Dr. D Bolhuis. In 2012 she was selected for the European Nutritional Leadership Program (ENLP). Next to her PhD project, Anne performed intervention studies on the glycaemic index and satiating value of teff, the glycaemic index of palm sugar, and the glycaemic index of camel milk in collaboration with multiple research partners. Currently, she is appointed as a postdoctoral researcher at the Division of Human Nutrition in Wageningen.

List of publications

Publications in peer-reviewed journals

Brouwer IA, Wanders AJ, Katan MB. Trans fatty acids and cardiovascular health: research completed? Eur J Clin Nutr [In press, doi:10.1038/ejcn.2013.43]

Wanders AJ, Jonathan MC, van den Borne JJ, Mars M, Schols HA, Feskens EJ, de Graaf C. The effects of bulking, viscous and gel-forming dietary fibres on satiation. Br J Nutr. 2012 Jul 31:1-8. [Epub ahead of print]

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de Roos B, Wanders AJ, Wood S, Horgan G, Rucklige G, Reid M, Siebelink E, Brouwer IA. A high intake of industrial or ruminant trans fatty acids does not affect the plasma proteome in healthy men. Proteomics. 2011 Oct;11(19):3928-34.

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Submitted publications

Wanders AJ, Jonathan MC, Feskens EJ, , de Graaf C, Mars M. Pectin is not pectin: The effect of different physicochemical properties of dietary fibre on appetite.

Wanders AJ, Mars M, Borgonjen-van den Berg KJ, de Graaf C, Feskens EJ. Satiety and energy intake after single and repeated exposure to gel forming dietary fibre: post ingestive effects.

Rienks J, Wanders AJ, van Woudenbergh GJ, van Rooij FJ, Hofman A, Kuijsten A, Witteman JC, Franco OH, Feskens EJM. Intake of dietary fibre types and associations with change in BMI and waist circumference: results from a population-based prospective cohort study.

Overview of completed training activities

The Graduate School

VLAG

With the educational activities listed below the PhD candidate has complied with the educational requirements set by the Graduate VLAG (Food Technology, Agrobiotechnology, Nutrition and Health Sciences).

Description	Organisor and location	Year
Discipline specific activities		
Courses and workshops		
Masterclass Health Food Innovation: 'Research, Development and Claim Substantiation'	Nutrim/VLAG, Maastricht	2010
Sensory Perception and Food Preference	Graduate school VLAG, Wageningen	2011
Gut-Brain communications: 'A new dimension in food and health research'	ABS graduate school, Kuopio (FI)	2011
ILSI Europe Workshop on 'Satiety and appetite control claims: Getting it right for consumers'	ILSI, Brussels (BE)	2012
Pre-congress workshop SSIB: 'Measurement of gastrointestinal motility in humans'	ETH/SSIB, Zurich (CH)	2012
Conferences and meetings		
Wageningen Nutritional Sciences Forum	Division of Human Nutrition, Arnhem	2009
Symposium: 'Meer voedingsvezels: welke, waarom en hoe?'	NVVL-FNLI, Utrecht	2009
Annual meetings NWO Voeding	NWO, Deurne	2009, 2011
4th and 5th international Dietary Fibre conference	ICC, Vienna (AT) , ICC/INRAN Rome (IT)	2009, 2012
34th British Feeding and Drinking group	BFDG, Maastricht	2010
9th Vahouny Fiber conference	NutraSource Research, Bethesda (USA)	2010
Annual symposium Voeding Nederland	Voeding Nederland, Nieuwegein	2011, 2012
Annual meeting Society of Study Ingestive Behaviour	SSIB, Zurich (CH)	2012
General courses and workshops		
Afstudeervak organiseren en begeleiden	Docenten Ondersteuning, Wageningen	2008
Philosophy and ethics of food science and technology	Graduate school VLAG, Wageningen	2009
Techniques for writing and presenting scientific papers	Graduate school SENSE, Wageningen	2009
Good Clinical Practice	Clinical Trial Service, Ede	2009
PhD competence assessment	Wageningen Graduate Schools (WGS)	2010
Scientific writing	Wageningen Graduate Schools (WGS)	2010
Talent classes: 'Creative thinking' and 'Negotiation'	NWO, Den Haag	2010
Masterclass Linear and Logistic Regression	Graduate school VLAG, Wageningen	2010
Design of Experiments	Graduate school WIAS, Wageningen	2010
Mixed Linear Models	Graduate school PE& RC, Wageningen	2011
European Nutrition Leadership Programme (ENLP)	ENLP, Luxembourg (LU)	2012
Optional courses and workshops		
Preparation research proposals and research presentations	Division of Human Nutrition, Wageningen	2008-2012
MSc course: Concepts and Methods in Epidemiology	Division of Human Nutrition, Wageningen	2008
PhD Study Tour Nordic Countries	Division of Human Nutrition / Graduate school VLAG, Wageningen	2009
Symposium preceding 93rd Dies Natalis	Wageningen University, Wageningen	2011

Colophon