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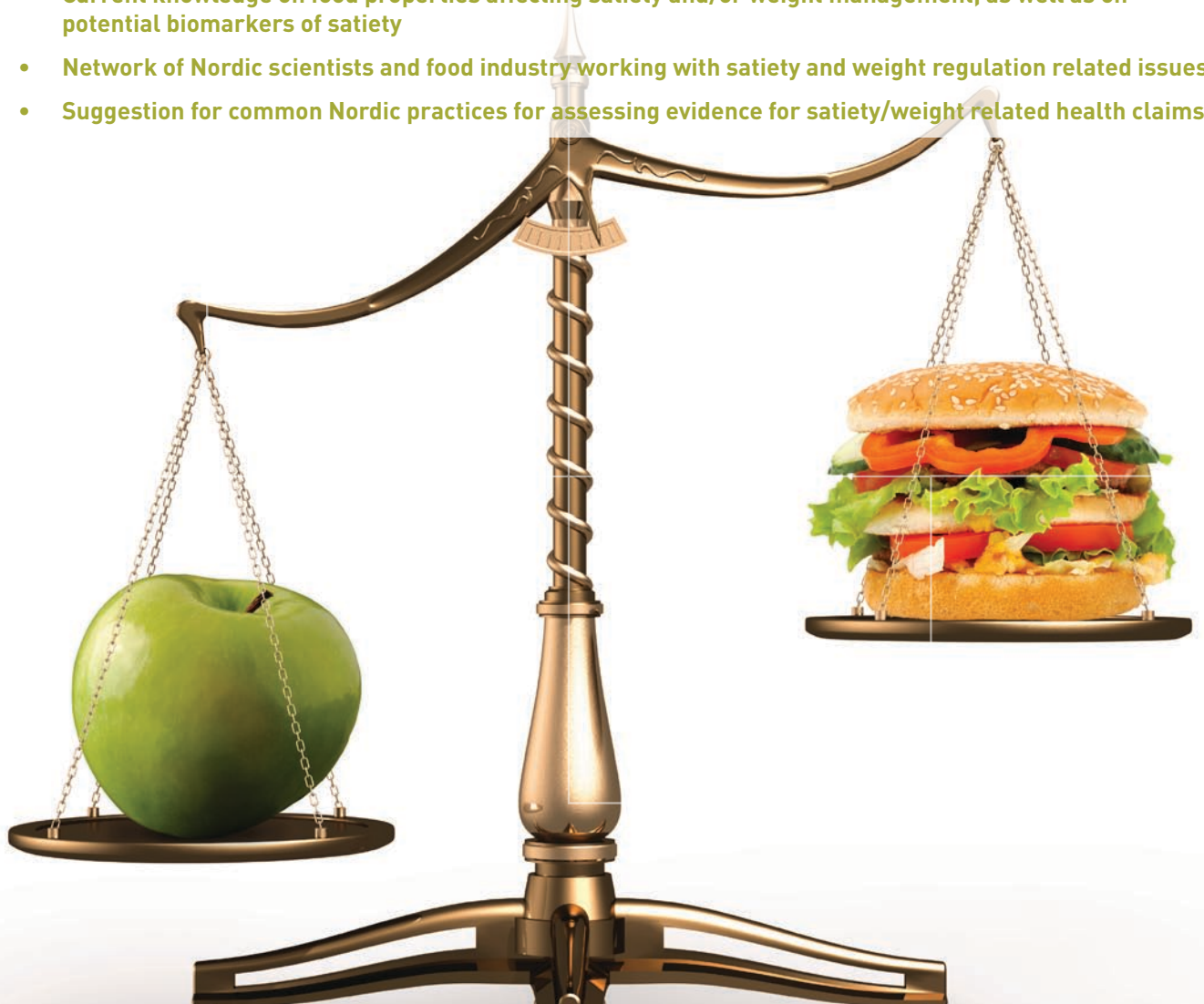
Nordic Innovation Centre

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# Satiety, weight management and foods

## Literature review

- Current knowledge on food properties affecting satiety and/or weight management, as well as on potential biomarkers of satiety
- Network of Nordic scientists and food industry working with satiety and weight regulation related issues
- Suggestion for common Nordic practices for assessing evidence for satiety/weight related health claims



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# **Satiety, weight management and foods**

## **Literature review**

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## Abstract

Obesity is becoming an increasing health problem. It is a major burden for healthcare costs because it is related to many chronic diseases such as type 2 diabetes, elevated blood pressure and cardiovascular disease. Body weight is determined by a complex interaction of genetic, environmental and psychosocial factors. Obesity results when energy intake exceeds energy expenditure.

Food has a crucial role in weight management. The new EU legislation on nutrition and health claims permits the use of weight regulation related health claims on foods, if they are based on generally accepted scientific evidence. In this literature review the current knowledge on food properties and potential biomarkers, that have been proposed to affect satiety and/or energy expenditure and thus might be useful in weight control are considered regarding the scientific evidence behind different factors.

The short-term regulation of food intake is mediated via neural and humoral signals from GI tract to different regions in brain. Different macronutrients, carbohydrates, protein, fibre and fat, affect the release of satiety related peptides from stomach and different parts of intestine. For example, the release of glucagon-like peptide 1 (GLP-1) and peptide YY (PYY) from the intestine after meal increase satiety. In the long-term regulation of food intake the hormones leptin from adipose tissue and insulin from the pancreas play a significant role.

There is no single, standard method to measure satiety. Different methods have been used in measuring sensations related to the promotion and inhibition of eating, such as satiety, appetite, hunger and fullness. Generally satiety has been measured by rating subjective feelings before and after consumption of a test food/meal, and/or by measuring the energy intake after the test food/meal. A visual analogue scale is the most commonly used method to assess subjective ratings of satiety. In the scale the end points are verbally anchored, e.g. "I'm extremely full" and "I'm not at all full". If the satiety related feelings are rated e.g. for 120 min after ingestion of the food at certain intervals, a graph can be drawn as a function of time, and the area under the curve can be used as a measure of e.g. fullness produced by the meal/food. Satiety index and satiety quotient help in the comparison of satiety values of different foods. The search for the physiological biomarkers of appetite is active at the moment, but so far no clear winner has been found.

The energy density of foods (kJ or kcal/g of food) is considered an important factor in the regulation of energy intake. In short term studies, low energy density foods have been shown to effectively increase satiety and decrease feeling of hunger with relation to their energy content, and reduce energy intake. In long term studies low energy density foods have been shown to promote weight reduction.

The results on the effects of different macronutrients on satiety and weight control are not conclusive, although research in this field has been active. However, as several studies have shown that the energy density of carbohydrates and protein is lower and satiating power greater than those of fats, favouring them as a means to regulate food intake is of interest. Particularly, many studies indicate that dietary fibre may be associated with satiation, satiety and reduction of energy intake via several different mechanisms. High protein food has shown to produce increased satiety and to promote weight regulation after weight loss. In addition, current research on the role of quality of fat and glycaemic index of food in the regulation of weight, satiety and hunger is actively ongoing but the results so far are inconclusive.

The physical properties of food are also important in the satiating effect of food. Food macrostructure effects the rate with which food exits the stomach and the rate of absorption of nutrients. This in turn is correlated to blood glucose and insulin responses and may also affect the feeling of satiety.

Some bioactive compounds such as caffeine, compounds in green tea and capsaicin have been proposed to have an effect on energy metabolism and may thus contribute to weight loss. Although some promising short-term effects on energy expenditure and fat oxidation have been found, more data are needed to draw conclusions on the long-term weight control effects. There is also evidence that dairy calcium may play a role in body weight regulation, but the results are still contradictory and need further studies.

Gut microbiota has been of research interest also from the weight management perspective. It can be hypothesized that gut microbiota influences the energy balance of the host, but further studies are needed to find out what kind of role gut microbiota could have in the development of obesity in humans.

At the moment it appears that the scientific evidence behind the satiating effect of dietary fibre and protein is the most convincing, but so far no dose-response relationship has been defined. Many other potential links between different nutrients, dietary composition and weight management exist. However, further studies are needed to verify these effects in order to achieve the scientifically sound proof required for the weight management and satiety related health claims on foods.

## Preface

This literature review has been written within ‘Substantiation of weight regulation and satiety related health claims on foods’ project. This two-year project started in 2006 and is mainly financed by Nordisk InnovationsCenter and belongs to the Functional Food focus area.

The aim of this project is to create a network of Nordic scientists who work with satiety and weight regulation related issues and create a possible suggestion for common practices for assessing the evidence for satiety/weight related health claims in the Nordic countries. This literature report reviews the latest knowledge on food properties that have been proposed to affect satiety and might therefore be useful in weight control. The literature on potential biomarkers of satiety is also explored.

The project is coordinated by VTT Technical Research Centre of Finland, with project partners from the University of Kuopio, Finland; University of Lund, Sweden; University of Copenhagen, Denmark; University of Iceland & Landspítali-University Hospital, Iceland; MS Icelandic Dairies, Iceland; Atria Finland Ltd, Finland; Fazer Bakeries Ltd, Finland; Valio Ltd, Finland; Danish Meat Association, Denmark; Skåne Dairy, Sweden and Lantmännen Food R & D, Sweden.

This literature review is aimed at researchers, food authorities, food industry and others working with satiety and weight management related issues.

Espoo, January 2008

On behalf of the project group,

Marika Lyly, project leader

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# 1. Introduction

Obesity is now recognized as a chronic disease almost in all countries, although with great variation between and within countries. Because the risks of diabetes, cardiovascular disease and hypertension rise continuously with increasing weight, there is much overlap between the prevention of obesity and the prevention of a variety of chronic diseases, especially type 2 diabetes (Report of a Joint WHO/FAO Expert Consultation on ‘Diet, nutrition and the prevention of chronic diseases’). Against this background, identification of food properties able to influence specific physiological functions linked with body fat accumulation may be helpful for the prevention and management of overweight. Once the health effects of foods have been identified, they should be communicated to the general public to help consumers benefit from this important information. This could provide new business opportunities for Nordic food industries, but demands knowledge on the validation process of health claims for foods in relation to body weight control.

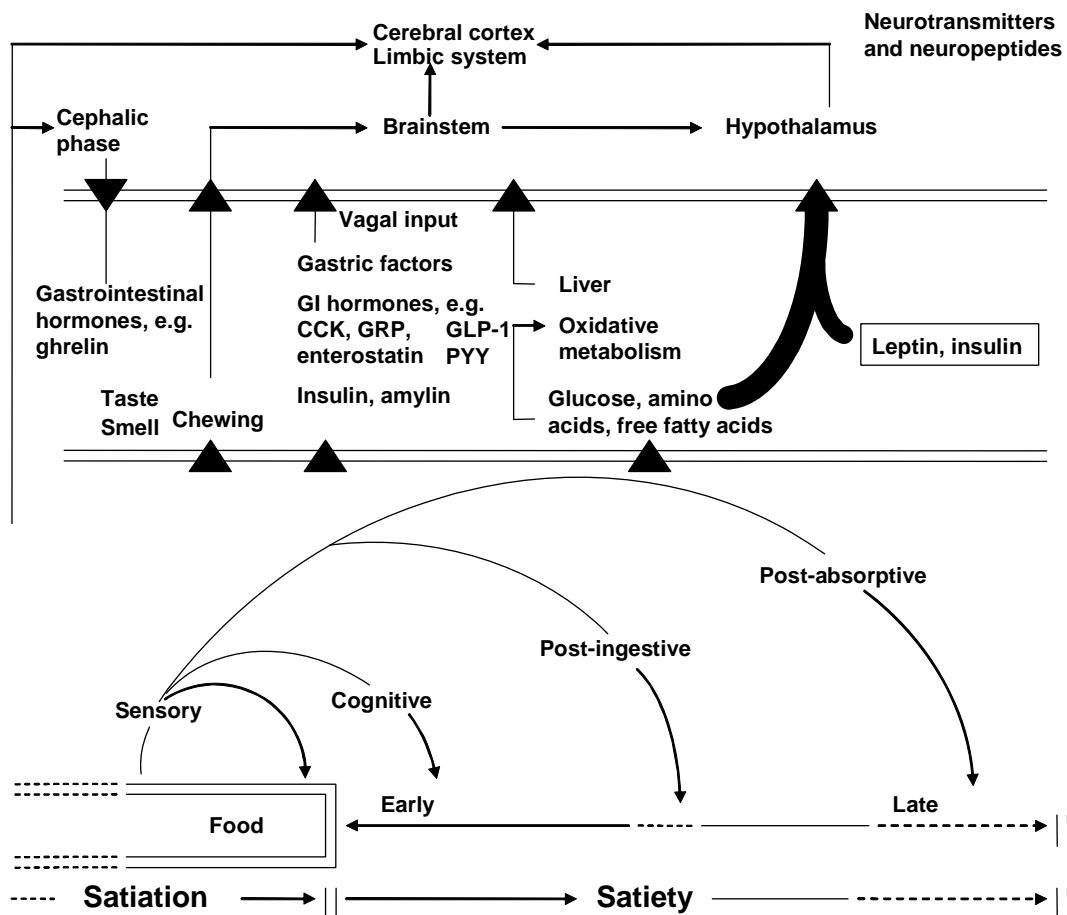
Regarding body weight regulation, key elements are the control of energy intake, which is regulated at the simplest level by sensations of hunger, and satiety, and the control of energy efficiency, which influences the amount of energy dissipated as heat instead of being stored as fat. Potential weight regulation related health claims could be based both on the measurable target functions such as body mass index (BMI) and body fat deposition and the associated marker functions such as sensation of satiety and satiety related hormones, energy expenditure and lipid oxidation.

The new EU legislation on nutrition and health claims permits the use of weight regulation related health claims on foods. The criteria for the scientific substantiation of health claims have been built as a result of PASSCLAIM (Process for the Assessment on Scientific Support for Claims on Foods) and FUFUSE (Functional Food Science in Europe) projects. These criteria provide general rules for substantiating health claims but they do not give clear guidelines of how these rules are substantiated in such complex questions as weight control and satiety: what kind of evidence is sufficient and how results gained with different methods can be interpreted?

Although food industry may use health claims to advertise and promote their products, the intended purpose of health claims is to benefit consumers by providing information on healthful eating patterns that may help reduce risk of certain diseases. Therefore, all health claims used in the labelling, advertising or promotion of food or food supplements must be substantiated. In addition, health claims must be based on a systematic and objective compilation of all the available scientific evidence. They should also be based on human data, primarily from intervention studies with an appropriate design and a relevant end-point. All this raises important practical questions: what evidence is needed to build weight regulation related claims and how substantiation process proceeds?

## 2. Short-term regulation of food intake

Short-term regulation of food intake controls what, when and how much we eat within a single day or a meal. Short-term regulation results from a coordinated series of neural and humoral signals that originate from the gastrointestinal (GI) tract in response to mechanical and chemical properties of ingested food (Cummings and Overduin 2007). Multiple sites in the GI tract, including the stomach, proximal and distal small intestine, colon, and pancreas are involved in this process. In different phases of regulation, different signals originating in these sites are essential (Blundell et al. 2001) (**Fig. 1**). Moreover, although the short- and long-term regulation of food intake is mediated through distinct mechanisms, there is also a lot of interaction between them. This ensures that energy balance can be maintained, even despite the usually large variation in day-to-day energy intake (Havel 2001). The major regulators of long-term energy balance, such as the adiposity hormones leptin and insulin, modulate the sensitivity of an organism to the GI satiation signals.



**Figure 1.** Main regulatory mechanisms of short-term regulation of food intake. Modified from Blundell et al. 2001.

Ingested food evokes satiety in the GI tract primarily by two effects, i.e. by mechanical stimulation and by the release of peptides through the chemical effects of food (Cummings and Overduin 2007). However, pure mechanical stimulation, such as gastric distention, is insufficient to terminate ingestion, but contributes to satiety when acting in concert with pregastric and postgastric stimuli (Ritter 2004). Instead, the intestine seems to play a key role in satiety through various peptides secreted in response to ingested food (Cummings and Overduin 2007). Furthermore, many of the intestinal peptides also inhibit gastric emptying, thus enhancing gastric mechanoreceptor stimulation, too.

The hindbrain is the principal central site receiving input from the GI satiety-related signals (Berthoud 2003, Cummings and Overduin 2007). The other brain region strongly involved in this regulation is the hypothalamus. In the perception of satiety, higher forebrain centres are, of course, also important. The GI satiety-related signals are transmitted to central nervous system both neurally, through vagal afferents, as well as humorally, through gut-derived peptides.

The access of many substances into the central nervous system (CNS) from the systemic circulation is very strictly controlled by the blood-brain barrier (BBB) in order to maintain and regulate the optimal neural microenvironment in the brain (Saunders 1999). Despite the extensive coverage of BBB in the CNS, there are some specialized areas called sensory circumventricular organs (e.g. median eminence, area postrema) which are lacking this barrier (Fry and Ferguson 2007). These areas serve as crucial regions in the CNS and are responsible for sensing the internal milieu of the body (such as serum osmolarity) or are involved in either sensing hormone levels or releasing hormonal factors into the circulation. Thus, the BBB has a dynamic and vital role in the passage of several internal circulating signals serving both energy metabolism and regulatory functions of the brain.

In the next chapters, the current knowledge about the effects of different macronutrients on the release of GI satiety-related peptides in humans will be reviewed. Summary of the main findings of the effects of different macronutrients on postprandial release of satiety-related gastrointestinal peptides in humans is presented in **Table 1**.

*Table 1. Summary of the main findings of the effects of different macronutrients on postprandial release of satiety-related gastrointestinal peptides in humans.*

Peptide	Carbohydrate	Fibre	Fat	Protein
<b>CCK</b>	increase	increase	increase	increase
<b>Ghrelin</b>	decrease	blunted or inhibited decrease / decrease / no effect	decrease / no effect / increase	decrease / increase / no effect
<b>GLP 1</b>	increase	blunted increase / no effect / increase	increase	increase
<b>PYY</b>	increase	increase / no effect	increase	increase
<b>Obestatin</b>	decrease (a mixture of carbohydrates, protein and fat)		decrease (a mixture of carbohydrates, protein and fat)	decrease (a mixture of carbohydrates, protein and fat)
<b>Gastric leptin</b>	○	○	○	○
<b>GIP</b>	increase	○	increase	no effect / increase
<b>Oxyntomodulin</b>	○	○	○	○
<b>Enterostatin</b>	○	○	○	○
<b>Insulin</b>	increase	blunted increase (soluble fibres)	increase	increase
<b>Amylin</b>	increase	○	○	○
<b>Pancreatic polypeptide</b>	increase	no effect	increase	increase

○: no studies available

## 2.1 Satiety-related peptides released from the stomach

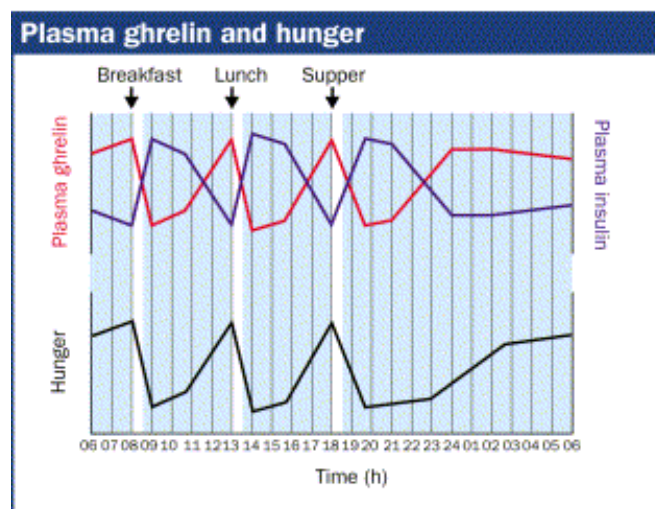
### 2.1.1 Ghrelin

Ghrelin is an acylated 28-amino acid peptide hormone produced primarily by the stomach (Kojima et al. 1999). Gastric fundus is the most abundant source of ghrelin (Ariyasu et al. 2001, Gnanapavan et al. 2002). Relatively large amounts are also produced in the duodenum and lower concentrations are expressed throughout the small intestine. In addition, minor amounts of ghrelin are produced in lungs, pancreatic islets, adrenal cortex, placenta, kidney and brain (Kojima et al. 1999, Hosoda et al. 2000). Ghrelin receptors are expressed widely in the brain and peripheral tissues, especially in

the pituitary, stomach, intestine, pancreas, thymus, gonads, thyroid and heart (Cummings 2006). Ghrelin crosses the BBB and stimulates food intake by acting in the brain on several important weight and energy balance regulatory centres, including the hypothalamus, hindbrain/caudal brainstem and mesolimbic reward centers.

Ghrelin has many biological functions and was originally identified as the natural ligand for the growth hormone secretagogue receptor. However, the role of ghrelin in the regulation of energy homeostasis is generally viewed as its most important function (Cummings 2006).

Ghrelin is the only mammalian substance that has been shown to increase appetite and food intake when delivered to humans (Wren et al. 2001, Druce et al. 2005, Druce et al. 2006). Ghrelin can exert this effect both when injected peripherally and centrally. Contrary to gastrointestinal satiety peptides, ghrelin increases GI motility and decreases insulin secretion. Also, in contrast to satiety peptides, circulating levels of ghrelin normally rise shortly before and fall shortly after meals (**Fig. 2**). Thus, ghrelin has a role in mealtime hunger and meal initiation (Cummings and Overduin 2007). Accordingly, ghrelin enhances food intake by increasing the number of meals initiated without altering meal size. Preprandial ghrelin secretion also seems to be a cephalic response participating in the anticipatory processes that prepare an organism for ingestion of food (Drazen et al. 2006).



**Figure 2.** Typical curves of circadian changes in plasma ghrelin (and insulin) concentrations in healthy subjects (Pinkney and Williams 2002).

Ghrelin also has a role in the long-term regulation of energy balance and body weight. Circulating ghrelin levels respond in a compensatory manner to body weight changes; diet-induced weight loss increases, and weight gain decreases the circulating levels of ghrelin (Cummings et al. 2002).

### *Nutrients and ghrelin release*

The postprandial ghrelin response is affected by the macronutrient composition of a meal. However, in contrary to what was first expected, postprandial suppression of ghrelin seems not be mediated by nutrients in the stomach or duodenum (Cummings 2006). Rather, it results from post-ingestive increases in lower intestinal osmolarity (via enteric nervous signaling) as well as from insulin surges (Cummings 2006). The release of ghrelin also seems to depend upon the length of small intestine exposed; no postprandial decrease was seen if less than 60 cm from the upper part of the intestine was exposed to glucose (Little et al. 2006). Pure stomach expansion, by e.g. ingestion of water, is neither a sufficient condition to modify ghrelin secretion (Shiyya et al. 2002, Blom et al. 2005).

Among different macronutrients, carbohydrates have been shown to be most effective at suppressing postprandial ghrelin concentration (Monteleone et al. 2003, Tannous dit El Khoury et al. 2006). Decreased concentrations have been seen after intravenous and oral administration of glucose (Shiyya et al. 2002) as well as after ingestion of simple (e.g. maltodextrin) or complex (e.g. exopolysaccharide) carbohydrates (Blom et al. 2005). Different carbohydrate preloads suppress ghrelin concentrations in proportion to their energy content.

The effect of fibre on postprandial ghrelin is currently not well understood due to a limited number of studies as well as a wide range of fibres with different physical and chemical properties. Increased fibre content of meals has been shown both to decrease postprandial ghrelin concentration as well as to inhibit the postprandial decrease of ghrelin. In one study, consumption of a small amount (4 g) of non-caloric soluble psyllium fibre with water was as effective at suppressing postprandial plasma ghrelin concentrations in healthy subjects as was a 585-kcal mixed meal (Nedvidkova et al. 2003). By contrast, in another study no postprandial ghrelin decrease was seen after the ingestion of a 300 kcal solid meal, enriched with a great amount (23 g) of psyllium-fibre (Karhunen et al. 2005). Similarly, no postprandial decrease in ghrelin was reported after the intake of a non-caloric liquid containing 21 g of guar gum (Erdmann et al. 2003). Moreover, in a study by Möhlig et al. (2005), soluble-like arabinoxylan fibre (6 g) enriched breakfast induced a shorter postprandial decrease in ghrelin when compared to a control breakfast. Similarly, enrichment of bread with 10 g of insoluble wheat fibre blunted the decrease in postprandial ghrelin concentrations, whereas the same amount of insoluble oat fibre did not, as compared with white wheat bread of same energy and carbohydrate content (Weickert et al. 2006). In our own study, postprandial ghrelin responses did not differ after eucaloric puddings enriched with 10 g insoluble wheat or 10 g oat fibre (Juvonen et al. 2006). Addition of insoluble carob fibre (5, 10 or 20 g) to a liquid meal decreased acylated ghrelin without dose-dependent effects but did not affect

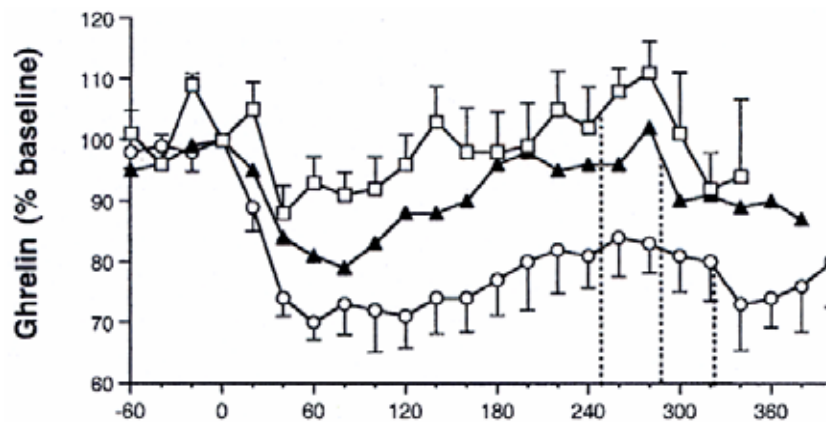
total or nonacylated plasma ghrelin in comparison to a non-fibre meal (Gruendel et al. 2006). There could thus be differences also between acylated and non-acylated forms of ghrelin.

The results of studies investigating the effect of protein on postprandial ghrelin concentration have been quite conflicting. In some studies, postprandial ghrelin concentrations did not change (Greenman et al. 2004) or even increased after the ingestion of a protein-rich meal (Erdmann et al. 2003, Erdmann et al. 2006) or a physiologic dose of essential amino acids (Groschl et al. 2003, Knerr et al. 2003). By contrast, other studies have shown a high-protein test breakfast (enriched with milk-based proteins) (Al-Awar et al. 2005, Blom et al. 2006) or liquid preloads of whey, casein, soy and gluten (Bowen et al. 2006a, Bowen et al. 2006b) to cause a prolonged suppression of ghrelin as compared with carbohydrate. The type of protein might thus play a role in modulating postprandial ghrelin release. A decrease in postprandial ghrelin concentration has been seen quite consistently after milk-based proteins (Aziz and Anderson 2007) whereas the increase has been seen after the meat protein (Erdmann et al. 2003, Erdmann et al. 2006). Nevertheless, it has also been suggested that although the kinetics of the ghrelin response to ingested proteins and carbohydrates could differ, the overall magnitude of suppression after isocaloric intake of these two macronutrient types would be relatively similar (Cummings 2006). In line with this, ghrelin levels were equivalent among people in energy balance consuming isocaloric high- vs. normal-protein diets with constant fat content (Lejeune et al. 2006). Thus, calorie for calorie, carbohydrates and proteins might suppress postprandial ghrelin levels equally (Cummings 2006).

The effect of dietary fat on postprandial release of ghrelin is still unclear. Intravenous lipid infusion does not seem to affect ghrelin concentrations (Möhlig et al. 2002, Murray et al. 2006). After oral ingestion of a high-fat meal, ghrelin concentrations have both been shown to decrease (Monteleone et al. 2003, Greenman et al. 2004) or to increase (Erdmann et al. 2004). Moreover, if ghrelin decreased, the decrease has been characterised by a slower return to baseline than after a high-carbohydrate meal (Romon et al. 2006, Otto et al. 2006). There is also some evidence that fat-induced suppression of ghrelin is dependent on fat digestion (Feinle-Bisset et al. 2005). Moreover, the effect of intraduodenal fatty acids on ghrelin secretion seems to be dependent on the chain length (Feltrin et al. 2006). Fatty acid, 12 carbon atoms in length (C12, lauric acid), markedly suppressed plasma ghrelin compared with a fatty acid, 10 carbon atoms in length (C10, decanoic acid), which had no effect.

However, when the calorie content of meals is varied but the volume, macronutrient distribution, and all other features are kept constant, the depth and duration of postprandial ghrelin suppression are dose-dependently related to the number of ingested

calories (Callahan et al. 2004) (**Fig. 3**). More energetic meals do thus suppress ghrelin more than do the small ones.



**Figure 3.** Temporal profiles of plasma ghrelin after ingestion of meals containing 7.5% (□), 16% (△), and 33% (○) of total daily energy expenditure (Callahan et al. 2004).

In conclusion, the role of ghrelin as a satiety-related peptide is not at all clear and it is not even not known what kind of postprandial profile is most efficiently associated with enhanced satiety. Both increased and decreased concentrations have been reported after meals with typically higher satiety value, such as those high in fibre or protein. On the other hand, the association between ghrelin and feelings of hunger and satiety has not been seen in all studies. By contrast, the role of ghrelin as a meal initiator is quite clear. The role of ghrelin in the regulation of short-term food intake might thus be different before than after the ingestion of a meal (Erdmann et al. 2004).

### 2.1.2 Obestatin

Obestatin is a recently discovered gut-derived 23-amino acid peptide (Zhang et al. 2005), which is derived from the processing of the ghrelin gene. In rodents, obestatin has been shown to reduce food intake and body weight as well as to decelerate gastric emptying (Zhang et al. 2005, Lagaud et al. 2007). Against this background, obestatin may function as a physiological counterpart of ghrelin. However, the accurate role of obestatin has not been completely determined (Gourcerol et al. 2007, Bassil et al. 2007). Moreover, obestatin actions to reduce food intake and to inhibit gastrointestinal (GI) motility *in vivo* and *in vitro* have not been reproduced by other groups (Gourcerol et al. 2007, De Smet et al. 2007). Thus, although it is obvious that obestatin is a functionally active circulating peptide in humans, its role in the regulation of food intake and energy balance waits for further substantiation.



### *Nutrients and obestatin release*

In a study by Guo et al. (2007), a habitual Chinese breakfast containing about 500–600 kcal with a mixture of carbohydrates, protein, and fat decreased postprandial obestatin concentrations in both normal-weight and obese subjects. To our knowledge this is the only published human study on the postprandial release of obestatin.

#### **2.1.3 Gastric leptin**

Gastric leptin, a recently found stomach-derived form of leptin, has been identified in the epithelium of the lower half of the fundic glands (Bado et al. 1998, Cinti et al. 2000). Gastric leptin is released upon vagal stimulation (Sobhani et al. 2002), and during food ingestion, but its secretion is also stimulated by pepsinogen secretagogues such as CCK, gastrin, or secretin (Sobhani et al. 2000, Lewin and Bado 2001). The increased secretion occurs within minutes after a meal, both in the circulation and the gastric lumen (exocrine secretion). Vagal stimulation of leptin release in the human stomach suggests that leptin is released during the cephalic phase of gastric secretion (Sobhani et al. 2002). Luminal leptin may thus be involved in vagus-mediated intestinal functions.

Gastric leptin possesses different physiological functions that are mediated through exocrine and endocrine pathways (Strader and Woods 2005). Since gastric leptin remains stable in gastric fluid (Sobhani et al. 2001) it could exert its effects locally in the stomach to influence gastric functions. Gastric leptin may also serve as an efficient regulator of the intestinal absorption of luminal nutrients due to the occurrence of unbound leptin and the expression of leptin receptors on the brush border (Guilmeau et al. 2004). In addition, gastric leptin has been shown to stimulate CCK release, and together leptin and CCK can potentiate their own actions by cross-stimulating secretion (Guilmeau et al. 2004, Bado et al. 1998).

Gastric leptin operates as a short-term regulator of digestion, gastric emptying, absorption of nutrients by the intestinal epithelium, and secretion of gastric, intestinal and pancreatic hormones. Several animal studies indicate that gastric leptin is sensitive to nutritional state, being rapidly mobilized in response to food intake after fasting. A brief period of re-feeding is capable of emptying all the leptin stores within the gastric granules of rodents (Bado et al. 1998, Cinti et al. 2000). Thus leptin secreted by gastric mucosal cells and by adipocytes, could have an effect on the regulation of feeding behaviour both on a short- and long-term basis.

### *Nutrients and gastric leptin release*

Although food intake seems to stimulate the secretion of gastric leptin in humans, there is yet no data available regarding the potential effects of different nutrients on the secretion of gastric leptin. However, in rodents food composition has been shown to play a major role in the release of gastric leptin. Leptin mRNA expression in rat gastric mucosa is upregulated by sucrose-rich but not by fat-rich diets (Lindqvist et al. 2005). Similarly, fasted rats refed with a carbohydrate-rich diet showed an increased synthesis of gastric leptin (Sanchez et al. 2004).

## **2.2 Satiety-related peptides released from the proximal intestine**

### **2.2.1 Cholecystokinin**

Cholecystokinin (CCK) is a polypeptide hormone produced by I cells in the duodenal and jejunal mucosa in the upper small intestine (Cummings and Overduin 2007). CCK is also produced in the brain and enteric nervous system. CCK has peripheral and central receptors; CCK receptor 1 (CCK1R) predominates in the GI system, CCK receptor 2 (CCK2R) in the brain. CCK1R mediates CCK-induced satiation (Kopin et al. 1999). This receptor is expressed on vagal afferents, and peripheral CCK administration increases vagal-afferent firing, as well as neuronal activity in the hindbrain region receiving visceral vagal input. CCK1R is also expressed in the hindbrain and hypothalamus indicating that CCK might relay satiation signals to the brain both directly and indirectly, and central CCK also contributes to satiation.

The satiating effect of CCK has been confirmed in numerous species, including humans. It is however short-lived, lasting less than 30 minutes. Accordingly, CCK inhibits food intake within meals by reducing meal size and duration but does not affect the onset of the next meal (Kissileff et al. 1981).

Gastric distention augments the anorectic effects of CCK in humans and the mechanism by which CCK suppresses appetite is the delay of stomach emptying (Kissileff et al. 2003). Accordingly, full stomach is a necessary condition for the appetite-suppressing effect of CCK (Melton et al, 1992). Some vagal-afferent fibres respond synergistically to gastric distention and CCK. However, evidence suggests that CCK causes satiation also through mechanisms additional to enhancing gastric distention signals.

### *Nutrients and CCK release*

Gastrointestinal release of CCK is mediated in response to nutrients in the lumen, with fat and protein producing greater postprandial concentrations than carbohydrates (Hopman et al. 1985, Moran and Kinzig 2004).

Nevertheless, also carbohydrates increase plasma CCK concentrations. This has been seen after the oral ingestion of glucose (Hasegawa et al. 1996, Bowen et al. 2006b) as well as after intraduodenal perfusion or oral ingestion of isocaloric diets with various amounts of carbohydrates (55–79%) (Mössner et al. 1992). The response is rapid and seen within 15 min of ingestion. After carbohydrates, the increase in CCK concentrations is, however, quite short-lived and returns close to baseline within less than one hour (Bowen et al. 2006b).

The results of studies investigating the effects of different fibres on CCK secretion are limited. Different dietary fibres, including hydrolyzed guar gum (Heini et al. 1998), beta-glucan in barley pasta (Bourdon et al. 1999), or fibre in bean flakes, and fibre mostly from oatmeal and oat bran (Bourdon et al. 2001), have been shown to produce greater postprandial increases in CCK concentrations, as well as prolonged elevations of the hormone than low fibre meals or placebo. This effect may be related to the delayed gastric emptying and thereby retarded/inhibited carbohydrate absorption, although the role of CCK might be contributory to that of glucagon-like peptide 1 in the inhibition of gastric emptying after a mixed meal (Enc et al. 2001).

Protein preloads have been followed by higher CCK than the carbohydrate ones. CCK remained elevated after liquid whey, casein, soy and gluten preloads or after a whey protein isolate enriched dairy product meal compared with glucose and lactose (Bowen et al. 2006a, 2006b, Blom et al. 2006). The gastric emptying time was also reduced after the whey protein isolate enriched meal. Higher CCK responses after proteins (whey, casein) also correlated with satiety but did not affect food intake (Bowen et al. 2006a). In some studies, the postprandial CCK release has been greater after whey than casein (Hall et al. 2003). Whey was also more satiating than casein.

Both the load, and duration, of small intestinal lipid exposure influence antropyloroduodenal motility and patterns of CCK release (Pilichiewicz et al. 2005, Feltrin et al. 2007). Triglycerides must be hydrolyzed to fatty acids to stimulate CCK secretion and the fatty acid acyl chain must be at least 12 carbon atoms in length to markedly stimulate CCK (Matzinger et al. 2000, Feltrin et al. 2004, Moran and Kinzig 2004). Fats with long-chain fatty acids do thus result in higher CCK concentrations than fats with short-chain fatty acids. They are also more efficient in suppressing appetite and energy intake (Feltrin et al. 2004). High fat intake seems to have long-lasting effect on CCK; after a high-fat

evening meal CCK concentrations remained elevated until the following morning (Robertson et al. 2002). High-fat, low-carbohydrate feeding does, however, reduce CCK-induced satiety, possible due to a down-regulation of vagal CCK1R receptors (French et al, 1995). There also seem to be gender differences in the CCK response after a high fat intake (Burton-Freeman et al. 2004, Burton-Freeman 2005). Also, other characteristics, such as dietary restraint, have been shown to be associated with postprandial CCK response; CCK response was blunted in those with higher dietary restraint (Burton-Freeman 2005).

In conclusion, CCK has an important role in the causal chain leading to satiation or meal termination. Foods that have a high potency for releasing CCK may thus be those with a higher satiating effect (de Graaf et al. 2004).

### **2.2.2 Glucose-dependent insulinotropic polypeptide (GIP)**

Glucose-dependent insulinotropic polypeptide / gastric inhibitory polypeptide (GIP) is a 42-amino acid polypeptide that shares the insulinotropic effect with glucagon-like peptide 1 (GLP-1) to potentiate meal-induced insulin secretion from the pancreas (Drucker 2006). GIP is released from intestinal K cells in response to the presence of nutrients in the intestinal lumen. GIP-secreting K-cells are found predominantly in the duodenum but can be found in principle throughout the gastrointestinal tract (Mortensen et al. 2003). The secretion of GIP is closely correlated to the secretion of GLP-1, although the mechanism underlying this co-secretion is still unclear.

The predominant stimulus for GIP secretion is nutrient intake and GIP concentration increases within 5–15 min after nutrient ingestion (Drucker 2006). The concentration peaks 30–60 minutes postprandially depending on meal size and composition (Vilsboll et al. 2001). GIP is rapidly degraded by the proteolytic enzyme dipeptidyl-peptidase IV (DPP IV) yielding the biologically inactive fragment of GIP (GIP<sub>3-42</sub>) (Drucker 2006). After the cleavage, GIP has lost its incretin effect regarding the stimulation of insulin secretion. Circulating GIP represents a mixture of active (GIP<sub>1-42</sub>) and inactive GIP (GIP<sub>3-42</sub>).

In addition to its role in the regulation of endocrine pancreatic secretion and thus glucose metabolism, GIP exerts various peripheral effects on adipose tissue and lipid metabolism in the postprandial state. As an anabolic hormone GIP stimulates lipoprotein lipase activity (Eckel et al. 1979) and promotes fatty acid incorporation into adipose tissue (Beck and Max 1983), thereby leading to increased lipid deposition and fat storage. It does, however, not affect gastric emptying in humans (Meier et al. 2004). The role of GIP in the regulation of satiety is, however, questionable (Strader and Woods 2005).

## *Nutrients and GIP release*

The major stimuli for GIP release are dietary fat and carbohydrates (Cataland et al. 1974, Falko et al. 1975, Sarson et al. 1980, Krarup et al. 1985, Elliott et al. 1993, Herrmann et al. 1995). Proteins seem to have no effect (Sarson et al. 1980, Elliott et al. 1993), although some evidence exists indicating that amino acids can stimulate GIP release (Thomas et al. 1976).

Among different carbohydrate sources, glucose, but not fructose, increased GIP concentration, although they both were equally effective in suppressing food intake in the test meal (Vozzo et al, 2002). Moreover, the ingestion of equivalent portions of carbohydrate either in a simple (glucose) or a complex form (boiled brown rice or barley) were followed by different size GIP responses; the increase was the largest following glucose and the smallest following the barley meal (Elliott et al. 1993).

Among different fat sources, the postprandial GIP release might be affected by the saturation of the fatty acids; olive oil induced higher concentrations of GIP than did butter, which may point to a relation between fatty acid composition, incretin responses and triacylglycerol metabolism in the postprandial phase (Thomsen et al. 1999).

## **2.3 Satiety-related peptides released from the distal small intestine and colon**

### **2.3.1 Glucagon-like peptide 1 (GLP-1) and oxyntomodulin**

Glucagon-like peptide 1 (GLP-1) and oxyntomodulin are cleaved from proglucagon, which is expressed in the gut, pancreas, and the brain (Drucker 2006). Post-translational cleavage of proglucagon generates different breakdown products depending on the tissue. In the gut the process results in the end products of glicentin, glucagon-like peptide 1 (GLP-1) and GLP-2. Glicentin (also known as enteroglucagon) is then further cleaved to produce oxyntomodulin (Wynne and Bloom 2006). In the pancreas, the end product of proglucagon is glucagon (a counter-regulatory hormone). Although several of these peptides are implicated in satiation, evidence is strongest for GLP-1 and oxyntomodulin (Cummings and Overduin 2007).

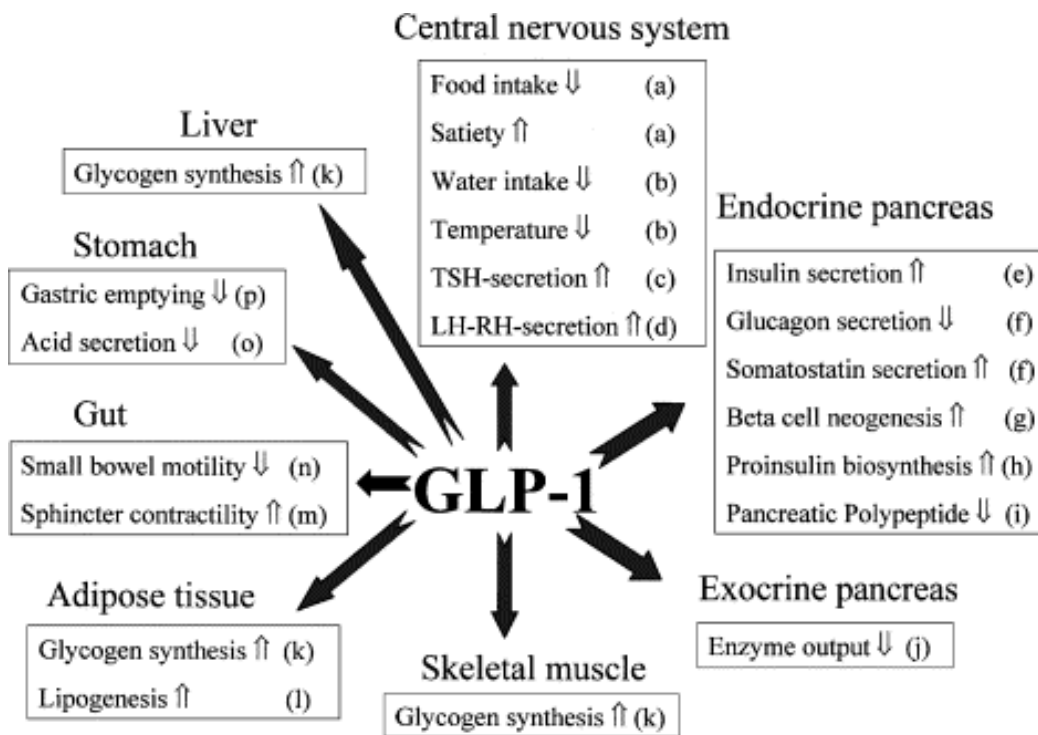
#### Glucagon-like peptide 1

GLP-1 is an incretin hormone released by L cells in the distal small intestine and colon in response to food intake (Drucker 2006). At the site of production, GLP-1 colocalizes with oxyntomodulin and peptide YY (PYY) (Cummings and Overduin 2007).

The two equipotent bioactive forms, GLP1<sub>7-36</sub> amide and GLP1<sub>7-37</sub>, are rapidly (within few minutes) inactivated in the circulation by dipeptidyl peptidase-4 (DPP4) (Drucker 2006). The effect of GLP-1 on food intake is thus a typical short-term effect.

GLP-1 is thought to play an important part in the “ileal brake” mechanism (ie, adjustments of stomach and gut motility after food ingestion) that causes a moderate and stable (digestible) flow of nutrients from the stomach into the small intestines. This is probably also the mechanism by which GLP-1 exerts its effect on appetite (Cummings and Overduin 2007). In addition to the ileal brake, GLP-1 accentuates glucose-dependent insulin release, inhibits glucagon secretion, and increases pancreatic  $\beta$ -cell growth (Drucker 2006). The multiple functions of GLP-1 are presented in **Fig. 4**.

The mechanisms underlying GLP-1-induced anorexia are not fully known but involve vagal and possibly direct central pathways (Cummings and Overduin 2007). Anorectic effects are mediated specifically by GLP-1 receptors (GLP1R). GLP1R is expressed in the gut, pancreas, brainstem, hypothalamus, and vagal-afferent nerves (Drucker 2006). The vagus is required for peripheral GLP-1-induced anorexia. The peptide can cross the BBB, but it seems unlikely that physiologically relevant quantities of endogenous peripheral GLP-1 evade peripheral DPP4 degradation and penetrate the brain. However, GLP-1 is also produced by brainstem neurons that project to hindbrain and hypothalamic areas important in the regulation of energy homeostasis.



**Figure 4.** Multiple functions of glucagon-like peptide 1 (Meier et al. 2002).

### ***Nutrients and glucagon-like peptide 1 release***

Plasma concentrations of GLP-1 rise rapidly within minutes of food intake (Drucker 2006). Ingested nutrients stimulate GLP-1 secretion thus by indirect, duodenally activated neurohumoral mechanisms, already before digested nutrients traverse the small bowel, as well as later by direct contact with the enteroendocrine L cells in the distal intestine (Brubaker and Anini 2003).

Carbohydrates are strong stimuli to GLP-1 release, consistently with the role of GLP-1 as an incretin (Elliott et al. 1995, Hermann et al. 1995, Brubaker and Anini 2003). Nevertheless, there could also be differences in the GLP-1 responses between different carbohydrates. After equivalent portions of carbohydrates as pure glucose or as complex carbohydrates, plasma GLP-1 concentrations increased only following the glucose (Elliott et al. 1993). Among different monosaccharides, oral glucose seems to have a bigger effect on GLP-1 release than fructose, although glucose and fructose have similar effects on appetite (Kong et al. 1999).

Closely related to the different GLP-1 responses among carbohydrate meals, the fibre content of meals also modifies postprandial GLP-1 response. Elevated, inhibited and unaffected GLP-1 responses have been reported, possible related to the fibre type or amount. A meal combined with galactose and guar gum (Adam and Westerterp-Plantenga 2005) increased and extended GLP-1 release. In contrast, resistant (pregelatinised) starch produced a lower GLP-1 response than digestible starch (Raben et al. 1994a). Similarly, Juntunen et al. (2002) demonstrated that whole-kernel and whole-meal rye bread and dark durum pasta produced lower GLP-1 responses than low-fibre wheat bread and rye bread containing oat  $\beta$ -glucan concentrate. In our own study, a test meal enriched with a great amount (23 g) of soluble psyllium fibre in combination with soya protein completely abolished the postprandial GLP-1 response, but not when the protein was replaced with carbohydrate (Karhunen et al. 2005). This suggests also some other component interactions that modify the postprandial GLP-1 responses as well. On the other hand, a smaller amount of psyllium fibre (1.7 g) did not modify postprandial GLP-1 responses (Frost et al. 2003), and neither did pea fibre (Raben et al. 1994b).

Protein stimulates GLP-1 release, even more than carbohydrates (Blom et al. 2006 AJCN, Lejeune et al. 2006). Among meals rich in protein, fat, carbohydrate or alcohol, GLP-1 responses were the highest after a protein rich meal (Raben et al. 2003). Among different protein sources, whey protein has been shown to increase postprandial GLP-1 secretion more than casein (Hall et al. 2003). Whey was also more satiating than casein (Hall et al. 2003). Also, in a study by Blom et al. (2006) a high-protein dairy product, enriched with a whey protein isolate, stimulated GLP-1 secretion along with reduced

rate of gastric emptying more than did a high-carbohydrate meal, although subjective sensations of hunger and *ad libitum* energy intake during the lunch were not significantly different between the meals.

GLP-1 concentration increases also after fat (Hermann et al. 1995), although the increase may be delayed as compared with carbohydrate (Elliott et al. 1993). The type of fat might modify the GLP-1 response; fat, rich in monounsaturated fatty acids (i.e. olive oil), induced higher concentrations of GLP-1 than did butter (Thomsen et al. 1999). The effect of fatty acid saturation on GLP-1 response has, however, not been seen in all studies (Brynes et al. 1998). The postprandial GLP-1 response to intraluminal fats may also depend on the chain length of fatty acids released during lipolysis (Feltrin et al. 2004). Fatty acid with 12 carbon atoms (C12, lauric acid) stimulated GLP-1, whereas the shorter one (C10, decanoic acid) did not (Feltrin et al. 2004).

### Oxyntomodulin

The effects of oxyntomodulin, a 37-amino-acid peptide product of the preproglucagon gene secreted from distal intestinal L cells, are mediated via the same receptor as GLP-1, although the affinity of oxyntomodulin for this receptor is substantially lower. Even so, oxyntomodulin and GLP-1 are equally effective in inhibiting food intake, which suggests that other pathways are also involved (Dakin et al. 2004). In line with that, oxyntomodulin and GLP-1 have different targets in the CNS. Oxyntomodulin activates the CNS neurons primarily in the hypothalamus, whereas GLP-1 activates the ones in the hindbrain and other autonomic areas (Murphy et al. 2006).

Oxyntomodulin is released into the circulation 5–10 min postprandially, in amounts proportional to ingested calories (Ghatei et al. 1983, le Quiellec et al. 1992). In human studies, oxyntomodulin has been shown to acutely suppress appetite and reduce caloric intake as well as reduce body weight and increase activity-related energy expenditure (Cohen et al. 2003, Wynne et al. 2005, 2006). Within the gastrointestinal tract, oxyntomodulin delays gastric emptying and decreases gastric acid secretion (Schjoldager et al. 1988).

### ***Nutrients and oxyntomodulin release***

To our knowledge, there are so far no published human studies on the effects of different nutrients on postprandial oxyntomodulin metabolism in humans.



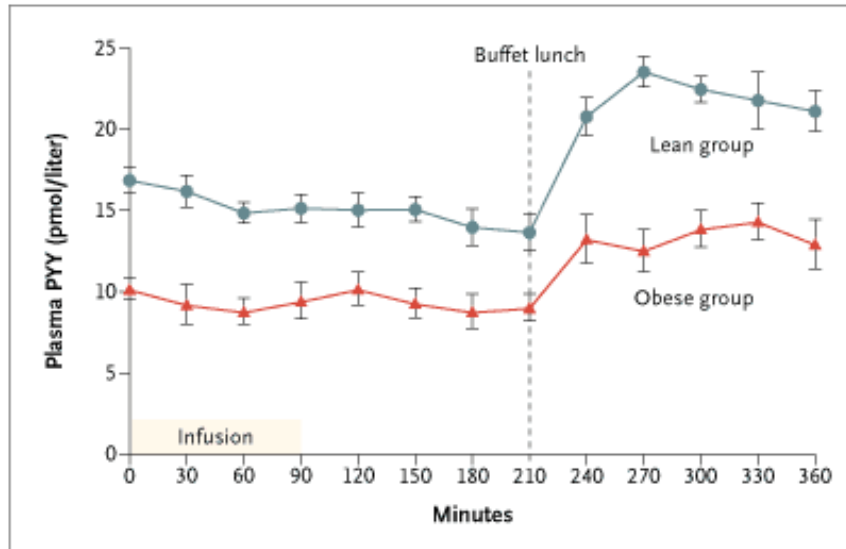
### 2.3.2 Peptide YY (PYY)

Peptide tyrosine-tyrosine (PYY) is a member of the pancreatic polypeptide–fold (PP-fold) family which also includes neuropeptide Y (NPY) and pancreatic polypeptide (PP) (Cox 2007, Cummings and Overduin 2007). PYY is synthesized and released in response to food intake primarily from the endocrine L-cells in the distal parts of the GI tract, especially ileum, colon and rectum (Adrian et al. 1985). Smaller amounts of PYY are also produced in the upper parts of the small intestine. According to animal studies, PYY is also present in the CNS, with PYY immunoreactive nerve terminals in the hypothalamus, medulla, pons, and spinal cord. Receptors that mediate the effects of PYY belong to the NPY receptor family and include Y1, Y2, Y3, Y4 and Y5. Among some other functions, PYY mediates ileal and colonic brakes, mechanisms that ultimately slow gastric emptying and promote digestive activities to increase nutrient absorption (Cox 2007). PYY is also involved in a wide range of digestive functions including regulation of insulin secretion and glucose homeostasis (Boey et al. 2007).

A marked amount of postprandially released PYY is rapidly proteolyzed by DPP4 to PYY<sub>3-36</sub>. The biological activity of PYY is not abolished by the conversion, rather there is a subtle change in pharmacology; full length PYY activates receptor types Y1, Y2 and Y5, whereas PYY<sub>3-36</sub> activates receptor types Y2 and Y5 (Cox 2007). This change in target activity may be important to the effects of PYY on digestive and feeding behavior, as well as satiety after the meal. However, quite a little information is available with respect to circulating molecular forms of PYY (Beglinger and Degen 2006).

#### *Nutrients and PYY release*

PYY increases after meal ingestion and decreases during fasting in a manner consistent with a meal-related signal of energy homeostasis (**Fig. 5**). However, it does so independently of regulation by leptin (Chan et al. 2006). PYY secretion occurs even before nutrients have reached the PYY-containing cells of the ileum. The postprandial PYY secretion is thus biphasic, stimulated initially by atropine-sensitive neural projections from the foregut, followed by direct nutrient stimulation in the gut.



**Figure 5.** Postprandial plasma peptide YY concentrations before and after a buffet meal in lean and obese subjects (Batterham et al. 2003).

Nutrients stimulate PYY plasma levels within 30 min of ingestion of a meal, reaching usually the maximum within 60 min (Adrian et al. 1985). The release of PYY is proportional to calorie intake; the greater the energy intake, the greater the PYY release. However, the composition of the meal also affects postprandial PYY release. Dietary fat, carbohydrates and protein have all been shown to stimulate PYY release but to a different degree and with different time-courses (Cox 2007). By contrast, PYY is not altered by gastric distension (Oesch et al. 2006), water loading (Pedersen-Bjergaard et al. 1996) or sham feeding (Soffer and Adrian 1992).

The ranking order of the stimulatory effects of different nutrients on PYY has differed across studies. In a study by Adrian et al. (1985), fat (as double cream) elicited the largest increase in postprandial PYY concentration, protein (as steamed cod) a more moderate increase, whereas glucose solution caused only a transient and minor release. The order between lipid and glucose was also the same in a study by MacIntosh et al. (1999). In contrast, in a study by Pedersen-Bjergaard et al. (1996), the PYY concentrations increased after the protein and the carbohydrate meal and there was only a slight rise after the fat meal. Both during the intraduodenal infusion of lipids and glucose there have been positive correlations between changes in plasma PYY concentrations and changes in fullness ratings (MacIntosh et al. 1999).

All fats do not stimulate PYY release equally. Fat-induced stimulation of PYY is dependent on fat digestion (Feinle-Bissett et al. 2005). Furthermore, both the load, and duration, of small intestinal lipid exposure influence antropyloroduodenal motility and pattern of PYY release (Pilichiewicz et al. 2006, Feltrin et al. 2007). The effects of intraduodenal fatty acids on PYY also depend on fatty acid chain length. A 12-carbon

fatty acid (C12) increased PYY compared with a control and a 10-carbon one (C10), while C10 had no effect (Feltrin et al. 2006). Similarly, perfusion of long-chain triglycerides (sodium oleate) increased the plasma PYY concentration more than did medium-chain triglycerides (sodium caprylate) (Maas et al. 1998). By contrast, a fat replacer (sucrose polyester) did not change PYY concentration at all (Maas et al. 1998). On the other hand, in another study, plasma PYY levels were consistently higher after the ingestion of oleic acid-enriched liquid mixed meal than after the ingestion of linoleic acid (sunflower oil) enriched meal (Serrano et al. 1997). Also, in another study ileal infusions of oleic acid solutions induced a dose-dependent increase of PYY (Pironi et al. 1993). In both of these studies, oleic acid also slowed gastric emptying and the slower rate of gastric emptying was dose-dependently related to increased plasma PYY concentrations (Pironi et al. 1993, Serrano et al. 1997).

Psyllium-fibre enrichment of meals induces slower but a more prolonged increase in plasma PYY concentrations as compared with eucaloric meals with no added fibre (Karhunen et al. 2005). However, there might be differences in the postprandial PYY responses between different fibre types. In a recent study, postprandial PYY release was greater after the ingestion of oat-fibre enriched bread or white wheat bread than after the intake of bread with wheat fibre (Weickert et al. 2006). In our own study, postprandial PYY responses did not differ after eucaloric puddings enriched with the same amounts of wheat (insoluble) or oat bran (partly soluble) (Juvonen et al. 2006).

The stimulatory effect of protein on PYY has been seen after the ingestion of different protein solutions of similar energy density (whey or casein whole protein, whey or casein hydrolysate) (Calbet and Holst 2004). There might still be differences in the time course of postprandial PYY secretion among different protein sources. In a study by Sangaard et al. (2004), ingestion of fermented milk resulted in slightly greater PYY concentrations compared with whole milk in the initial part of the study, but after the crossover the whole milk meal resulted in higher PYY concentrations than the fermented milk. Soy isoflavone supplementation for eight weeks has also been shown to increase plasma PYY concentrations in healthy postmenopausal women (Weickert et al. 2006b). However, the increased soy protein content of a single meal does not modify the PYY release (Karhunen et al. 2005).

In conclusion, PYY increases after meal and decreases after fasting in a manner consistent with a meal-related signal of energy homeostasis. Dietary fat, carbohydrates and protein all stimulate PYY release but to different degrees and time-courses. Slower rate of gastric emptying is dose-dependently related to increased plasma PYY concentrations, although the role of PYY seems to be contributory for that of GLP-1 in the inhibition of gastric emptying after a mixed meal (Enc et al. 2001).

## **2.4 Other gastrointestinal satiety-related peptides**

### **2.4.1 Enterostatin (ENT)**

Enterostatin (ENT) is an aminoterminal pentapeptide, a by-product formed during the cleavage of pancreatic procolipase to colipase in the stomach and small intestine (Larsson and Erlanson-Albertsson 1991). An active colipase is an essential activator for intraluminal fat digestion. ENT may also regulate the intake of dietary fat. In animals, when administered either centrally or peripherally, ENT selectively inhibits the intake of dietary fat (Okada et al. 1991, Erlanson-Albertsson et al. 1991, Lin et al. 1993). In addition to decreasing dietary fat intake, ENT reduces body weight and body fat by increasing thermogenesis. It also decreases insulin secretion.

#### ***Nutrients and enterostatin release***

Until now, only few studies have investigated the effects of food intake on ENT release in humans. Prasad et al. (1999) found that ENT levels in premenopausal lean and obese women did not differ when pre- and postprandial levels were compared after a standardized 1000-calorie mixed meal. However, there was a slight reduction in the serum levels after a meal with increasing obesity, suggesting a delay in the appearance of satiety in obesity.

### **2.4.2 Apolipoprotein A-IV (apo A-IV)**

Apolipoprotein A-IV (apo A-IV) is a 46-kDa glycoprotein that is only synthesized by the small intestine enterocytes in humans (Green et al. 1980) during the packaging of digested lipids into the triglyceride-rich lipoproteins, known as chylomicrons (CM). Subsequently, apo A-IV is secreted together with chylomicrons into the blood and exchanged rapidly from the surface of CMs by other apolipoproteins during CM metabolism in the circulation (Weinberg and Spector 1985).

Apo A-IV synthesis by the epithelial cells of small intestine is stimulated by active lipid absorption (Green et al. 1980, Apfelbaum et al. 1987, Hayashi et al. 1990, Kalogeris et al. 1994). Furthermore, Hayashi et al. (1999) demonstrated that the formation and secretion of CMs are responsible for the stimulation of apo A-IV synthesis and secretion after lipid feeding, but not the digestion, uptake, or the re-esterification of monoglycerides and fatty acids to form triglycerides. Apo A-IV synthesis and secretion is also stimulated by PYY (Tso and Liu 2004).

## *Nutrients and apolipoprotein A-IV*

Postprandial increase in apo A-IV synthesis and secretion after a high-fat meal has been demonstrated (Green et al. 1980, Bisgaier et al. 1985, Miyata et al. 1986, Dallongeville et al. 1997). Moreover, plasma apo A-IV concentrations seem to rise in a dose-dependent manner with increasing dietary fat content (Weinberg et al. 1990). However, there seems to be adaptation in human plasma apo A-IV levels in response to prolonged fat consumption and the elevated plasma apo A-IV levels seem to disappear over time (Weinberg et al. 1990). Apo A-IV production might thus be autoregulated in response to diets with high fat or energy content. Apo A-IV levels might also be altered in obesity. Postprandial apo A-IV increase after an oral fat load was higher in the obese subjects than in the normal-weight ones (Verges et al. 2001).

## **2.5 Satiety-related peptides released from the pancreas**

### **2.5.1 Insulin**

Insulin is a major endocrine and metabolic polypeptide hormone, secreted by the islet  $\beta$  cells of the endocrine pancreas, and one of the key adiposity signals described to act in the brain to influence energy homeostasis (Schwartz et al. 1992). Plasma insulin concentrations are in direct proportion to changes in adipose mass; insulin concentrations are increased at positive energy balance and decreased during negative energy balance. Additionally, plasma insulin concentration is largely determined by peripheral insulin sensitivity which is related to the amount and distribution of body fat (Porte et al. 2002). Thus, insulin provides information to the central nervous system, both about the size and distribution of adipose mass as well as recent changes in metabolic status, and in that way it regulates food intake, energy balance, and body adiposity in the long term (Havel 2001).

In addition to the long-term effects of adiposity on insulin concentrations, the well-known occurrence of insulin is related to the postprandial metabolism of energy providing nutrients. The secretion and circulating concentration of insulin is influenced by recent energy intake and dietary macronutrients, which is manifested as a rapid insulin surge after food ingestion (Polonsky et al. 1988). The postprandial rise in insulin concentration is a consequence of nutrient ingestion and stimulation by incretin hormones such as GIP and GLP-1 (D'Alessio et al. 2001). Moreover, insulin concentration decreases during energy-restriction and fasting, independent of body fat changes, ensuring that feeding is triggered before body energy stores become depleted (Havel 2001).

However, the role of insulin in short-term appetite regulation is controversial. Increased insulin concentrations have been shown to promote hunger and thereby increase energy intake at a subsequent *ad libitum* meal (Rodin et al. 1985).

In the light of the aforementioned evidence, there is a considerable consensus that insulin is an important short- and long-term regulator of food intake and energy balance. That is, circulating insulin aids in modulating the short-term signaling of satiety and the long-term levels of adipose stores in the body in any particular environment (Havel 2001).

### ***Nutrients and insulin release***

The endocrine cells of the pancreatic islets respond rapidly to nutrients in the blood stream. Only small monomeric molecules, such as monosaccharides, long-chain fatty acids, L-amino acids, and ketone bodies are affecting secretion while large polymeric nutrients, such as glycogen or triglycerides, do not (Newgard and Matschinsky 2001). It is noteworthy, that there is no nutrient-induced inhibition of insulin secretion; rather, all the nutrients have a stimulatory effect on insulin secretion. However, nutrients might inhibit insulin secretion indirectly by affecting secretion of other inhibitory hormones, like somatostatin or glucagon, which in turn diminish insulin secretion (Kiefer et al. 2001, Patel 1999). Metabolic endproducts or intermediates, such as lactate, pyruvate, glycerol, and citrate, do not affect insulin secretion.

Considering the sources of digestible carbohydrates, glucose is the most powerful stimulator of insulin secretion and independent of other fuels while it can potentiate other stimuli (Newgard and McGarry 1995). Accordingly, dietary glucose causes a greater insulin release than an equal amount of e.g. starch (Ullrich and Albrink 1985). By contrast, the digestible carbohydrate, fructose, does not stimulate insulin secretion. Amino acids and fatty acids are ineffective in the absence of glucose, or stimulate insulin secretion only weakly when circulating glucose concentrations are low (i.e. in fasted state). Circulating glucose concentrations, higher than 5 mM, stimulate insulin release (Newgard and Matschinsky 2001) with the highest release rate at glucose concentrations ranging from 5 mM to 10 mM (Henquin et al. 2006).

Indigestible complex carbohydrates, i.e. diverse forms of dietary fiber, may exert beneficial effects on postprandial insulin action. High fiber foods cause a much lesser insulin response than does glucose (Ullrich and Albrink 1985). Dietary fiber could displace some of the carbohydrates that would normally be absorbable in the small intestine, or could translocate the carbohydrate to a point lower in the intestinal tract where less effect on insulin secretion would be observed. Moreover, the extreme fluctuations between the fed and fasted states seen with low fiber intake are dampened

by high fiber diets. Accordingly, consumption of foods high in fiber is associated with beneficial effects on insulin sensitivity and insulin resistance (Jenkins et al. 2000, Bessesen 2001, Erkkilä and Lichtenstein 2006). This effect has been seen especially after the ingestion of soluble viscosity-producing fibres, such as oat  $\beta$ -glucan, although insoluble fibers, primarily from the cereal products, have also been associated with lower incidence rates of e.g. cardiovascular diseases. Several recent studies have also suggested that diets low in glycemic index may improve insulin sensitivity (Ludwig et al. 1999, Wolever 2000).

Protein behaves as an insulin secretagogue (Simpson et al. 1985), though there seem to be differences in postprandial insulin responses after different kind of dietary proteins (von Post-Skagegård et al. 2006). For example, milk protein has been shown to produce a larger postprandial insulin response than fish (cod) or plant (soya) protein. Furthermore, of the milk proteins, whey leads to higher insulin concentrations compared to casein (Dangin et al. 2001). Indeed, amino acids differ in their capability to release insulin. In general, alanine, glutamine, lysine and branched chain amino acids (leucine, isoleucine, valine) stimulate insulin release (Newgard and Matschinsky 2001, Nilsson et al. 2004). However, amino acid stimulated insulin release requires permissive levels of blood glucose (2,5 mM to 5 mM). The only exception is leucine, which stimulates insulin secretion even in the absence of glucose. That is due to the twofold action of leucine on the metabolism of  $\beta$ -cells (Newgard and Matschinsky 2001). The role of arginine on insulin secretion is controversial. Some reports argue that arginine stimulates insulin release, especially when administered together with glucose (Copinschi et al. 1967, Palmer, et al. 1975). However, the opposite has also been reported (Gannon et al. 2002).

The role of free fatty acids on insulin secretion is controversial. It is known that short-term elevation of plasma free fatty acids is beneficial for insulin secretion profile (Newgard and Matschinsky 2001). Elevation of non-esterified fatty acids upon fasting is required for the glucose-stimulated insulin release (Stein et al. 1996). The chain length and saturation degree of fatty acids might play a role in stimulation capacity, i.e. saturated long-chain fatty acids (especially palmitate and stearate) had the highest capacity to stimulate insulin secretion, whereas the medium-chain saturated fatty acids were not as potential in isolated perfused rat pancreas (Stein et al. 1997).

However, when free fatty acids are elevated chronically, insulin secretion capability of pancreatic  $\beta$ -cells is disturbed (McGarry 2002). In line with that, the association of elevated free fatty acids, obesity and type II diabetes is well established (Kahn et al. 2006). Chronic elevation of free fatty acids is initially increasing insulin secretion during a low glucose concentration, but subsequently, impairing the insulin response to high concentrations of glucose (Prentki et al. 2002). In addition, it has been suggested

that free fatty acids could compete with glucose for substrate oxidation leading to inhibition of subsequent signalling cascade (Randle 1998).

### **2.5.2 Amylin**

Besides insulin, pancreatic  $\beta$ -cells additionally secrete amylin (also known as islet amyloid polypeptide, IAPP). Amylin is a novel 37 amino acid peptide hormone that is secreted in conjunction with insulin from the pancreas in response to nutrient stimulus. Amylin was first isolated from pancreatic amyloid deposits typically found in type II diabetics (Cooper et al. 1987). Amylin is an anorexigenic peptide shown to reduce meal size and in some studies the number of meals as well (Lutz et al. 1995, Lutz 2006). The inhibitory effect of amylin on food intake is thought to be due to the inhibition of gastric emptying (Reda et al. 2002). Amylin is stored in same granules as insulin and cosecreted in response to stimuli evoking insulin release (Cooper 2001). Amylin also inhibits gastric acid and glucagon secretion (Cummings and Overduin 2007, Lutz 2006). Hence, amylin is considered to be required for the proper function of insulin in the control of nutrient flux by its ability to regulate nutrient appearance and postprandial glucose concentrations (Lutz 2006).

#### ***Nutrients and amylin release***

Concerning amylin as a satiety inducing hormone, it is clearly established that amylin is released during meals (Lutz 2006) and the effects of nutrients in amylin secretion are similar to that of insulin (Moore and Cooper 1991). In human studies, it has been shown that plasma amylin concentrations rise after a glucose load (Mitsukawa et al. 1990), a meal rich in carbohydrates (van Hulst et al. 1996), and after mixed meals (Butler et al. 1990, Heptulla et al. 2005). To our knowledge, there is only one published human study on the effects of dietary fat on amylin, showing no differential effects on postprandial amylin after moderate changes in dietary fatty acid profile (Poppitt et al. 2004).

### **2.5.3 Pancreatic Polypeptide**

Pancreatic polypeptide (PP) belongs to the same PP-fold peptide family that includes neuropeptide Y (NPY) and peptide YY (Kojima et al. 2007/2), and is secreted by F cells of the endocrine pancreas, comprising approximately <5% of islet volume (Taborsky 2001). Other sites of PP expression include the exocrine pancreas, colon and rectum (Wynne et al. 2004). The main function of PP is thought to be the inhibition of the exocrine pancreas. Secretion of PP is controlled by the parasympathetic nervous system, and therefore it is often used as a marker of the activation of pancreatic parasympathetic



nerves (Rossi et al. 2005). Atropine almost completely blocks PP secretion (Okita et al. 1997). PP has been shown to affect energy balance by suppressing food intake and gastric emptying (Kojima et al. 2007).

Pancreatic polypeptide is secreted in a biphasic manner in proportion to food intake (Kojima et al. 2007, Jesudason et al. 2007). The main stimulus for the release of PP is the activation of the parasympathetic nervous system by food intake (Wynne et al. 2004). The quantity of PP release is related to the nutritional state: release is low in the fasting state but increased throughout the phases of digestion (Adrian et al. 1977, Batterham et al. 2003). There is also evidence that sham feeding and even sole water ingestion stimulate PP secretion (Witteaman et al. 1994, Robertson et al. 2002, Simonian et al. 2005, Crystal and Teff 2006).

### ***Nutrients and pancreatic polypeptide release***

Different dietary factors potentiate PP release and several studies have reported increased postprandial PP after mixed meal conditions (Adrian et al. 1977, Tasaka et al. 1980, Holmbäck et al. 2003, Simonian et al. 2005, Feinle-Bisset et al. 2005). Glucose as well as starch ingestion stimulates PP secretion (Sive et al. 1979, Waldhäusl et al. 1983, Taylor et al. 1985, Layer et al. 1989). However, considering the effects of indigestible carbohydrates, it seems that they have no effect on PP release. In a study by Schwartz et al. (1982, 1988), a diet supplemented with dietary fiber (20 g/d; apple pectin, alpha-cellulose) over four weeks had no relevant effects on postprandial PP concentrations. Negative results have also been demonstrated in later studies performed with dietary fibers (Trinick et al. 1986 (20 g, guar gum), Fuessl et al. 1987 (5g, guar gum), Di Lorenzo et al. 1988 (15 g of pectin/ methylcellulose)). On the other hand, there is also evidence that some dietary fibers, such as soy polysaccharide (10 g), could still affect PP concentrations, although in an attenuating direction (Tsai et al. 1987).

Protein-rich meals stimulate secretion of PP (Schmid et al. 1989, Schmid et al. 1992) in a dose dependent manner (Zipf et al. 1983). This is due to increased levels of circulating amino acids and PP response depends on the respective plasma amino acid concentrations. However, only 35% of postprandial PP levels can be ascribed to the rise of plasma amino acids (Schmid et al. 1992) suggesting that other neural and/or endocrine factors can also contribute to the activation of islet cell function. Indeed, the stimulatory effect of dietary protein on postprandial PP release has been seen even in the sham-fed condition (Witteaman et al. 1994).

Dietary fat increases postprandial PP as well (Owen et al.1980, Lawson et al. 1983, Robertson et al. 2002, Robertson et al. 2004). On the other hand, daily supplementation with excess fat (as cream and peanuts) over a three week period led to decreased

postprandial PP levels (Robertson et al. 2004). Similarly, reduced fasting concentrations of PP were observed in the following morning after a high-fat evening meal (Robertson et al. 2002).

## **3. Methods to measure satiety**

### **3.1 Definition of satiety**

Appetite is influenced by a large number of biological, behavioural, and environmental stimuli. To be able to discuss the biological and physiological processes that stimulate and inhibit food consumption, a number of general terms and concepts have been defined (e.g. Gerstein et al. 2004). The biological drive that forces us to search for food is hunger. The feeling of hunger is an important component in determining what, how much, and when to eat (Blundell and MacDiarmid 1997). When eating reduces hunger, physiological processes are stimulated that inhibit further eating. This process of feeling full and consequently stopping to eat is termed satiation. Satiation increases during eating and tends to bring the period of eating to an end. Satiation (intrameal satiety), therefore, reduces hunger and limits the amount of energy consumed during that meal (Blundell and MacDiarmid 1997). Satiety (intermeal satiety), on the other hand, develops after foods have been ingested. It is the state of satiety that determines the intermeal period of fasting and may reduce food consumption at the next meal (Gerstein et al. 2004).

The mechanisms that regulate hunger, satiation, and satiety, and the consequent food intake, have a physiologic basis but are also strongly influenced by environmental factors, e.g. availability of food or sensory stimulation, or cognitive issues like health beliefs and habitual meal times (Blundell and MacDiarmid 1997, Mattes et al. 2005). Although on the scale of appetite sensation hunger is usually placed on the opposite end from satiation or satiety, one is not simply the absence of the other. The sensations that promote and inhibit eating are regulated both by overlapping and distinct mechanisms. Satiation and hunger can even be simultaneously elevated, e.g. when a palatable sweet is presented after a large meal.

**Appetite** is the desire to eat food, felt as hunger. Appetite regulation is a complex process involving the gastrointestinal tract, many hormones, and both the central and autonomic nervous systems.

**Fullness** is a physical feeling related to the degree of stomach filling.

**Hunger** is a feeling experienced when the glycogen level of the liver falls below a threshold, usually followed by a desire to eat. The usually unpleasant feeling originates in the hypothalamus and is released through receptors in the liver. The sensation of hunger typically begins after several hours without eating.

**Satiation** is the feeling that develops during the meal and finishes intake.

**Satiety** is the feeling between meals that prevents a new intake occasion, the disappearance of hunger after a meal. It is a process mediated by the ventromedial nucleus in the hypothalamus. Various hormones, first of all cholecystokinin, have been implicated in conveying the feeling of satiety to the brain. Leptin increases during satiety, while ghrelin increases when the stomach is empty. Therefore, satiety refers to the psychological feeling of "fullness" or satisfaction rather than to the physical feeling of being engorged, i.e. the feeling of physical fullness after eating a very large meal.

Foods and beverages vary in their capacity to affect appetite. This can be attributed to several properties of food, such as energy content, taste sensation, and physical properties. Assessment of the effects of different properties of foods on appetite provides us with information on factors which contribute to control of appetite control and also factors which can induce overeating. It is useful to measure quantitative effects of foods on short term appetite as this enables comparison of the effects of different foods on hunger and satiety. Hill and Blundell (1982) and Mattes et al. (2005) have reviewed hunger and measurement of satiety. Measurements using different methods, like fixed-point scales, visual analogy scales or psychophysical techniques such as magnitude estimation, show that subjective sensation of hunger increases steadily as mealtime approaches, and decreases sharply after eating. A common belief is that the higher the hunger rating, the more food will be consumed. However, the actual correlation between pre-meal hunger ratings and the amount of food consumed varies. In a similar way, ratings of satiety may not be correlated with consumption. According to Hill and Blundell (1982), measuring only hunger and fullness does not sufficiently describe eating behaviour, as only separate sensations are asked. Hill et al. (1984) have developed a multidimensional formulation in which subjects can partition their subjective experience into physical, emotional, and cognitive aspects. Several terms improve reliability of the measurement and help subjects to relate to the terms that are relevant for them.

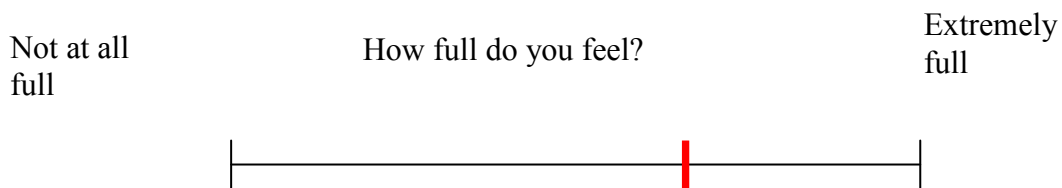
### 3.2 Methods to measure satiety

There is no single, standard method to measure satiety. The problem in measuring satiety is that there is a lot of variation on how people perceive satiety in foods, partly due to their individual eating style and habits and partly due to the subjective nature of the term. As satiety is a subjective concept, it can only be measured indirectly. Two methods are commonly used: 1) satiety has been measured by rating subjective feeling of satiety before and after eating a test meal (e. g. Holt and Brand-Miller 1994, Porrini et al. 1995, Turconi et al. 1995, Holt et al. 2001, Rolls et al. 1998, Flint et al. 2000), 2) satiety has also been measured as the amount of food/energy intake eaten after the test meal (e g. Holt and Brand-Miller 1995, Porrini et al. 1995, Holt et al. 1995, 1996, Guinard and Brun 1998, Zandstra et al. 1999, Flint et al. 2000). These two methods can also be used together, which gives a better estimate of satiety/satiating effect of the test food. Blood tests are also often used in measuring satiety (e. g. blood glucose, insulin). Other methods, such as the microstructure of eating (number of chews, rate of eating) or salivation have been used to measure appetite, but they have not been widely accepted as valid indices of appetite (Barkling et al. 1995, Myers and Epstein 1997, Spiegel 2000, Yeomans 2000).

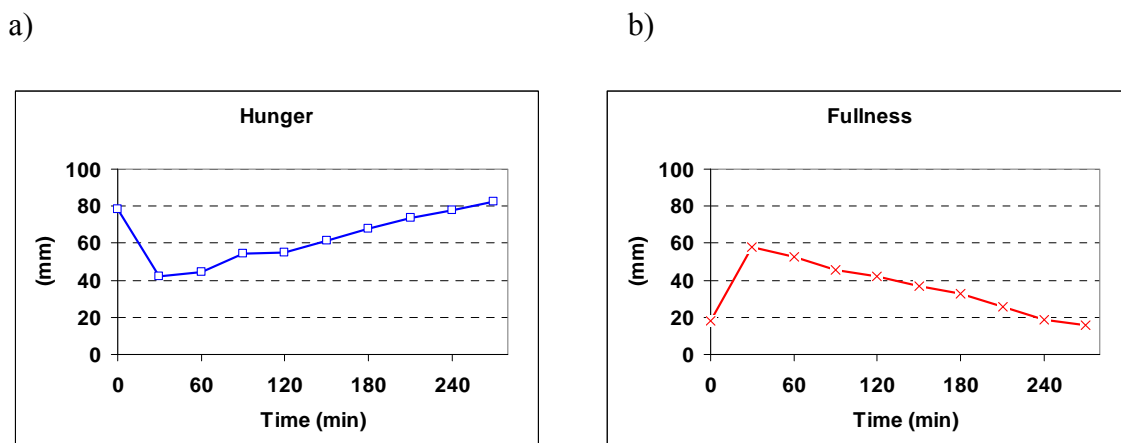
**Table 2** lists a number of satiety measurements, in which the experimental design varies widely. Questions asked to measure satiety vary in the different experiments. Usually in addition to satiety feelings of fullness, hunger and desire to eat have been asked (Kissileff et al. 1984, Holt and Brand-Miller 1994, 1995, Porrini et al. 1995, Turconi et al. 1995, Holt et al. 1995, 1996, 2001, Green and Blundell 1996, Himaya et al. 1997, Crovetti et al. 1997, Guinard and Brun 1998, Rolls et al. 1998, de Graaf et al. 1999, Zandstra et al. 1999, Flint et al. 2000, Bell et al. 2003). In addition to subjective feelings, questions about the food have been asked, e.g. palatability (Porrini et al. 1995), taste, texture, saltiness and sweetness (Guinard and Brun 1998). Time used in the tests vary. Usually feeling of satiety has been measured before and after eating the test food, and at fixed intervals for two to four hours after eating the test food by filling a questionnaire.

In addition to the questionnaire a freely chosen meal (*ad libitum*) or another test meal has been served after defined time (e.g. two hours is commonly used) after eating the test food. The amount eaten is measured and the ingested energy intake is used to measure the feeling of satiety (Holt et al. 1995, 1996, Porrini et al. 1995, Green and Blundell 1996, Guinard and Brun 1998, Zandstra et al. 1999, Flint et al. 2000). Eating patterns have also been used as a means to assess appetite. The assumption is that there is a direct relationship between the intermeal interval and hunger. There are data supporting an association between the size of a meal and the postmeal interval, but intake at a meal is not strongly associated with the time since the last meal (de Castro and Kreitzman 1985).

A visual analogue scale (VAS) is the most commonly used method to assess subjective ratings of satiety. The end points have been anchored verbally, e.g. ‘I’m extremely full’ and ‘I’m not at all full’ (**Fig. 6**). The scales require the participant to respond to a question by placing a mark on a line, which is usually 100 mm or 150 mm in length. The mark is changed to a number by measuring the distance from the left end of the line to the mark. When the measurement is done, before and after eating the test food, and at certain time points after the test meal, a graph can be drawn and the area below the curve can be used as a measure of fullness (**Fig. 7**), hunger or other feelings related to appetite (Flint et al. 2000).



**Figure 6.** Measuring feeling of fullness on a 100 mm visual analogue scale (VAS). Measured at certain intervals before and after eating the test food, e.g. 0, 10, 30, 60, 90, 120, 180, 240 minutes.



**Figure 7.** Feeling of a) fullness and b) hunger measured on a 100 mm visual analogue scale (Flint et al. 2000). 0 min = fullness/hunger before eating the test food, other times after eating the test food.

Sensory specific satiety can affect the results, as satiety/satiation can be towards a specific food item just eaten/ a specific taste or sensory property, and is then not directed to other tastes/ sensory properties. Rolls et al. (1981a, b) have shown that when several foods, differing in taste, appearance and texture, are served one after the other, food intake is greater than when only one food is served. Also, liking of the food decreased faster if only one food was served, in comparison to eating different foods (Ernst and Epstein 2002). The sensory specific satiety caused by a test food can vary

depending on the food item, and is dependent on the sensory properties of the food, but nutrient composition does not cause a similar satiation (Johnson and Vickers 1992, 1993). It is supposed, that sensory specific satiation is to guarantee a sufficiently varied diet. Hetherington et al. (2002) tested the palatability of chocolate and sandwiches and observed that desire to eat chocolate decreased faster than desire to eat sandwiches.

A method commonly used in the UK (Stubbs et al. 2000) contains six different questions (**Fig. 8**; Hill et al. 1984). The measurement uses 100 mm verbally anchored visual analogy scales. Four questions measure appetite: 1) How strong is your desire to eat? 2) How hungry do you feel? 3) How full do you feel? 4) How much food do you think you could eat? In addition two questions are asked about the food: 5) How pleasant have you found the food? 6) How satisfying have you found the food?

Very weak	How strong is your desire to eat?	Very strong
Not at all hungry	How hungry do you feel?	As hungry as I have ever felt
Not at all full	How full do you feel?	Very full
Nothing at all	How much food do you think you could eat?	A large amount
Not at all pleasant	How pleasant have you found the food?	Very pleasant
Not at all satisfying	How satisfying have you found the food?	Very satisfying

*Figure 8. Questions of the visual analogy scales developed by Hill et al. 1984.*

There are only a few studies about reliability and repeatability of the VAS-method. The validity of the test is difficult to measure, as there are no impartial measures for satiety. The validity of a short term satiety measurement can be correlated to energy intake. However, Flint et al. (2000) measured repeatability of the VAS-method by using 55

healthy, normal-weight, 19–36 years old males as subjects. They filled the questionnaire before and after the test lunch and at 30 min intervals after the lunch for 4 hours. After 4 hours they were served an *ad libitum*-lunch, which they ate until they were pleasantly full. The same group made the test twice. Eight questions were asked using a 100 mm verbally anchored visual analogue scale (**Fig. 9**). The subjects were divided into two groups, the other had a defined diet for two days before the test. The diet appeared to have no effect on measured satiety. The measured satiety correlated with energy intake at the *ad libitum* meal (Flint et al. 2000). On the second test day the correlation was better than on the first day, which was supposed to show that the subjects learned to use the scales. Their conclusion was that satiety measurement is valid, in spite of the variation between repeats, when appetite is measured.

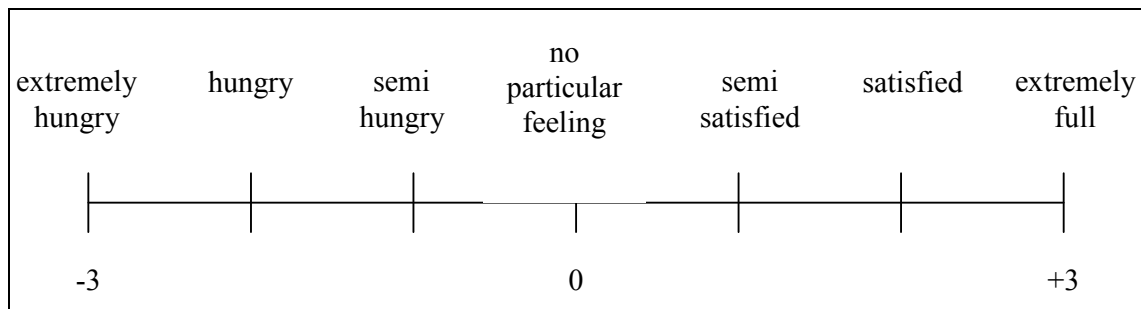


I am not hungry at all	How hungry do you feel?	I have never been more hungry
I am completely empty	How satisfied do you feel?	I cannot eat another bite
Not at all full	How full do you feel?	Totally full
Nothing at all	How much do you think you can eat?	A lot
Yes, very much	Would you like to eat something sweet?	No, not at all
Yes, very much	Would you like to eat something salty?	No, not at all
Yes, very much	Would you like to eat something savoury?	No, not at all
Yes, very much	Would you like to eat something fatty?	No, not at all

**Figure 9.** Questions used by Flint et al. (2000) to measure appetite.

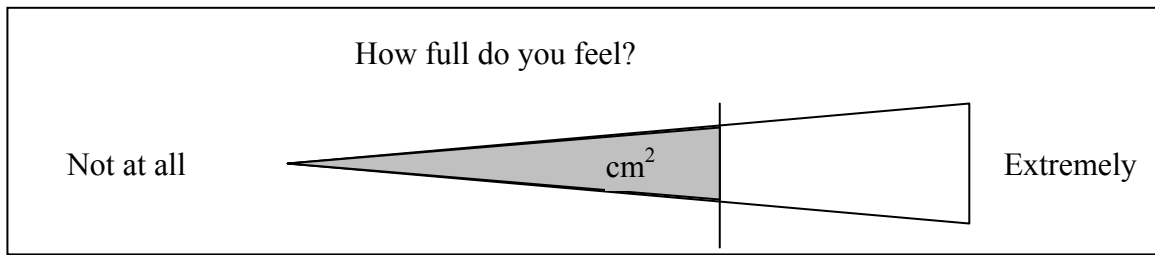
Stubbs et al. (2000) have reviewed the reliability and validity of visual analogue scales in terms of 1) their ability to predict feeding behaviour, 2) their sensitivity to experimental manipulations, and 3) their reproducibility. VASs correlate with, but do not reliably predict, energy intake, and are sensitive to experimental manipulations. They conclude that VAS are more reliable and valid under controlled laboratory conditions than in real life. It is important to consider what people mean when they use the terms hunger, appetite and satiety, that the words have both objective (physiological) and subjective (learned) components – different people feel hunger in different ways (Stubbs et al. 2000).

Both a 100 mm verbally anchored visual analogue scale (Green and Blundell 1996, Himaya et al. 1996, Guinard and Brun 1998, Rolls et al. 1998, Bell et al. 2003) and a 150 mm scale have been used to measure satiety (de Graaf et al. 1999, Zandstra et al. 1999). Holt and her collaborators have used a slightly different 7-point scale to measure hunger/satiety (**Fig. 10**; Holt and Miller 1994; Holt and Brand Miller 1995; Holt et al. 1995, 1996, 2001). The other end of the scale is extremely hungry (-3), at 0 is no particular feeling, and at the other end extremely full (+3). They found that the results were more reproducible using the 7-point scale than with the 100 mm VAS-scale. The subjects found the scale easy to use to measure feelings of hunger and fullness (Holt et al. 1995). Also, the food consumed after 2 hours correlated well with the results.



**Figure 10.** 7-point scale to measure appetite (Holt et al. 1995).

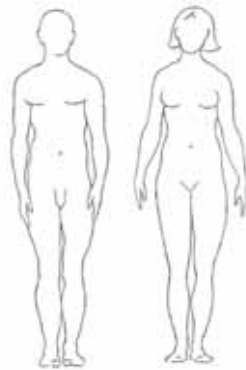
Porrini et al. (1995b) verified reproducibility of three questions related to fullness, satiety and desire to eat, rated on an unmarked triangle (**Fig. 11**). The questions were: “How satiated do you feel?”, “How full do you feel?”, and “How great is your desire to eat?”. The subjects were asked to rate their sensations by drawing a line, parallel to the baseline, across an isosceles triangle (height 15 cm, base 3 cm) oriented horizontally on the paper with the base to the right. The apex of the triangle was verbally anchored as minimum (not at all), and the base as maximum (extremely). The ratings were expressed as area (cm<sup>2</sup>). The triangle rating scale was chosen in preference to fixed point scales to avoid any recall of previous rates: numbers are easily remembered and might be used by the subjects to reflect not only feelings of satiety, but also the preconception of what should be felt during a meal. In the triangle the area increases were expected to help subjects to better quantify hunger and satiety sensations which have an increasing and decreasing trend. There was a good linear relation between intake and satiety ratings, the method could discriminate sensations felt after two loads of the same food with different energy content. The differences in the sensations felt were confirmed by the food intake data (Porrini et al. 1995b). The same triangle scale and questions have also been used in other studies by Porrini and her collaborators (Porrini et al. 1995a, Crovetti et al. 1997, Berti et al. (2005).



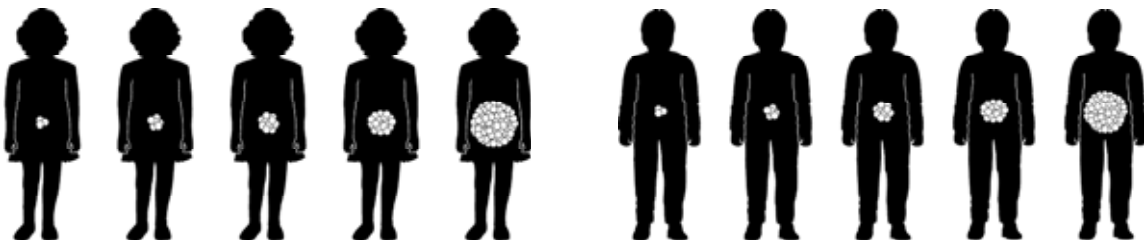
**Figure 11.** Appetite measurement using a triangle scale (Porrini et al. 1995).

Friedman et al. (1999) used figurative measure to assess subjective hunger sensations (**Fig. 12**). In the study, the subjects indicated where they felt hungry on a drawing of a human figure. Approximately half of the subjects indicated the abdominal area with slight hunger, the proportion of subjects indicating other or additional body sites grew significantly with increasing hunger states. Lowe et al. (2000) compared the figurative measure of Friedman et al. (1999) to verbal hunger measures. They observed that the figurative assessment provides information complementing the information provided by traditional verbal measures. The method has also been modified to a silhouette satiety scale for children, which corresponds to a one to five ordinal scale (Faith et al. 2002).

a)



b)



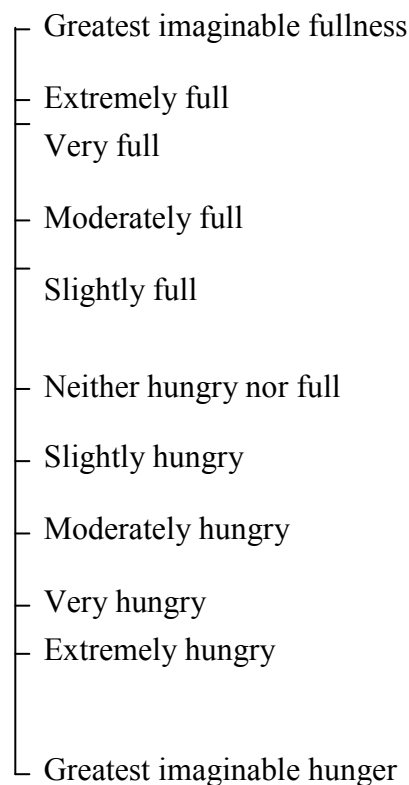
**Figure 12.** Pictorial measures of appetite: a) a figurative measure of subjective hunger sensations (Friedman et al. 1999), b) two silhouette satiety scales for children (females and males; Faith et al. 2002).

Merrill et al. (2002) assessed the sensitivity and reliability of five different 100 mm visual analogue scales of satiety: 1) a bipolar hunger-fullness scale (extremely hungry – extremely full), 2) a unipolar hunger scale (extremely hungry – not at all hungry), 3) a unipolar fullness scale (not at all full – extremely full), 4) a unipolar ‘amount could eat’ scale (a large amount – none at all), and 5) a 7-point equal interval, bipolar scale of hunger/fullness (1 = extremely hungry, 2= hungry, 3=semi hungry, 4=no particular feeling, 5= semi satisfied, 6= satisfied, 7 = extremely full). Foods were prepared in 240 kcal portions. Subjects rated their baseline subjective hunger/fullness on each of the 5 test scales, after which they were served one of the test foods. Subjects ate these foods within 10 min and then rated their liking/disliking on a 9-point hedonic scale; hunger/fullness was then rated at 10-min intervals for 1 h using the 5 test scales presented in random order, after which an *ad libitum* continental breakfast was provided. The same procedure was repeated with the same subjects one week later to assess test-retest reliability. Changes in scale ratings of all sensations followed the same general pattern. All measures declined monotonically with time; there was also an effect of foods and a time x food interaction. The first bipolar hunger/fullness scale had the highest correlation for both weeks of study, followed by the equal-interval bipolar scale. The unipolar ‘amount could eat’ scale was least reliable and had the lowest association with the other scales. Individuals were better able to differentiate hunger than fullness. Another aspect of the data concerned the amount of time required to index the satiety value of a food. Measuring satiety over the course of one hour may be underestimating the area under the curve for more satiating foods, a longer period of time may be necessary to accurately predict that satiating capacity of such foods. However, correlations among ratings at 30 and 60 min showed a high degree of association between the ratings, suggesting that a 30-min testing may be as predictive of the satiety value of a given food as a 60-min testing period.

A new 100 mm labelled magnitude scale of satiety was developed, based on the study, to establish a simple, more quantitative technique to index perceived hunger and/or fullness (**Fig. 13**, Merrill et al. 2004, Cardello et al. 2005). Thirty-seven subjects rated the semantic meaning of 47 phrases describing different levels of hunger/fullness using a magnitude estimation. Eleven phrases were then selected using criteria of response consistency, symmetry, bipolarity, and inclusion of the end-point anchors of ‘greatest imaginable hunger (fullness)’. These phrases were placed along a vertical line scale at positions corresponding to their geometric mean magnitude estimates to create a labelled magnitude scale of satiety (Cardello et al. 2005). This Satiety Labelled Intensity Magnitude (SLIM) scale was compared to VAS scales for sensitivity and reliability in two studies. The SLIM scale was shown to have greater sensitivity, also reliability was found to be highest for the SLIM scale.

Perceived satiety value of different military ration items were indexed using the SLIM scale, and effect of nutrient composition, physical characteristics and sensory properties on satiety were assessed (Merrill et al. 2004). 2 commercial food items and 17 military ration items, each of 300 kcal portions, were tested. Satiety levels were measured before eating, just after eating, and then every 15 min for 1 h. Sensory attributes and acceptability were rated. Overall satiety responses for each item were quantified using the area under the 75-min response curve (AUC). The mean AUC for each food item was divided by that of a reference food to obtain a satiety index (SI). Results showed that among the 19 foods, there were significant differences in perceived satiety. Oatmeal had the greatest AUC. Perceived satiety was influenced by 4 variables: perception of fatty/oily/creamy; protein content; fat content; and initial satiety. Lower perceived satiety was linked to higher initial satiety and higher fat content, whereas greater perceived satiety was linked to higher protein content and higher fatty/oily/creamy ratings. The positive association of the perception of fatty/oily/creamy to satiety value was suggested to be through cognitive influence related to the belief that such foods are energy dense and therefore more filling. In context of perceived satiety, a belief that a food is energy dense may increase perceptions of fullness.

#### How hungry or full you are right now?



**Figure 13.** Labelled magnitude scale of satiety, note the unequally spaced intervals (SLIM, satiety labelled intensity magnitude) (Merrill et al. 2004).

### 3.3 Satiety index and satiety quotient

Feeling of satiety can be evaluated as a function of time, but it is not the “whole story”. If satiety feelings are to be compared, a number value that can be referenced to known materials/foods is needed. A satiety index –system has been developed in Australia (satiety index, SI), that can be used to compare the satiety values of different foods (Holt et al. 1995, Holt 1998). Satiety index can be compared to glycaemic index. Satiety index gives the short term satiety effect of a food in relation to satiety caused by isoenergetic amount of white bread (Holt 1998). Holt et al. (1995) calculated the satiety index as follows: satiety response curve of one subject consuming 1000 kJ test meal followed for 120 min is measured. The area below the curve is divided by the average AUC of a group having consumed 1000 kJ of white wheat bread and the result is converted to percentages by multiplying with 100. The satiety index of a given food was then calculated as an average of the satiety indexes calculated for each subject. With this method the satiety index of white wheat bread is 100. If the satiety index is <100, the satiety effect of the food is less than that of white wheat bread, if it is >100, the food is more satiating than white wheat bread. A similar satiety index has also been developed by Merrill et al. (2004).

Green et al. (1997) have introduced the term SQ, satiety quotient, to describe the satiety effect of a food. SQ is calculated by subtracting the value of desire to eat before eating from desire to eat after eating a given food and by dividing the difference with the weight or energy of the food eaten. SQ is calculated at several different time points to give the development of satiety over a given time period. Drapeau et al. (2005) modified the SQ by not measuring it over time because of the rather short interval of appetite ratings after the meal in their study. Instead, they used the mean post-meal appetite sensations to evaluate SQ or the satiety signal capacity in response to a standardized meal test (**Fig. 14**). In addition, SQ values were multiplied by 100 to obtain a more meaningful range of values. SQ has been shown to be associated with energy intake (Drapeau et al. 2005) and is considered a more valid indicator of satiety than the 1 h postprandial AUC because it takes into account the pre-meal appetite sensations and the caloric content of the meal. Drapeau et al. (2007) evaluated the use of appetite sensations to predict overall energy intake and body weight loss using a buffet style *ad libitum* test lunch and a three-day self-report dietary record as measures of energy intake. Their results showed that appetite sensations are relatively useful predictors of spontaneous energy intake, free-living total energy intake and body weight loss. They also confirmed that SQ for fullness predicts energy intake, at least in women. However, in predicting body weight loss, fasting state appetite sensation for desire to eat, hunger and prospective food consumption (on visual analogue scales) represented the best markers (Drapeau et al. 2007).

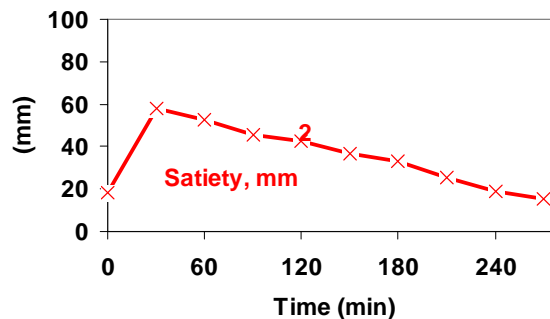
$$\begin{aligned}
 & \text{[SQ](mm/kcal)} \\
 & = \frac{(\text{fasting AS} - \text{mean 60 min post meal AS})}{\text{energy content of the test meal(kcal)}} \times 100.
 \end{aligned}$$

**Figure 14.** Calculation of satiety quotient (Drapeau et al. 2005).

The satiety effect of a food cannot be evaluated based only on energy intake and nutrients, as also the sensory quality and physical properties of the food affect the satiating effect. Holt et al. (1995) have proposed that the energy:satiety –relation of foods would be a welcome addition to caloric value tables to indicate, which foods give much in relation to their satiating effect (**Fig. 15.**; Holt et al. 1995, Holt 1998).

$$\text{Satiety index (\%)} = \frac{A_{\text{sample}}}{A_{\text{reference}}} * 100$$

where A is area under the curve:



**Figure 15.** Calculation of satiety index (Holt et al. 1995, Holt 1998).

### 3.4 Physiological biomarkers

The search for the physiological biomarkers of appetite is active at the moment, but so far no clear winner has been found. Many physiologic changes, such as gut peptide concentrations, are related to appetitive ratings or food intake and can be used as biomarkers of appetite. Interest in the use of biomarkers to measure hunger and satiety is based on their presumed lower susceptibility to subjectivity and modification by environmental factors. A useful biomarker must be sensitive to changes in appetite sensations and relate to the physiology of appetite.

### **3.4.1 Blood glucose**

Fluctuations in blood glucose concentration, even those within the normal postprandial range, affect gastric emptying in rats (Louis-Sylvestre and LeMagen 1985). Hypoglycemia accelerates (Liu et al. 1999) and hyperglycemia slows (Fraser et al. 1990, Russo et al. 2005) gastric emptying. Therefore it has reasonably been proposed that blood glucose concentration also affects appetite and food intake. This hypothesis has been backed up by studies that have revealed the presence of glucoreceptors in both the central (Lavin et al. 1996) and enteric nervous system (Ritter et al. 2000). However, studies have failed to show any significant inhibition of food intake and appetite ratings after intravenous infusions of glucose (Kong et al. 1999). On the other hand, there is considerable evidence that a decrease in blood glucose concentration is associated with meal initiation (Melanson et al. 1999a, b). Thus, it is not clear whether blood glucose intrinsically is associated with short-term regulation of appetite.

### **3.4.2 Blood insulin**

Like blood glucose, insulin has been suggested to be involved in short-term appetite regulation (Lavin et al. 1996). However, the role of insulin in short-term appetite regulation is controversial. Increased insulin concentrations have been shown to promote hunger and thereby increase energy intake at a subsequent ad libitum meal (Rodin et al. 1985), whereas some studies show no association between insulin concentrations and appetite sensations (Woo et al. 1984; Gielkens et al. 1998). Speechly and Buffenstein (2000) found that insulin concentrations before a test meal were inversely related to subsequent ad libitum energy intake in normal weight, but not in obese males. Since high concentrations of blood glucose and insulin are associated with obesity (Bonadonna et al. 1990), it seems possible that the potential effects of blood glucose and insulin in the short-term appetite regulation may differ between normal weight and overweight or obese participants.



*Table 2. Studies measuring effects of different foods on satiety.*

Aim of the study, reference	Subjects f = female m = male	Food tested	Experimental design		Satiety measurement			Other measurements
			Before the test	Others	Timing	Questions asked	Scale	
Effect of soup on satiety and energy intake  Kissileff et al. 1984	59 f, 6 men	Soup, crackers, cheese, apple juice	Pre-test meal	Test meal 15 min after preload	After preload and after test meal	Feelings and desire to eat something more	6-point scale, the suitable number was circled	Question about the food
Effect of particle size on satiety and glycaemic response  Holt and Brand-Miller 1994	n = 10; average age 22 years	Muffins made of wheat of different particle size, cooked grains	Fasting for 12 hours	Low-fat milk and the test product, water added to adjust volume of the meal, one week between tests	Before meal, and 15, 30, 45, 60, 90 and 120 min after it	Satiety/hunger	7-point scale, - 3 very hungry, +3 very full	Blood samples before and 15, 30, 45, 60, 90 and 120 min after, blood glucose and insulin
Satiety, glycaemic and insulinemic response  Holt and Brand-Miller 1995	n = 9; 19–26 y	Boiled rice, rice cake	Fasting for 10 h	Water to add meal volume to 600 ml, <i>ad libitum</i> meal 2h later	Before meal, and 15, 30, 45, 60, 75, 90, 105 and 120 min after it	Satiety/hunger	7-point scale, - 3 very hungry, +3 very full	Blood samples (blood glucose and insulin), Palatability, Difficulty to eat Desire to eat more
Repeatability of test  Porrini et al. 1995	12 m; 23–26 y	Pasta, meatballs	Fasting from the evening before	Three energy levels, <i>ad libitum</i> meal after	Before and after test meal, 2 h later	Satiety Fullness Desire to eat	Isosceles triangle, 15 cm	Blood samples (blood glucose) Palatability after test meal
Effect of fibre on satiety  Turconi et al. 1995	12 f and 12 m; 21–36 y	Two breakfast cereals	-	-	Before and after test meal, and 30, 60, 120, 180 and 240	Fullness Satiety Desire to eat	Area from satiety curve	-

Aim of the study, reference	Subjects f = female m = male	Food tested	Experimental design		Satiety measurement			Other measurements
			Before the test	Others	Timing	Questions asked	Scale	
					min after test meal			
Satiety index Holt et al. 1995, 1996	41 students: 11–13 per food item	37 food items: fruit, bakery products, snacks, sweets, breakfast products rich in protein or carbohydrates	Questionary of food eaten the night before and physical activity	Standard portion 1000 kJ, 220 ml water, white wheat bread as reference, <i>ad libitum</i> meal after	at 15 min intervals for 120 min	Hunger/satiety, How much you would like to eat this food, something else, something sweet	Linear 10 cm, 7-point two-direction scale Extremely hungry-extremely full	Satiety index Blood samples (blood glucose and insulin), difficulty to eat, adequacy of the portion size
Satiating effect of a snack bar Green and Blundell 1996	16 m; normal weight, 18–26 y	20 snack bars: salty-high fat, salty-high carbohydrate, sweet-high fat, sweet-high carbohydrate	standard breakfast + standard lunch	minimum 72 h between tests	Before and after lunch, 1 and 2 h after lunch; before and after <i>ad libitum</i> test meal plus at 30 min intervals four times	Hunger Fillingness	Linear 10 cm, very/not at all	Questions about palatability, taste, saltiness and sweetness
Satiety effect of fat Himaya et al. 1997	12 m; 19–24 y	2 test meals	7 day food diary, identical breakfast and dinner at each test time	-	Before and after meal, every 30 min until dinner	Hunger	Linear 10 cm, Not at all/very	Blood samples (blood glucose and insulin), palatability

Aim of the study, reference	Subjects f = female m = male	Food tested	Experimental design		Satiety measurement			Other measurements
			Before the test	Others	Timing	Questions asked	Scale	
Satiety, sweet taste reactivity  Croveti et al. 1997	8 m; 23–26 y	Baked macaroni, meat balls	Fasting for the night before	Maximum 300 ml water during the test, Small and large portion Large portion + <i>ad libitum</i> test meal	Before and after the meal, and 120 min after	Satiety Fullness Desire to eat	Isosceles triangle	Blood samples (blood glucose), palatability
Sensori-specific satiety  Guinard and Brun 1998	16 m and 16 f; young adults, normal weight	8 test foods and 4 lunches Salty vs. sweet Hard vs. soft texture	Normal breakfast	All 8 foods tasted one after the other, then <i>ad libitum</i> lunch	-	Hunger Fullness How much can eat	Linear 10 cm	pleasantness of taste and texture, saltiness, sweetness
Effect of volume on satiety  Rolls et al. 1998	20 m; normal weight	3 milk based beverages, isoenergetic, three volumes (300, 450, and 600 mL)	Evening meal, physical activity and breakfast identical each time	Lunch 30 min after test beverage, dinner over 4 h later	Before and after breakfast, after test beverage and lunch, 3 h after lunch and after dinner	Hunger Thirst Fullness Nausea	Linear 10 cm, Not at all/very	-
Palatability/satiation and satiety  de Graaf et al. 1999	29 f and 9 m; 18–26 y	Tomato soup, standars bread	-	-	Before and after test meal	Hunger	Linear 15 cm	-
Prediction of food intake  Zandstra et al. 1999	30 f and 6 m	5 yoghurts with different sugar content	-	Defined volume test food, <i>ad libitum</i> meal	Before and after test meal	Desire to eat food, something sweet, snack Oversatiation Hunger	Linear 15 cm	

Aim of the study, reference	Subjects f = female m = male	Food tested	Experimental design		Satiety measurement			Other measurements
			Before the test	Others	Timing	Questions asked	Scale	
Repeatability of linear scale measurement  Flint et al. 2000	55 m; 19–36 y	Breakfast	standard diet the day before (part of the group)	<i>ad libitum</i> lunch four h after test breakfast	Before breakfast and after at 30 min intervals for 4 h	Hunger Satiety Feeling of fullness How much can eat Desire to eat something sweet, salty, fatty	Linear 10 cm	-
Effect of different types of bread on satiety, blood glucose and food intake  Holt et al. 2001	n = 10; 19–39 y	7 breads	Identical dinner before each test, fasting for 1–12 h	Minimum 1 day between tests, reference bread	before, after and at 15 min intervals for 120 min after test meal	Fullness Amount of bread needed to suppress hunger Alertness	7-point linear scale for fullness	Blood samples (glucose) Satiety index Questions about bread
Volume and energy effects on sensory specific satiety  Bell et al. 2003	36 students	Milk-based beverage, different volume and energy content	-	-	Before and after	Hunger Satiety Desire to eat Thirst Nausea	Linear 10 cm	-
Sensitivity and reliability of 5 different 100 mm visual analogue scales of satiety  Merrill et al. 2002	n = 19	yoghurt, multigrain bread, maple and brown sugar oatmeal and croissants; 240 kcal portions		Subjects ate these foods within 10 min and then rated their liking/disliking on a 9-point hedonic scale;	at 10-min intervals for 1 h, after which a full continental breakfast was provided	Fullness	a bipolar hunger-fullness scale; a unipolar hunger scale; a unipolar fullness scale; a unipolar 'amount could eat' scale; and	

Aim of the study, reference	Subjects f = female m = male	Food tested	Experimental design		Satiety measurement			Other measurements
			Before the test	Others	Timing	Questions asked	Scale	
							a 7-point equal interval, bipolar scale of hunger/fullness	
To index the perceived satiety value of food items, to assess the relationship of the foods nutritional and sensory properties to satiety, to determine the ability of the sum of the satiety indices of individual food items to predict total meal satiety  Merrill et al. 2004	In total 73 m, 15 f	19 different food items, 300 kcal/portion	usual breakfast	Test at lunch time	at 15 min intervals for 1 h	Hunger/fullness	"Satiety labelled intensity magnitude scale" + 100 mm linear scale, area under the 75 min response curve was used to calculate a satiety index for the food items	Ratings of acceptability and sensory attributes
Effect on appetite control of minor cereal and pseudocereal products  Berti et al. 2005	bread study 15 m, pasta 14 m, quinoa study 12 m	Oat bread, oat and buckwheat pasta, quinoa risotto compared to corresponding wheat or rice foods	Fasting overnight, usual breakfast	Test at lunch time	Subjects were instructed to eat each food, together with 500 ml water, until they felt "comfortably full"	Satiety Fullness Desire to eat	Isosceles triangle	Pleasantness (after consumption of foods)
Effect of palatability on the effect of	Experiment 1: 16 m	Experiment 1: Low and high	Fasting overnight	Exp. 1: Test at breakfast	Subjects were	Exp. 1: Hunger,	From 0 (not at all) –	Exp. 1 & 2: Mood related

Aim of the study, reference	Subjects f = female m = male	Food tested	Experimental design		Satiety measurement			Other measurements
			Before the test	Others	Timing	Questions asked	Scale	
energy density on short-term food intake and changes in rated appetite  Yeomans et al. 2005	Experiment 2: 16 m	energy density oat porridge, both as bland and palatable (optimally sweetened) version Experiment 2: Palatable (Exp 1) low and high energy density oat porridge, both with either cinnamon or blueberry flavouring, with or without pink food colouring		time between 9.00–11.00 Exp. 2: Test at breakfast time between 08.00–09.30.	instructed to eat as much as they liked	fullness, food pleasantness after every 50 g of food consumed Exp. 2: Hunger, fullness, food pleasantness before and after eating	500 (very)	ratings, food intake

y = years

## 4. Energy density

Energy density of foods, as opposed to their sugar and fat content, is considered an important factor in the regulation of energy intake (Poppitt and Prentice 1996, Prentice and Poppitt 1996, Rolls et al. 1999, Drenowski 1999). Energy density (kJ or kcal / g) is defined as the amount of available energy per weight of food. Water content, content of energy nutrients (fat, protein, and carbohydrate), content of fibre and sweeteners affect the energy density. The energy density of fat is double the energy density of carbohydrate and protein (9 kcal/g = 37.6 kJ/g vs. 4 kcal/g = 16.7 kJ/g), and therefore, fat has a high influence on the energy density value of foods. Addition of dietary fibre and the substitution of sucrose with less energy dense sweeteners can reduce the energy density. Addition of water or air also adds volume and dilutes/reduces energy density.

Energy density has been proposed to play a central role in determining energy intake (Stubbs et al. 1995, Poppitt and Prentice 1996, Prentice and Poppitt 1996, Drenowski 1998, Rolls 2000, Yao and Roberts 2001). In short term studies, low energy density foods have been shown to increase satiety, decrease feeling of hunger and reduce energy intake. In a study of Bell and Rolls (2001), energy density influenced energy intake across all fat contents in both lean and obese women; energy intake of the group partaking low energy density meals (5.23 kJ/g) was 20% lower than in the high energy density (7.32 kJ/g) meal group. Despite this 20% lower energy intake, there were only small differences in hunger (7%) and fullness (5%). The *ad libitum* meals chosen by the testees had the same volume in both groups. In long term studies low energy density foods have been shown to promote weight reduction (Yao and Roberts 2001). In a multiethnic cohort study (191 023 participants) a 1 kJ/g increase in energy density was associated with an increase in BMI of approximately 1 kg/m<sup>2</sup> in each ethnic sex group (Howarth et al. 2006). This same increase in energy density was associated with a significantly increased risk (4–34%) of being overweight in all ethnic sex groups.

## 5. Macronutrients

Macronutrients exert different effects on satiation and satiety, independent of their caloric value. The most satiating macronutrient seems to be dietary protein when compared with fats and carbohydrates in human subjects and rats; fat has the lowest satiating value and carbohydrates intermediary (Johnstone et al. 1996, Prentice and Poppitt 1996, Stubbs et al. 1996, Porrinin et al. 1997, Reid and Hetherington 1997, Poppitt et al. 1998, Marmonier et al. 2000, Astrup et al. 2000, Bensaid et al. 2002, Westrup-Plantenga 2003, Anderson and Moore 2004). However, in several studies differences in the satiating value of energy-giving nutrients have not been seen (Barkeling et al. 1990, Rolls et al. 1991, deGraaf 1992, Prentice and Poppitt 1996). In some studies the poor satiating capacity of fat is connected to susceptibility to obesity (Prentice and Poppitt 1996).

In spite of the large number of studies, the results on the effects of different macronutrients on satiety and weight control are not conclusive. However, as several studies have shown that the energy density of carbohydrates and protein is lower and satiating power greater than those of fats, favouring them as a means to regulate food intake is of interest. The present conception is that a diet low in fat (fat about 30% of energy) and rich in complex carbohydrates gives the best results in weight management.

### 5.1 Protein

#### 5.1.1 Effect of protein on satiety

High protein food has been shown to cause higher sensory specific satiety and decrease the feeling of hunger more than similar low protein food (van Dewater and Vickers 1996). Several mechanisms have been proposed to the satiety maintaining effect of protein (Havel 2001; Dye and Blundell 2002; Raben et al. 2003). Protein stimulates effectively the secretion of several satiety mediating hormones like insulin, glucagon and cholekystokininin. The concentration of some amino acids, like tryptophan and tyrosin, can also be of importance, as they function as precursors for the satiety increasing mediators, serotonin and dopamine. Protein also increases heat generation after meal (thermogenesis) more than fat or carbohydrates. Rate of oxidation of the different nutrients is expected to affect development of the feeling of satiety.

A high protein meal has been shown to cause a higher feeling of satiety in subjects, whose normal diet is low in protein (Long et al. 2000). In some studies a diet low in fat (~30 E%) and high in protein (~25 E%) has been shown to cause more weight reduction than a diet low in protein (~12 E%) (Skov et al. 1999). Protein has also been shown to



promote weight regulation after weight loss. Lejeune et al. (2003) and Westerterp-Plantenga et al. (2003) observed a significantly smaller weight gain after a low energy diet period in a study group ingesting a higher daily protein diet (18 vs. 15 E%). Studies measuring effects of different proteins on satiety are presented in **Table 3**.

### 5.1.2 Effect of protein source

Different protein sources seem to exert different effects on satiety (Uhe et al. 1992), energy intake (Borzoei et al. 2006), and energy expenditure (Mikkelsen et al. 2000). However, Lang et al. (1998, 1999) found no difference in satiety between egg albumen, casein, gelatin soy and bean protein or wheat gluten. No differences were observed in 24 h energy intake either. In the latter study (1999) differences in post-meal levels of glucose and insulin were observed, which were suggested to depend on differences in stomach emptying rates caused by the different proteins. Mikkelsen et al. (2000) compared the effects of isoenergetic diets rich in pork, soy protein (28% of energy) or carbohydrates (61% of energy, cereal products and potato as carbohydrate sources) on 24 h energy expenditure. Diets rich in pork or soy increased energy intake by 3% compared to the diet rich in carbohydrates, and the diet rich in pork by 2% compared to the diet rich in soy.

Uhe et al. 1992 observed higher satiety after the ingestion of white fish compared to equal protein portion of lean meat or chicken. This was suggested to be due to differences in protein digestion and plasma concentrations and profiles of amino acids. Another study showed that fish protein reduced subsequent energy intake in normal-weight men, compared to isoenergetic beef protein, without any significant differences in appetite (Borzoei et al. 2006). Also, Holt et al. (1995) observed higher satiety with fish than cheese, egg, bean, lentil or beef. A mycoprotein, produced by fermentation of *Fusarium graminearum*, decreased appetite and the amount of food consumed, three hours after the test meal, compared to chicken protein. It also decreased energy intake during the rest of the day in comparison to chicken (24%), without compensation the following day (Turnbull et al. 1993).

There is a continuing consumer interest in vegetarianism, and more generally in the choice of occasional meat-free meals as part of a varied diet (Sadler 2004). An increasing range of main ingredients (pulses, cereal protein, fungi, nuts, vegetables) for the manufacture of meat substitute products are available. The health benefits of mycoprotein include satiety effects (Rodger 2001, Sadler 2004). Effects of tofu or mycoprotein preloads were compared to chicken meat preloads regarding their ability to affect satiety during consumption of lunch and also for their effects on increased eating (compensation) at a subsequent dinner meal (Williamson et al. 2006). Preloads of tofu

or mycoprotein were associated with lower levels of food intake at lunch compared with chicken preloads. Also, these lower levels of food intake at lunchtime were not associated with an increased food intake at dinner. The authors suggested, therefore, that tofu and mycoprotein have satiating properties that persist for several hours after a meal, and that these foods may be useful in the development of low calorie foods that are also filling (Williamson et al. 2006).

The milk peptide, caseinomacropeptide, has been shown to regulate appetite via cholecystokinin and the secretion of stomach and pancreas enzymes in test animals. Gustafson et al. (2001) did not observe a corresponding effect on human appetite or energy intake at a meal two hours after the administration of a beverage containing caseinomacropeptide. Hall et al. (2003) compared the effect of milk casein and whey on blood amino acid profile, secretion of gut hormones, and appetite, and observed that whey caused higher secretion of cholecystokinin, GLP-1 and GIP and had a higher satiating effect than casein. After whey ingestion the blood concentration of branched amino acids was significantly higher than after ingestion of casein. No differences were observed in the concentrations of phenylalanine, often connected with the development of satiety.

The different satiating effects of different types of protein may depend on differences in their digestion, and absorption. It is also possible that it may be caused by other factors, such as fat structure or fat quality. Casein, unlike whey, coagulates in the stomach, due to its precipitation by gastric acid (Hall et al. 2003). Therefore, the time of gastric emptying for casein is longer, which results in a smaller postprandial increase in plasma amino acids compared with whey. The concept of 'fast' and 'slow' proteins has been introduced to describe these differences in the digestion and absorption of proteins. According to this, a fast protein, such as whey, would be more satiating than a slow protein, such as casein (Boirie et al. 1997).

### **5.1.3 Amino acids**

The diet based amino acid tryptophan acts as a precursor for the production of the neurotransmitter serotonin (5-hydroxytryptophan, 5-HTP). 5-HTP has been shown to lower appetite and promote weight loss. Cangiano et al. (1992) observed significant weight loss in obese subjects who had 5-HTP before meal, both when energy intake was limited or not limited. No weight loss was observed in the placebo group. In the 5-HTP-group, ingestion of carbohydrates was decreased and satiety at meals developed fast.

Phenylalanine has been shown to affect satiety. Ballinger and Clark (1994) observed a high dose of phenylalanine (10 g) to cause the secretion of cholecystokinin and thus decrease food intake at a meal, 20 minutes later. However, in a study by Hall et al. (2003a), aspartame (consisting of phenylalanine and asparagine acid, 400 mg), or the

amino acids as such (176 + 224 mg), had no effect on the secretion of cholecystokinin, satiety or energy intake.

*Table 3. Studies measuring effects of different proteins on satiety.*

Aim of the study	Subjects f = female m = male	Food tested	Experimental design		Satiety measurement			Other measurements	Reference
			Before the test	Others	Timing	Questions asked	Scale		
Effect of three different types of protein on satiety	6 m	50 g of protein; beef, chicken or fish as a part of a standard meal	Overnight fast  (meal at 08:30 or 09:00)	Test meal finished within 15 minutes, chewed thoroughly, within-subjects design,  one week between tests	15 min. before meal, immediately before, and 15, 30, 45, 60, 90, 120, 150, and 180 min. after meal (Before each blood sample)	Satiety/hunger	7-point scale,  -3 (very hungry), +3 (very full)	Blood samples 15 min. before, immediately before, and 15, 30, 45, 60, 90, 120, 150, and 180 min. after. Blood glucose, insulin, amino acids, triglycerides.	Uhe et al. 1992
Comparison of the effects of fish protein and beef protein on satiety	23 m	Cod or beef as a part of a standard lunch.  Lunch: 47% protein, 20% fat, 33% CHO	Standard breakfast 4 hours prior to test lunch	Within-subjects design, one week between tests	Immediately before and after meal, every hour between meals	Hunger, satiety, desire to eat, prospective consumption	Visual analogue scale (100 mm)	Energy intake in an ad-libitum meal, 4 hours after test meal	Borzoei et al. 2006
Comparison of the effects of different proteins on satiety	12 m	Proteins: egg albumin, casein, gelatin, soy protein, pea	Overnight fast. Standard breakfast (08:30)	Within-subjects design, two-tailed Latin-square	At 30–60 min. intervals from 08:30 to 22:30	Hunger, satiety, fullness, appetite, desire to eat	Visual analogue scale (100 mm)	Pleasantness of food (after each meal). Energy intake in an ad-libitum	Lang et al. 1998

Aim of the study	Subjects f = female m = male	Food tested	Experimental design		Satiety measurement			Other measurements	Reference
			Before the test	Others	Timing	Questions asked	Scale		
		protein, wheat gluten. Lunch: 61–70% protein.	before test (12:00).	design, one week between tests				dinner (20:00). Blood samples (11:00–19:30) every 30–60 min. Glucose, insulin, triacylglycerol, cholesterol	
Comparison of the effects of casein and whey on satiety	1 m 8 f	Isoenergetic, liquid preloads of casein or whey (1700 kJ) at 11:00.	Subjects told to avoid high-protein meals the evening before and until the study. Standard breakfast before 8:00.	Randomized, single-blind, within-subjects design, one week between tests	Before and after test, and at 20 min. intervals for the next 3 hours.	Hunger, satiety, desire to eat.	Visual analogue scale (100 mm)	Blood samples before and 5, 15, 35, 45, 60, 75, 90, 120, 180 min. after preload. Glucose, amino acids, insulin, GLP-1, GIP and CCK.	Hall et al. 2003
Comparison of the effects of chicken protein and mycoprotein on appetite	13 f	Chicken or mycoprotein (130 g)	Overnight and morning fast	Randomized, not blind, within-subjects design, one week between	Immediately before and after test meal	Hunger, fullness, desire to eat, prospective consumption	Visual analogue scale (100 mm)	Pleasantness of meal	Turnbull et al. 1993

Aim of the study	Subjects f = female m = male	Food tested	Experimental design		Satiety measurement			Other measurements	Reference
			Before the test	Others	Timing	Questions asked	Scale		
				tests					
Comparison of the effects of mycoprotein, chicken and tofu on satiety	42 f	Pasta preload with mycoprotein, tofu or chicken (220 g).	12 hour fast, standard breakfast 4 h prior to test meal.	Randomized, within-subjects design. At least 1 day between tests.	At specific intervals during the day (08:00–22:00)	Hunger, desire to eat, fullness, motivation to eat, thirst.	Visual analogue scale (100 mm). UEM scales.	Compensation of food intake (MSSP). Food intake (UEM).	Williamson et al. 2006
Comparison of the effects of casein, gelatine and soy protein on satiety	9 m	Casein, gelatine and soy protein.	11 hour fast. Standard breakfast 3.5 h before test meal.	Randomized, within-subjects design. 1 week between tests. Protein served at two energy levels.	Every hour during the test day. (08:00–22:00).	Hunger, satiety.	Vertical visual analogue scale (100 mm).	Food intake. Blood samples; glucose, insulin, glucagon. Pleasantness of food (after each meal).	Lang et al. 1999

#### **5.1.4 Effect of protein ingestion on hormonal secretion**

Protein in the diet has been shown to stimulate the release of several gastrointestinal hormones, such as cholecystokinin (Liddle et al. 1985, Bowen et al. 2006a, 2006b, Blom et al. 2006), and glucagon-like peptide-1 (GLP-1; Herrmann et al. 1995, Verdich et al. 2001, Blom et al. 2006, Lejeune et al. 2006, Raben et al. 2003). Ghrelin has been shown to decrease after high protein mixed meals, with yogurt as the primary protein source (Al-Awar et al. 2005, Blom et al. 2006). It has also been suggested that the higher satiety associated with the consumption of protein may partially be mediated by prolonged ghrelin suppression (Bowen et al. 2006) as well as the type of protein ingested (Aziz and Anderson 2007). In another study, ghrelin levels rose to a plateau after the ingestion of a high-protein meal, consisting of turkey (99% protein) (Erdmann et al. 2003). These conflicting findings may be due to differences in the time of digestion and absorption of the test food (Bowen et al. 2006). Both cholecystokinin and GLP-1 have been shown to be satiety signals (Kissileff et al. 1981, Turton et al. 1996, Verdich et al. 2001), whereas ghrelin is a hunger signal (Wren et al. 2001).

## **5.2 Fats**

Several studies have demonstrated that fat is the least satiating of the macronutrients (Blundell and MacDiarmid 1997). Many studies have suggested that fat holds a weaker satiety value than carbohydrates (Lawton et al. 1993, Schutz et al. 1989, Blundell and MacDiarmid 1997) and protein (Blundell and MacDiarmid 1997). Fats are rarely found to be more satiating than carbohydrates (Rolls 1995).

### **5.2.1 Fat and food intake**

There is plenty of evidence that high fat diets increases energy intake. High intake of fat can promote the development of obesity by several different mechanisms:

*Palatability:* High fat foods can often promote excessive consumption, because of their deliciousness. Many aroma compounds are fat soluble and affect the taste of fatty foods. Also, the texture of fat and the mouthfeel it gives are generally considered pleasant (Drewnowski 1997a). The satiating effects of palatable foods develop slower than that of unpalatable foods and therefore the portions eaten are often larger when the food is palatable (de Castro et al. 2000). In some studies obese people have had a higher preference for fatty foods (Drewnowski 1997b).

*Less need of chewing:* High fat foods usually require less chewing and are easier to eat than foods rich in dietary fibre and complex carbohydrates, and are therefore eaten faster. When eating is faster and easier, the portion eaten is often larger (Golay and Bobbioni 1997).

*Volume/weight of food:* A constant amount (volume or weight) of food is usually eaten independently of the energy amount. Therefore, energy intake is easily much higher when eating high fat food compared to low fat food.

*Weaker satiating effect of fat:* The satiating effect of fat is weaker per energy unit than that of carbohydrates or protein (Astrup et al. 2002). After a meal, fat is metabolised slower than carbohydrates or protein, and the satiating effect of free fatty acids in blood circulation is delayed (Reid and Hethernington 1997). Fat does not cause an increase of blood glucose. The reason for the weaker satiating effect of fat can be connected to the hormones mediating information of energy balance. Fat does not stimulate insulin secretion and therefore does not cause insulin-mediated feeling of satiety in the brain. Also, leptin is secreted less after a high fat meal than a high carbohydrate meal (Romon et al. 1999). On the other hand, fat is known to stimulate the secretion of cholecystokinin in the small intestine (Havel 2001), and thus promoting the development of the feeling of satiety. Fat also slows stomach emptying rate, which is expected to lengthen the feeling of satiety.

Lawton et al. (1993) observed that after a low energy lunch obese subjects ingested more energy at dinner when the meal was a high fat one as compared to a high carbohydrate meal. High fat breakfast meals were less satiating and caused a greater food intake in than high carbohydrate breakfasts (Holt et al. 1999). A high carbohydrate breakfast rich in fibre also decreased the whole day energy intake in comparison to breakfast meals rich in fat. Marmonier et al. (2000) observed that the want to eat dinner appeared earlier after a snack eaten two hours after lunch when the snack was high in fat compared to a snack high in protein (but not carbohydrate). However, none of the snacks decreased the amount of energy ingested at dinner. In contrast, Vozzo et al. (2003) observed no differences between test meals regarding subjective feelings of hunger, the spontaneous timing of the next meal, or energy intake during the next seven hours. Also, Raben et al. (2003) noted no difference in the feeling of satiety or energy intake following a fat, carbohydrate, protein, or alcohol test meal.

### **5.2.2 Fat balance**

Energy balance is not correlated with carbohydrate or protein balances, whereas energy balance of lean people is well correlated with fat balance (Golay and Bobbioni 1997).



Fat is mostly used or stored in response to day-to-day fluctuations in energy balance. Obese people appear to have a particularly limited capacity for fat oxidation. The positive correlation between fat intake and lipid oxidation appears not to be present in obese people; increase of dietary fat increases fat storage. Studies in humans show that while carbohydrate and protein stores are closely regulated, fat stores are much less so; we are designed to store excess fat as a reserve for leaner days. Only very large surfeit of carbohydrates will induce lipogenesis (Poppit and Prentice 1996; Golay and Bobbioni 1997).

A variety of evidence indicates that the oxidation of fatty acids in the liver influences feeding behaviour (Friedman 1998, Friedman et al. 1999). It has been hypothesized that increases in fatty acid oxidation in the liver enhance satiety signals (Langhans 1996a, b). This has been demonstrated in experiments showing that the food intake of rats is increased after treatment by agents that inhibit the oxidation of fatty acids (Friedman et al. 1986, Scharrer et al. 1986). Carnitine palmitoyltransferase I (CPT I) transports long-chain fatty acids into mitochondria, the principal site of fatty acid oxidation. In rats, inhibition of long-chain fatty acid oxidation with methyl palmoxirate, which blocks carnitine palmitoyltransferase I and consequently decreases the transport of long-chain fatty acids to mitochondria, stimulates feeding (Friedman et al. 1999).

### **5.2.3 Effect of fat structure**

The physiochemical properties of dietary fats are affected by their structure. Chain length and degree of saturation has an effect on the rate of absorption, oxidation in the liver (Langhans 1996a, b), storage in adipose tissue, secretion of various appetite regulatory peptides, palatability, and fat perception in taste receptor cells (Gilbertson et al. 1997, Tepper 1999). The satiating effects of fatty acids have been investigated with regard to their structure. Two main areas associated with fat structure have been investigated; degree of saturation, and chain length.

A few studies have elucidated that ingestion of medium-chain triglycerides produces a satiating effect more rapidly compared to long-chain triglycerides in both rats and human subjects (Wymelbeke et al. 1998, Rolls et al. 1998). Moreover, medium-chain triglycerides (MCTs), added to a very-low energy diet, have been shown to increase satiety and enhance the rate of weight loss in the first 2 weeks of weight loss (Krotkiewski 2001). This may be explained by the fact that MCTs are absorbed and oxidized more efficiently and rapidly than long-chain triglycerides (LCTs). MCTs are absorbed directly into the portal circulation, whereas LCTs are transported in chylomicrons through the lymphatic system. Also, in contrast to LCTs, MCTs are not dependent on carnitine palmoyltransferase I (CPT 1) for their transport into mitochondria (Friedman 1986).

A number of studies have indicated that fatty acids varying in saturation have a differential effect on satiety (Alfenas and Mattes 2003). Unsaturated fatty acids seem to have a greater satiating effect than saturated fatty acids (Friedman 1998, Greenberg et al. 1999, French et al. 2000), which can be explained by the more efficient absorption and oxidation of unsaturated fatty acids (Stubbs et al. 1995, Piers et al. 2002). However, not all studies have shown differential effect of fatty acids varying in saturation on postprandial satiety or energy intake (Lawton et al. 2000, Kamphuis et al. 2001).

#### N-3 fatty acids in weight loss

Seafood-derived n-3 fatty acids have been shown to decrease the growth of the adipose cell, probably through stimulated beta-oxidation (Nakatani et al. 2003, Ukropec et al. 2003, Couet et al. 1997). Recently, this finding was supported by a study on mice showing that the anti-adipogenic effect of eicosapentaenoic and docosahexaenoic acids may involve a switch in adipocytes that includes increase in beta-oxidation and upregulation of mitochondrial biogenesis (Flachs et al. 2005). Furthermore, a recent review by Madsen et al. (2005) also describes that n-3 fatty acids may affect adipocyte differentiation. N-3 polyunsaturated fatty acids decrease adipose tissue mass and the development of obesity in rodents by targeting a set of key regulatory transcription factors involved in adipogenesis and lipid homeostasis.<sup>26</sup> The same set of factors are targeted by n-6 polyunsaturated fatty acids, but their effect seem to be dependent on feeding status and hormonal background and n-6 therefore react either as anti- or proadipogenic agents (Madsen et al. 2005). However, Garaulet et al. (2006) have recently showed, for the first time in humans, that n-3 and n-6 fatty acids are related to a reduced adipocyte size according to the tissue localisation. In another human study the inclusion of either lean or fatty fish, or fish oil as part of an energy-restricted diet resulted in approximately 1 kg more weight loss after 4 weeks, than did a similar diet without seafood or supplement of marine origin. Part of the effects might be attributable to seafood-derived n-3 fatty acids. Further studies in this area should be stimulated, but to-date there is not enough evidence to substantiate that n-3 fatty acids could support slimming efforts. According to a recent Cochrane study, the data is still inconclusive (Dewey et al. 2007).

#### **5.2.4 Effect of fat ingestion on hormonal secretion**

The secretion of several gastrointestinal hormones is increased in response to dietary fat. A mixture of fat and carbohydrate appears to be the most potent secretagogue of incretin hormones (Nordt et al. 1991), and the main stimulant of cholecystokinin secretion is the presence of dietary fat and proteins in the small intestine (Liddle et al. 1985). Furthermore, in animal studies, the satiety signals apolipoprotein A-IV (Fujimoto

et al. 1993, Liu et al. 2003) and enterostatin (Mei et al. 2002) have been shown to be regulated by the absorption and digestion of lipids. Cholecystokinin, apolipoprotein A-IV, and enterostatin have been shown to stimulate satiety and decrease food intake (Gibbs et al. 1973, Kissileff et al. 1981, Strader and Woods 2005).

### 5.2.5 Fat substitutes

Reduced-fat foods often lack the palatability of the familiar foods that they are replacing. Therefore, a number of fat mimetics that can reproduce the right mouthfeel of high fat foods, but contain less energy per gram, have been developed (**Table 4**).

One of the most studied fat substitutes is Olestra, a non absorbable sucrose polyester that is formed by linking fatty acids to the backbone of sucrose molecules (Stubbs 2001). The metabolizable energy content of olestra is zero, because the compound is not digested and absorbed in the human body. Olestra has similar physical and sensory properties as dietary fat, and it is heat stable, and can be used in cooking (Stubbs 2001).

Short-term studies have shown that a partial substitution of fat with olestra decreased both fat and energy intake in lean and obese subjects (Stubbs 2001, Eldridge et al. 2002). Bray et al. (2002) compared in a nine month study the effects of control diet (33% fat), low fat diet (25% fat) and test diet (25% fat + 8% olestra) on weight and body fat. Partial substitution of dietary fat with olestra reduced weight (6.27 kg) compared with the control (3.8 kg) and low fat diets (1.79 kg). Also, the amount of body fat decreased. In a ten week study, substitution of one third of the dietary fat with olestra decreased the weight of the subjects by 5.1 kg (Roy et al. 2002).

A fat emulsion formulated from palm- and oat oil fractions – Olibra – has been tested as a milk fat substitute in yogurts (Burns et al. 2000, 2001, 2002). In the studies, normal weight, over weight, and obese subjects ate normal control yoghurt (200 g) or test yoghurt (200 g), in which part (6 g) of the milk fat had been substituted with Olibra (5 g). The average energy intake after meal, four hours later, was lower among subjects who had eaten the test yoghurt (6700 kJ vs. 7700 kJ) compared with subjects who had eaten the control yoghurt. The effect was correlated with the amount of ingested Olibra. The long-term effects of Olibra have not been studied.

*Table 4. Fat substitutes (Mela et al. 1996).*

<b>Carbohydrate and protein-based materials</b> <ul style="list-style-type: none"><li>- modified glucosepolymers</li><li>- modified corn, potato, oat, tapioca and rice starches</li><li>- gums and algins</li><li>- cellulose and cellulose</li><li>- gelatin</li><li>- microparticulated proteins</li></ul>
<b>Poorly absorbed or non-absorbable lipids</b> <ul style="list-style-type: none"><li>- fatty acid esters of sugars and sugar alcohols (e.g. olestra)</li><li>- structured lipids containing specific fatty acids (e.g. caprenin)</li><li>- polycarboxylic acid and propoxylated glyceryl esters</li><li>- alkyl glyceryl ethers</li><li>- substituted siloxane polymers</li><li>- branched (sterically hindered) triglyceride esters</li><li>- specific naturally occurring lipids</li></ul>
<b>Emulsifiers and functional ingredients</b> <ul style="list-style-type: none"><li>- polyglycerol esters</li><li>- lecithins</li><li>- milk proteins</li></ul>

The effects of replacing the fat in beef sausage patties with inulin or lupin-kernel fibre on palatability, post-meal perceptions of satiety, and food intakes were investigated (Archer et al. 2004). The lupin-kernel fibre containing breakfast rated more satiating than the inulin and full-fat breakfasts. Total fat intake was 18 g lower on the day of the inulin and 26 g lower on the day of the lupin-kernel fibre breakfast than the full-fat breakfast day. Energy intake was lower (1521 kJ) only on the day of the inulin breakfast. Based on these results, the authors suggested that both inulin and lupin-kernel fibre might have potential as fat replacers in meat products and for reducing fat and energy intake in men (Archer et al. 2004).

### **5.3 Carbohydrates**

The satiating effect of carbohydrates appears to be caused by changes in blood glucose, changes in liver metabolism, end products of carbohydrate metabolism, and secretion of satiety hormones like insulin, GLP-1 and amylin (Feinle et al. 2002). Stimulation of mouth and throat by high fibre carbohydrates, slowed stomach emptying, and absorption of nutrients are important factors promoting the development and maintenance of satiety (Astrup et al. 2002). It has also been suggested that the oxidation of carbohydrates in the liver affects food intake (Friedman 1998).

### 5.3.1 Glycaemic index

Glycaemic index (GI) is the increase of blood glucose following ingestion of a carbohydrate source (50 g of absorbable carbohydrate) two or three hours after meal, measured as the surface area below the glucose curve in comparison to standard white bread or glucose. High GI products (fast degradation/fast absorption) increase blood glucose faster than low GI products (slow degradation/slow absorption). High GI products have also higher total area than low GI products and glucose level usually drops below fast level. Low GI products cause a lower glucose peak and the area is smaller. Low GI products are less likely to cause hypoglycaemia, as blood glucose stays longer above the fasting level. In addition, low GI breakfast has been shown to have a positive effect also on the glucose response after the next lunch (Liljeberg et al. 1999).

In general, high GI foods typically have a high carbohydrate content and are rapidly digested (Roberts 2000). High GI products have a high content of refined carbohydrates (because the effect of fat and protein on blood glucose is minimal compared with carbohydrate), high content of glucose and/or starch, low content of dietary fibre (especially soluble fibre), and soft, overripe or a highly processed structure (that is digested more rapidly than foods with more structure, such as firm raw foods, intact grains and harder pieces of food; Roberts 2000).

Low GI products on the other hand contain less absorbable carbohydrates and more water and dietary fibre, and therefore have lower energy density. They have been shown to have positive effects on metabolism: low GI products decrease insulin secretion after meals, upkeep insulin sensitivity and promote fat oxidation at the expense of carbohydrate, which can help in weight regulation. It has been proposed that weight regulation is easier and more effective on a low fat, slow carbohydrate diet than a low fat, fast carbohydrate diet (Ludwig 2000; Paman et al. 2003). In several intervention studies, energy restricted diets, containing low GI products, caused a higher weight reduction than a similar diet based on fast carbohydrate products (Brand-Miller et al. 2002). However, in several studies no differences between high and low GI products have been observed (Raben 2002, Sloth et al. 2004).

Low GI has also been coupled to increased satiety and slower development of hunger. Several short term studies have been conducted to explain the connection between GI and feelings of satiety and hunger. In about half of the 31 studies analysed by Raben (2002), low GI products decreased feeling of hunger or increased feeling of satiety more than high GI products. In two studies, high GI was correlated with increased satiety. In 15 of the studies, energy intake at a subsequent meal was also measured. In almost all cases, energy intake was slightly less after ingestion of low GI products, but the difference was significant in only seven of the studies. In some studies, the test meals

differed in e.g. energy density or palatability, which may have affected the results. In studies where energy intake, energy density, nutrient content, and palatability were standardised, the results were similar; in about half of them, low GI products increased satiety or decreased hunger, and the energy intake at a subsequent meal was reduced more than after the ingestion of high GI products (Raben 2002).

The results of studies, showing the importance of the glycaemic index in the regulation of weight, satiety and hunger, are inconclusive and more research is needed. The GI concept should be applied only to foods providing at least 15 g and preferably 20 g of available carbohydrates per normal serving, and comparisons should be kept within the same food group (Arvidsson-Lenner et al. 2004). As carbohydrates differ very much both in structure and in their effects on metabolism, it is important to pay attention to their quality. Recent dietary recommendations also guide towards the use of high fibre cereal products, vegetables and fruits instead of highly refined cereal products and sugar.

### **5.3.2 Effect of carbohydrate source**

The structure of carbohydrates affects their digestion and absorption in the gut. Sugars (mono- and disaccharides) and starch are digested and absorbed in the small intestine, and used as an energy source. Dietary fibre and oligosaccharides move to the large intestine, where the microbic flora digests them. The rates of digestion and absorption, and through them the GI, are not correlated with the length of the saccharide chain. Already, Wahlqvist et al. (1978) observed that glucose as a monosaccharide (glucose), disaccharide (maltose) and polysaccharide (starch) had a similar effect on the concentrations of blood glucose, insulin and fatty acids.

#### Mono- and disaccharides

The ingestion of glucose increases blood glucose and insulin levels fast. Sucrose (glucose+fructose) has a smaller effect and the effect of fructose is even smaller. The sweetness of these sugars is in the order glucose<sucrose<fructose, which means that at equal sweetness sucrose and fructose "save" energy. Other mono- and disaccharides in food are galactose, maltose (glucose + glucose, malt sugar) and lactose (glucose + galactose, "milk sugar"). Maltose is absorbed fast, lactose much slower.

Feinle (2002) has in a review reported studies in which fructose decreased food intake at a subsequent meal (after about 2 hours) more than glucose. Elliott et al. (2002) propose in their review, that a high and prolonged intake of fructose can cause overweight. This can be caused by no insulin secretion after fructose ingestion. As insulin partially regulates leptin production and has an independent satiety increasing effect in the brain, high intake of fructose can increase eating and promote weight gain (Havel 2001).

Intake of sucrose has in some studies decreased energy intake at the following meal (Lavin et al. 1997; Woodend and Anderson 2001). It appears that the energy of sucrose is compensated by reduced intake of energy from other sources. However, in several studies, no compensation of energy intake as sucrose at the following meal has been observed (Mattes 1996; Ludwig et al. 2001). When a part of starch in breakfast cereals was replaced with sucrose, the glucose and insulin responses three hours after intake of the cereals were reduced (Miller and Lobbezoo 1994).

Also, other monosaccharides and sugar alcohols, like D-tagatose (malabsorbed stereoisomer of fructose) and xylitol (pentose sugar alcohol) have awakened interest, as these can also be used as sweeteners like glucose. Several of them are absorbed less than glucose in the small intestine, which at least in theory might help reduce total energy intake. There is also some indication of the capacity of these compounds to reduce food intake at the next meal. King et al. (2003) observed that a yogurt snack containing xylitol, polydextrose, or a combination of both, decreased hunger and energy intake at the next meal more than the reference yogurt. The biggest problems, associated with the use of these sweeteners, are adverse gut effects like flatulence, diarrhoea and nausea. This actually could be the reason for the decreased food intake following the ingestion of the sugars (Feinle 2002). In normal-weight men, replacing 29 g of sucrose with 29 g of D-tagatose, as a sweetener to a breakfast meal, reduced energy intake at supper by 15% (Buemann et al. 2000). Gastrointestinal factors such as osmotic effects of unabsorbed D-tagatose, causing distension of the gut, might have mediated the acute appetite-suppressing effect.

The effects of replacing sucrose with artificial sweeteners on short-term regulation of food intake have not given a clear result; in some cases the intense sweeteners increased appetite, in some cases they had no effect (Drenowski 1998). It has also been proposed that regular users of intense sweeteners may learn to compensate for the missing calories. Increasing evidence demonstrates that simple sugars in drinks have a lesser satiating effect than simple sugars in solid foods. Therefore, a high intake of soft drinks is now regarded as a significant risk factor for weight gain and obesity (Astrup 2006, Dietz 2006). The effects of long-term supplementation (10 wk) with beverages and foods containing either sucrose or artificial sweeteners were investigated on *ad libitum* food intake and body weight in overweight subjects (Raben et al. 2002). Subjects who consumed relatively large amounts of sucrose (28% of energy), mostly as beverages, had increased energy intake, body weight, fat mass and blood pressure after 10 weeks, whereas body weight, fat mass and blood pressure decreased in the sweetener group.

## Starch

Native starch (e.g. from a raw potato) is digested slower than highly gelatinized starch (e.g. cooked potato), and starch rich in amylose (maize starch) is digested slower than normal starch. One of the problems of the western diet is that the starch it contains is digested and absorbed too fast (often as fast as pure glucose) and causes a fast rise in post meal blood glucose and insulin

Raben et al. (1997) have studied the effect of modified starch on blood glucose and the feeling of hunger and satiety. The starch products were potato starch, 1–2% acetylated potato starch (hydroxyl groups replaced with acetate groups giving a more stable starch gel) and potato starch containing 2% beta-cyclodextrin (cyclic sugar used as food stabilizer and antioxidant). Both types of modified starch produced higher ratings of satiety, and especially the beta-cyclodextrin containing starch decreased the blood glucose of the subjects (Raben et al. 1997). In another study (Raben et al. 1994), the use of resistant potato starch was correlated with decreased feeling of satiety compared to equal amount of gelatinized fully hydrolyzable and absorbable starch.

## Dietary fibre

Many studies indicate that dietary fibre may be associated with satiation, satiety and reduction of energy intake (Gerstein et al. 2004, Delzenne and Cani 2005; **Table 5**). The mechanisms by which dietary fibre promotes food intake are multiple and depend on the type of fibre involved (Delzenne and Cani 2005). Satiation may be influenced by a prolonged chewing and mastication period, gastric distension due to gelling, and delayed gastric emptying (Hoad et al. 2004, Slavin 2005). Howarth et al. (2001) calculated from 22 published research articles (no restriction of energy intake) that in average a 14 g addition of the daily fibre intake results in 10% reduction of energy intake and weight loss of 1.9 kg during 3.8 months. In overweight/obese subjects the effect was even bigger. The average energy intake was 82% of the normal, whereas in normal weight subjects the energy intake was 94%. Weight loss was in average 2.4 kg in overweight/obese subjects and 0.8 kg in normal weight subjects. The positive effects on energy intake and weight loss were obtained both with natural fibres and fibre additives.

In a study to examine the relative associations of dietary composition variables (especially fat and fibre intake) with body mass index (BMI) among young and middle-aged US adults only, energy percentage from fat was associated with BMI in men (Howarth et al. 2005). In women, a low-fibre (<1.5 g/MJ), high-fat (>35% energy) diet was associated with the greatest increase in risk of overweight or obesity compared with a high-fibre, low-fat diet.



Fibres which are soluble or insoluble in water have different physiochemical properties and may therefore be expected to exert different effects on post-ingestive satiety signals. Delargy et al. (1997) compared the effects of two isoenergetic high (22 g) fibre breakfasts, an isoenergetic low fibre breakfast and a low energy, 'light' breakfast, on short-term (24 h) appetite. Psyllium gum (the soluble fibre) and wheat bran (the insoluble fibre) were incorporated into breakfast cereals. According to hunger ratings, the subjects tended to be less hungry and they consumed significantly less energy at snack time after the high insoluble fibre breakfast than after the high soluble fibre breakfast cereal. The soluble fibre breakfast produced a greater suppression of snack intake than the light breakfast, but a smaller suppression than the other breakfasts. Interestingly, there was a trend toward reduced hunger and voluntary energy consumption following the soluble fibre compared with the insoluble fibre much later in the day (9.5–13.5 h after breakfast) although this was not significant. There was no significant effect of breakfast type on total daily energy intake. The results suggest that different types of fibre modulate the time course of appetite control and may produce alterations in the experience of motivation and patterns of eating without necessarily affecting total energy intake.

Dietary fibre can affect energy regulation by several different mechanisms (Burton-Freeman 2000, Howarth et al. 2001):

*Dilution of energy:* By definition, dietary fibre is not enzymatically degraded to subunits absorbable in the small intestine. Most fibres, especially soluble ones, are partially fermented in the large intestine. The short chain fatty acids formed are absorbed and used as energy. In average, only about 40% of the fibre is fermented, which means that the energy content of fibres per weight unit is low and addition of fibre to food is an effective way to lower energy density. In addition, the water binding ability of both soluble and insoluble fibres lowers energy density of fibre-rich food further. Equal amounts of food with lower energy density have been shown to increase satiety and lower intake of energy.

*Mastication:* Food naturally rich in fibre requires more mastication (time and force). This increases the stimulation of mouth area and increases the transmission of satiety signals to the brain.

*Gastric distension:* The increased mastication required of high fibre food can promote gastric distension by increased secretion of saliva and gastric acids. As some soluble fibres absorb large amounts of water and can form gels, they can promote gastric distension. This has been suggested to trigger satiety mediating signals to the central nervous system and thus promoting satiation at meals and increasing post meal satiety.

*Gastric emptying and rate of nutrient absorption:* Soluble fibres slow gastric emptying by forming a viscose gel matrix, that traps nutrients and slows their transit through the stomach, and digestion in the small intestine (Mälkki 2001). Diet rich in soluble fibre may reduce the rate of absorption and digestion of nutrients. The energy regulation model of Friedman (1995) assumes that availability/usability of circulating nutrients signals hunger and/or satiety. Therefore the ability of fibre to prolong the absorption time of nutrients can reduce the feeling of hunger and/or increase the feeling of satiety. In the small intestine, fibre can lower glucose- and insulin responses, and thereby delay the onset of hunger and reduce energy intake at the next meal.

*Gut hormones:* Dietary fibre can also affect energy intake and body weight through hormones, even though most of the suggested mechanisms are still a speculation. Slower absorption of macronutrients in the first part of the small intestine prolongs their contact with absorbing surfaces later in the small intestine. These unabsorbed energy nutrients in the last part of the small intestine have been coupled to slower gastric emptying time and ileal brake. Several gut hormones can mediate the ileal brake (GLP-1, peptide YY, neurotensine).

*Absorption of energy:* Some fibres, especially the more soluble and fermentable fibres of fruits and vegetables, decrease the total absorption of fat and protein. This can be a physical barrier effect caused by their presence in the gut diminishing contact between nutrients and the villi, which is a prerequisite of absorption. The intake of fibre and the digestibility of fat and protein have a negative correlation. Thus, a high fibre diet can directly decrease the amount of energy absorbed and promote long term weight control.

Epidemiological studies support the view, that obesity is less common in persons eating a high fibre diet. In evaluating the causes one must take into account that intake of fibre is linked with the intake of other nutrients. E.g. a low fibre diet typically contains high amounts of fat and the food has high energy density (Howarth et al. 2005, 2006).

Howarth et al. (2001) have reviewed studies that directly measure the effects of fibre intake on hunger and satiety either as physiological effects or/and using subjective analogy scales. The 38 studies reviewed had been made with healthy non-diabetic subjects. The control groups were given meals containing equal amounts of energy and fat as the test group meals. Most of the studies showed significant or non-significant increase in satiety between meals and/or decreased hunger in comparison to the control group with less fibre intake. None of the studies reported decreased satiety or increased hunger with a high fibre diet. No clear differences were observed between short and long term studies. In addition, no difference between the effects of soluble or insoluble fibre was shown. Increase in satiety was observed with both naturally fibre rich diet and fibre enriched diet. Turconi et al. (1995) observed increased feeling of satiety and fullness with increasing fibre amounts.

### **5.3.3 Effects of carbohydrate ingestion on hormonal secretion**

Ingestion of carbohydrates stimulates the secretion of a number of gastrointestinal hormones, such as amylin (Mitsukawa et al. 1990, van Hulst et al. 1996), and the incretins, glucagon-like peptide-1 (GLP-1), and glucose-dependent insulin-releasing polypeptide (GIP; Schirra et al. 1996, Burcelin 2005), and consequently insulin (Lavin et al. 1998). All of these hormones have been shown to be satiety signals (Turton et al. 1996, Flint et al. 2000, Verdich et al. 2001, Tempel and Leibowitz 1994), with the exception of GIP (Strader and Woods 2005).

Table 5. Postprandial studies on satiety and dietary fibres.

Reference Aim of the study	Fibre used / Fibre source	Subjects	Time scale	Satiety	Hunger	Biological responses	Food intake / <i>ad libitum</i>	Conclusions
<b>Studies with specified single dietary fibres</b>								
<b>Hoad et al. 2004</b>  To examine the satiating effects of 2 types of alginates which gel weakly or strongly on exposure to acid compared with guar gum whose viscosity is unaffected by acid	325 ml sweetened milk-based beverages with - weak-gelling <b>alginate</b> (AL-w) 1% of weight - strong gelling alginate (AL-s) 1% of weigh - viscouse <b>guar gum</b> (GG) 1% of weight - control (C)	n = 12 (3 m / 9 f), normal- weight, healthy	4 h	F↑, AL-s, GG, AL-w >C, (see figure)	H↓, AL-s, GG, AL-w >C, (see figure)	gastric emptying (by MRI) ±0	..	Agents that gel on contact with acid may be useful additions to weight-reducing diets, possibly due to distension in the gastric antrum and/or altered transport of nutrients to the small intestine in the lumps.
<b>Tomlin 1995</b>  To test whether a novel liquid fibre affects psychological factors connected with eating behaviour and short-term food intake	300 ml drinks - <b>Ethyl hydroxy ethyl cellulose*</b> drink (EHEC; 0.85% EHEC + sodium dodecyl sulphate) x 3 (at 9,12,18 o'clock) - placebo drink (incl. methyl- hydroxybenzoate) (C)  * liquid at room temperature, firm gel at body temperature	n = 17; 10 m / 7 f, oveweight/ obese, healthy	>5 h	F↑ with EHEC vs. C	(H↓ with EHEC vs. C)	..	Food intake ±0, ad lib (Food intake ↓ with EHEC vs. C later afternoon & next day)	The study suggests that gastric distension is a relateively unimportant influence on eating behaviour when non- restricted eaters are presented with an appetizing meal and that intestinal factors seems more important for prolonging satiety and reducing subsequent food intake.
<b>Wilmshurst and Crawley 1980</b>	200g portions - low-energy milk + <b>guar gum</b> 2 g (LMG)	n = 12; overweight	6 h	..	H↓, LMG>C	gastric emptying (by <sup>24</sup> Na) ↓	..	The mean transit time was increased by adding guar gum to test meal. There was a

Reference Aim of the study	Fibre used / Fibre source	Subjects	Time scale	Satiety	Hunger	Biological responses	Food intake / <i>ad libitum</i>	Conclusions
To measure gastric emptying time in obese using $^{24}\text{Na}$ and the effects of guar gum on gastric emptying and satiety	- low-energy milk (C)					with LMG vs. C		significant correlation between mean gastric emptying time and a subjective measure of satiety.
<b>Ellis et al. 1981</b> To determine the amount of guar gum required to be added to a wheat-flour bread to produce significantly reduced hyperglycaemic and insulinaemic response in non-diabetics. In addition, a satiety study with the same subjects.	<b>Guar gum (GG);</b> wheat bread with guar 0 (control, C), 50, 100 or 150 g/kg - portion 100 g bread	n = 11; 4 m / 7 f, normal / overweight, healthy	2 h	S $\pm$ 0 (GG vs. C)  S $\uparrow$ : GG 150 g vs. GG 50 g after eating; GG 150 g vs. GG 100 g at 60 min; GG 150 g vs. GG 50, GG 100 g at 120 min	..	gluc response $\pm$ 0 (except $\downarrow$ at 30 min 100 g guar vs. C)  ins response $\downarrow$ : GG 50, 150 g vs. C at 30 min, GG 50, 100, 150 vs. C at 60 min	..	Guar bread at the 100 g/kg level (59 g guar /kg bread) reduced the serum insulin by 48% at 60 min. More information is needed to demonstrate the possible satiating potential of guar bread.
<b>French and Read 1994</b> To determine whether the satiating effect of fiber are due to	- low / high-fat soup (LFS / HFS) with <b>guar gum</b> (GG); 3%, 12 g / 400 ml - low / high-fat soup without guar gum (LFS / HFS)	n = 8 m; normal / overweight, healthy	3 h 20 min	F $\uparrow$ (time to return to preprandial values) (particularly HFS + GG)	H $\downarrow$ (time to hunger returned) (partic. HFS + GG)	Gastric emptying (by gamma camera) $\downarrow$ after LFS+GG < HFS < HFS+GG	..	The delays in the return of hunger and decline of fullness were greater when GG was added to the fatty soup. These delays were not correlated with the small additional

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delaying gastric emptying or slowing absorption of meals						(the effect in this order) vs. LFS		delay in gastric emptying. This is more compatible with slowed absorption and prolonged contact of nutrients with intestinal chemoreceptors.
<b>Adam and Westerterp-Plantenga 2005</b>  To assess whether glucagon-like peptide 1 (GLP-1) release and appetite after a breakfast with or without an additional galactose/guar gum stimulation is different in normal-weight than overweight/obese subjects	Preload - <b>galactose</b> (50 g) + <b>guar gum</b> (2.5 g) (= 836 kJ) + 250 ml water - water 250 ml (C)  after preload a standard breakfast (1.9 MJ)	n = 58; 30 (15 m / 15 f) normal- weight (NW), 28 (9 m / 19 f) overweight / obese (OW/O)	2 h	S↑ (30 & 60 min) (NW vs. OW/O)	..	gluc conc. ↑ at 60 min after C vs. GG (NW)  ins conc. ↑ at 60 min after C vs GG (NW), at 90 min after GG vs. C (NW), at 120 min after GG vs. C (OW/O)  FFA conc. ↑ (decrease ↓) at 30 min after C vs. GG (NW)  GLP-1 conc. ↑ at 30 & 60 min after GG vs. C (NW, OW/O), at 90 min (OW/O)	..	After a standard breakfast with water, GLP-1 release was lower in OW/O than NW subjects. However, postprandial GLP-1 release in OW/O was not different from NW when galactose/guar gum was added to the breakfast. The latter was not mirrored by subjective feelings of satiety. Disturbed perception of the physiological feedback of a satiety hormone rather than disturbed feedback itself might contribute to obesity.
<b>Archer et al. 2004</b>  To examine whether replacing fat with inulin or	<b>Inulin (I) or lupin- kernel fibre (LKF)</b> (Lupinus angustifolius) (29,6 g/kg) in reduced- fat patty vs. full-fat sausage patty (C, 0 g/kg);	n = 33 m; normal/ overweight, healthy	4,5 h	S↑ LKF>I, C	..	..	Fat intake ↓(I, LKF, vs. C at test day) Energy intake ↓ (I vs. C at	Both inulin and LKF fibre appear to have potential as fat replacers in meat products and for reducing fat and energy intake in man.

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lupin-kernel fibre influenced palatability, satiety, and food intake	- a portion ~100 g						test day)	
<b>Zurakowski et al. 2005</b>  To investigate the effect of soluble fiber xantham gum on hunger, satiety and epigastric fullness in obese	- <b>Xantham gum</b> ; 0,5 g, (90kcal) - placebo (0 g)  with test meal (ham sandwich)	n = 21 f; obese, healthy	2 h	S ±0	H ±0	..	..	0.5 g of xantham fiber with test meal did not cause significant change of satiety. It is probably the effect of too low dose of xantham gum.
<b>Hulshof et al. 1993</b>  To investigate the effect of the physical state and fat content of a preload on hunger and satiety and subsequent food intake.	Preloads (550 ml) in three types of physical state (liquid (L), solid with <b>locust bean gum</b> (SLBG), solid with gelatin (SG)) at three energy levels (0.42 / 1.67/ 3.35 MJ)	n = 33 f; normal-weight	3,5 h	S ↑, S>L,  S↑, SLBG > SG	..	..	Energy intake ±0 (remainder of the day or the day after)	The solid preloads were more satiating than the liquid preloads and the solid preloads were more satiating with fibre (SLBG) than without fibre (SG).
<b>Marciani et al. 2000</b>  To evaluate the changes in meal viscosity during gastric emptying and correlate	<b>Locust bean gum</b> ; 0.25, 0.5, 1.0 or 1.5 g / 100 g; 500 ml nonnutrient liquid meals	n = 8; 3 m / 5 f, normal / overweight, healthy	1h 40 min	S↑ with ↑ initial viscosity	H↓ with ↑ initial viscosity	Gastric emptying (by EPI MRI) ↓ with ↑ viscosity (not a strong effect)	..	The stomach responds to meal ingestion by rapid intragastric dilution, causing a reduction of meal viscosity, and gastric emptying is minimally delayed. However, increased viscosity is associated with more

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them with meal dilution and satiety.								prolonged satiety.
<b>Di Lorenzo et al. 1988</b>  To evaluate the effect of adding pectin to a meal on gastric emptying, satiety and postprandial plasma cholecystokinin and pancreatic polypeptide levels	Solid meal with -15 g <b>pectin (P)</b> - 15 g <b>methylcellulose (MC)</b>	n = 9; obese	Postpr.	S↑ with P vs. MC	..	Gastric emptying ↓ with P vs. MC  CCK ±0 pancreatic polypeptide ±0	..	As pectin induces satiety and delays gastric emptying, it may be a useful adjuvant in the treatment of disorders of overeating.
<b>Tiwary et al. 1997</b>  to test the effect of pectin on satiety	- 5,10,15 & 20g <b>pectin (P)</b> in 448 ml orange juice - 448 ml orange juice (C)	n = 74; 49 m / 25 f, normal-weight	4 h + 60 min after second meal	S↑ with P (product x time, ns for pectin dose) vs. C	..	..	..	Pectin in doses as small as 5 g mixed with orange juice increases satiety and can aid in a program to reduce weight by limiting food intake.
<b>King et al. 2005</b>  To examine the immediate effects of polydextrose and xylitol given either alone or in combination, on consumption post-ingestion, as well as the extent to which	- yoghurt + 25 g xylitol (X) (0.686 MJ) - yoghurt + 25 g <b>polydextrose (P) (0.544 MJ)</b> - yoghurt + 12.5 g xylitol + 12.5 g polydextrose (XP) (0.611 MJ) - yoghurt + 25 g sucrose (C) (0.854 MJ)	n = 16 (8 m, 8 f), healthy, normal-weight	a fixed breakfast at 8:30, yoghurt at 11:00, ad lib meal at 12:30	F↑ with XP vs. C (with and without differential in energy content of yoghurt accounted for)			Energy intake ±0, however, when energy content of yoghurts accounted for Energy intake ↓ after P vs. C	Pre-loads of xylitol and polydextrose caused a mild increase in satiety and suppression of energy intake and the effects persist after repeated daily administration. The effects exerted by X and P did not arise from the differences in energy content of the yoghurt per se. Therefore, the usefulness of X and P as ingredients in



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any satiety-inducing effects would persist after repeated daily dosing for 10 d.								functional foods for appetite control are as a result of their lower energy content and suppression of appetite.
<b>Cybulski et al. 1992</b>  To evaluate a combination of psyllium fiber with nutrients in a commercially available wafer for its effectiveness in reducing food intake and appetite	<b>Psyllium (Ps)</b> ; no wafer and 4 different amounts (39, 104, 169, 234 kcal) of the fiber wafer with water, in a ratio of 13 kcal (and 0.565 g psyllium) wafer per 41.67 g water 30 min prior to a test meal of macaroni and beef. (=> preload: ~ 1,7 g psyllium / 39 kcal; 4,5 g /104 kcal; 7,4 g / 169 kcal or 10,2 g / 234 kcal)	n = 15 f; non-obese, healthy	Postpr.	..	H↓; 7,4 g (169 kcal), 10,2g (234 kcal)	..	Food intake ↓ <i>ad lib</i> , 7,4 g (169 kcal), 10,2g (234 kcal)	Methodologically, this work underscores the importance of testing the satiating effects of foods at multiple levels before conclusions are drawn about their satiating effectiveness and suggests that the threshold for significant reduction should be considered as a measure of the product's satiating effectiveness. The relative contributions of the nutrients, the fiber, and the water to the satiating effect still need to be determined.
<b>Bergmann et al. 1992</b>  To examine the correlation between ultrasonographic gastric emptying and appetite.	<b>Psyllium (Ps)</b> ; 10.8 g psyllium vs placebo (C)	n = 12; healthy	Postpr.	S↑ with Ps vs. C from 6. hour after the meal	H↓ with Ps vs. C from 6. hour after the meal	Gastric emptying ↓ with Ps from 3. hour  Correlation between gastric emptying and hunger and satiety after Ps and C	..	The association between echographic measurement and visual analogue scales is a simple method of evaluating the relationship between the stomach and appetite.
<b>Turnbull and Thomas 1995</b>	-20g <b>Plantago ovata</b> <b>semen and testa (=psyllium)</b> + 200 ml	17 f	3 h	F↑ with Ps vs. Pb / W at 1 h post-	..	..	Fat intake ↓ (at test day) with	This plantago ovata containing product which is already taken by many



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							intake $\pm 0$	
<p><b>Rigaud et al. 1998</b></p> <p>To assess whether psyllium could at an acceptable dose delay gastric emptying of a low-calorie meal and reduce hunger and energy intake without requiring intimate mixing with the meal.</p>	<p>- <b>Psyllium (Ps)</b> 7,4 g in 100 ml water) - 6,9 g placebo (gelatin) in 100 ml water (C)</p> <p>15 min before 450 kcal test meal</p>	n = 14; 7 m / 7 f, normal-weight, healthy	6 h	F $\pm 0$	H $\downarrow$ with Ps vs. C	<p>Gastric emptying (by standard double-radiolabeled meal) <math>\pm 0</math> (solid and liquid phases of the meal)</p> <p>gluc response <math>\downarrow</math> after Ps vs. C</p> <p>ins response <math>\downarrow</math> after Ps vs. C</p> <p>trigly: no increase after Ps, little signif. rise after C</p> <p>Correlation between gastric emptying and energy intake / hunger after test meal NS</p>	Energy intake after test meal $\downarrow$ after Ps vs. C	Psyllium reduces hunger and energy in normal subjects at reasonable dose and without requiring mixing with the meal. It does not act by slowing down the gastric emptying of hydrosoluble nutrients, but by increase in the time allowed for intestinal absorption, as suggested by the flattening of the postprandial serum glucose, insulin and triglycerides curves.
<p><b>Frost et al. 2003</b></p> <p>To assess whether the addition of</p>	<p>4 pasta meals (incl. 50 g available CHO); - <b>psyllium</b> (1.7g) enriched pasta with tomato-sauce without fat (Ps) (240 kcal)</p>	n = 10; 4 m / 6 f, normal / overweight, healthy	4 h	F $\pm 0$	H $\pm 0$	IAUC of gastric emptying (by paracetamol) $\downarrow$ after PsF vs. C / Ps, after CF vs. C / Ps; Ps	Energy intake $\pm 0$ (ad lib meal)	A dose of 1.7 g psyllium did not evoke measurable effects on gastric emptying, postprandial GLP-1, insulin or glucose metabolism, but the addition of 30 g oil and

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viscous fiber at an amount recommended by the US FDA to allow "low saturated fat, cholesterol, soluble fiber and coronary heart disease" health claim label on a food package and/or fat to a meal would affect gastric emptying, postprandial glucose, insulin and GLP-1.	- psyllium (1.7 g) enriched pasta with tomato sauce with fat (30 g sunflower oil + 3 g sodium propionate) (PsF) (520 kcal) - control meal with tomato sauce without fat (C) (240 kcal) - control meal with tomato sauce with fat (30 g sunflower oil + 3 g sodium propionate) (CF) (520 kcal)					vs. C±0  IAUC glucose ↓ after PsF vs. C / Ps / CF; Ps vs. C ±0  IAUC insulin ±0  IAUC GLP-1 ↑ after PsF vs. C / Ps; after CF vs. C / Ps; Ps vs. C±0		3 g of sodium propionate did reduce gastric emptying, increase GLP-1 and reduce glucose and insulin concentrations.
<b>Weickert et al. 2006</b>  To investigate effects of purified insoluble cereal fibres on postprandial peptide YY and ghrelin responses and their relation to satiety ratings.	Test breads (240 kcal, 50 g available CHO, 0.84 g fat, 7.3 g protein) - <b>wheat fibre (WF)</b> bread (13.4 g fibre) (WF) (94.5 g insoluble, 2.5 g soluble) - <b>oat fibre (OF)</b> bread (13.5 g fibre) (OF) (93% insoluble, 3% soluble fibre) - control (2.9 g fibre) (C)  - could not be distinguished by taste, smell or visual	n = 14 f, healthy, normal-weight	5 h		H ±0	postprandial peptide YY response ↓ after WF vs. C  postprandial ghrelin response ↓ after WF vs. C		Oat- and wheat fibre consumption result in different postprandial responses of PYY and ghrelin, but do not differ in satiety effects.

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	appearance							
<b>van Amelsvoort and Weststrate 1992</b>  To study the postprandial effects of changing the amylose-to-amylopectin ratio (Am:Ap) in the starch fraction of a meal.	Hot mixed lunches (protein 13 E%, fat 24 E%, mono- and disaccharides, 6 E%, polysaccharides 57 E%) in which Am:Ap was either 0:100 or 45:55.	n = 22 m, healthy, normal-weight /mildly overweight	6 h	F↑ after 45:55 vs. 0:100	H, D ↓ after 45:55 vs. 0:100	- after 45:55 lower initial responses but a small increase for glucose and decrease for insulin  - after 0:100 rises in free glycerol and free fatty acids ↑		An increase in Am:Ap in the meal has a significant effect on various postprandial responses. Although the effects of varying AM:Ap in the meals on the immediate postprandial responses look very promising, the long-term effects of an increased consumption of high-amylose diets on health indices are not yet known.
<b>Raben et al. 1994</b>  To study the effect of resistant starch on postprandial plasma concentrations of glucose, lipids, and hormones, and on subjective satiety and palatability ratings	50 g pregelatinized starch (0% <b>resistant starch</b> (RS) (S) or 50 g raw potato starch (54% RS) (R) together with 500 g artificially sweetened syrup	n = 10 m, healthy, normal-weight	5 h	S, F ↓ after the R meal than after the S meal.		After R meal postprandial glucose, lactate, insulin, gastric inhibitory polypeptide (GIP), glucagon-like peptide-1, and epinephrine ↓ compared with S meal.		The replacement of digestible starch with RS resulted in significant reductions in postprandial glycemia and insulinemia, and in the subjective sensations of satiety.
<b>Studies with meals rich in dietary fibres and/or non-specified single dietary fibres</b>								
<b>Sparti et al. 2000</b>	Two eucaloric diets (protein 18 E%, fat 30 E%, carbohydrate	14 subjects (7 m, 7 f), healthy,	24-h periods in a metabolic		- H ↓ after H than L diet	- H diet elicited lower and delayed rise of		The pattern of carbohydrate utilization is involved in the modulation of hunger

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To test hypothesis that isoenergetic diets differing only in their content of unavailable carbohydrates would result in different time courses of total, endogenous, and exogenous carbohydrate oxidation rates	52 E%) with a high (H) or low (L) content of unavailable carbohydrates. Different foods in each diets (H vs. L): puffed rice vs. breakfast cereals & sliced dried apple, white rice vs. barley, strawberry yoghurt vs. chickpea salad, cookie vs. dried apricots, instant mashed potatoes vs. buckwheat, vanilla custard vs. red bean salad, marzipan candy bar vs. pears in syrup	normal-weight	chamber; VAS throughout day before and after meals and at hourly intervals, final VAS completed following morning on waking up.		- differences in H between the diets associated with differences in the pattern of carbohydrate oxidation among diets	postprandial carbohydrate oxidation - total energy expenditure and substrate oxidation $\pm 0$		feelings. The greater suppression of hunger after the H diet than after the L diet may be helpful, at least over the short term, in individuals attempting to better control their food intake.
<b>Porikos and Hagamen 1986</b>  To test whether a high fiber preload can suppress food intake at a subsequent test meal	preload: 2 roast beef sandwich halves (à 400 kcal) and either 5.2 or 0.2 g of crude fiber in the bread.	n = 50 m: 31 normal-weight, 19 overweight	The preload eaten by subjects, their meal intentionally interrupted and then allowed to finish eating 30–45 minutes later (test meal)	F ↑ after high fiber preload in obese and normal-weight subjects.			Obese subjects ate fewer sandwich halves after high than low fiber preload. Obese subjects ate more than non-obese subjects in low fiber treatment.  The non-	These results support the hypothesis that fiber reduces caloric intake in obese people.

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							obese subjects ate the same amount in both treatments.	
<b>Burley et al. 1987</b>	breakfast meals (equal weight) of high (12.0 g) and low (3.0 g) fibre content; based on toast, breakfast cereal, milk, butter and orange marmalade.	n = 20 f, normal-weight, divided into high and low restraint groups	2.5 h	F ↑ after the high-fibre breakfast; no other differences			No difference in energy intake at lunch after high and low fibre breakfasts, or between the restraint groups.	The effect of fibre overall, was relatively weak compared to the differences between the two restraint groups, with the high restraint group consistently expressing significantly less hunger before, during and after the breakfasts compared to low restraint group.
<b>Levine et al. 1989</b>  To examine the effect of high-fiber cereals on short-term food intake	study I: one of five cereals (fibre 0 g (control), 11 g, 18 g, 35 g or 39 g/100g)  study II: a very-high-fiber (VHF) cereal (fibre 39 g/100g) or a very-low-fiber (VLF) cereal (fibre 0 g)  + 240 ml 2% milk and 120 ml orange juice.	study I: n = 14, healthy, normal-weight  study II: n = 19, healthy, normal/over weight	6 h		study I: H ↓ after higher-fibre cereals vs. cereal with no fibre; ↓ hunger fibre 35 g/100 g vs. 0 g or 18 g/100g  study II: no difference		study I: positive correlation between fibre content of cereals and energy intake at lunch; E intake ↓ at breakfast + lunch after cereals with 35 g and 39 g fibre/100g vs. cereal	Cereals containing relatively large quantities of dietary fiber may decrease short-term food intake.

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							with fibre 0 g  study II: no differences	
<b>Holm and Björck 1992</b>  To examine glucose and insulin responses to bread products as well as the rate of in vitro starch digestion and the content of in vitro resistant starch (RS)	3 white-wheat-bread (WWB) products varying in crust-crumbs ratio and monoglyceride addition (A), three bread products with a high soluble fiber content (HSFB) (B), and two coarse-wheat breads (C)  A:a. WWWB + monoglycerides = WWW-mg (control) (fibre total/soluble 3.5 g / 1.1 g) b. WWB without monoglycerides =WWB-tl (3.7 g / 1.1 g) c. WWB rolls = WWB-r (3.7 g / 1.1 g) B.3 breads high in soluble fibre (HSFB): a. HSFB + oat bran =HSFB-ob (10.9 g / 4.6 g) b. HSFB+linseed=HSFB-ls (13.5 g / 3.9 g) c. HFSB+high-fibre	n = 10, 3 m, 7 f, healthy, normal-weight	3 h	S ↑ after HSFBS and CBwwg vs. WWBs immediately after the test meal.		glucose ↓ after CBs, HSFB-mf, HSFB-ob vs. WWB-mg (control)  insulin ↓ after CB-wwg, HSFBS vs. WWB-mg (control)		Inclosure of intact wheat grains or oat bran show the most promising potential for developing lente bread. The whole-grain wheat bread also contained the highest level of resistant starch.



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	ingredients=HFSB-mf (15.1 g / 3.4 g) C. two coarse breads (CB) a. whole-grain wheat bread of intact wheat kernels (80%) and white wheat flour (20%) = CBwwg (11.4 g / 1.2 g) b. bread of spaghetti cuts (70%) and white wheat flour (30%) =CBsp (4.0 g / 1.2 g)  - all breads cont. 50 g starch							
<b>Burley et al. 1993</b>  To examine the effect of meals containing Quorn myco- protein or chicken upon satiety and satiation.	2 isocaloric meals, similar in every aspect except dietary fibre content (11 g (incl. Quorn myco-protein) vs 3 g (incl. chicken))	n = 18 (m+f), healthy, normal- weight	postprand.		D (and overall eating rate) $\pm 0$		an evening <i>ad libitum</i> meal energy intake $\downarrow$ (18% ) after high- fibre lunch vs. low- fibre lunch.	Quorn (high-protein, dietary fibre combination) has a strong impact on late satiety, but is similar in its effects during and immediately after consumption. These data have clear implications for the use of Quorn myco- protein for the control of appetite and body weight.
<b>Turnbull et al. 1993</b>  To examine the effect of mycoprotein, a food produced by continuous	an isoenergetic meal containing either 130 g mycoprotein ( <i>Fusarium            graminearum</i> ) (fibre 16.8 g) or 130 g chicken (fibre 10.1 g)	n = 13 f, healthy, normal- weight	3 h	F $\pm 0$	D and PC $\downarrow$ when measured 3 h after consumption of mycoprotein vs. chicken.		Energy intake $\downarrow$ at the day of the study (by 24%) and the next day (by 16.5%)	Evidence is increasing that fiber can have an effect on appetite and we have demonstrated that fiber- containing mycoprotein also has this affect.

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fermentation of <i>Fusarium graminearum</i> (Schwabe), on energy intake and appetite.					H $\pm$ 0		after eating mycoprotein (high fibre) compared with chicken (low fibre).	
<b>Gustafsson et al. 1993</b>	- eucaloric (2000 kJ) test meals (typical Swedish lunch) with different vegetables (carrots, peas, Brussels sprouts, spinach) in portions of 96–164 g. The added vegetables contained 4.4 g dietary fibre - control meals without vegetables - meals balanced with respect to digestible carbohydrates (59.7 g) and as far as possible also concerning protein and fat	n = 10 m, healthy	3.5 h	S $\pm$ 0		insulin and C-peptide response $\downarrow$ after meal with spinach vs. control meal  glucose $\pm$ 0		The meal with spinach elicited significantly lower insulin and C-peptide responses than the control meal.
<b>Raben et al. 1994</b>  To examine the effect of a high-fiber and an isoenergetic low-fiber meal on postprandial thermogenesis, substrate	isocaloric high-fiber (4.7 g/MJ) and an low-fiber (1.7 g/MJ) meals; net difference in fiber content attributed to pea fibre (3.5 g vs. 0 g)	n = 10 m, healthy, normal-weight	6.5 h	F $\uparrow$ after the high-fiber meal vs. low-fiber meal	D $\downarrow$ after the high-fiber meal vs. low-fiber meal	- diet-induced thermogenesis and postprandial fat oxidation $\downarrow$ after high-fiber meal vs. low-fiber meal - C-peptide $\uparrow$ less and nonesterified		In conclusion, a high-fiber meal decreased DIT and fat oxidation but increased fullness compared with a low-fiber meal.

Reference Aim of the study	Fibre used / Fibre source	Subjects	Time scale	Satiety	Hunger	Biological responses	Food intake / <i>ad libitum</i>	Conclusions
metabolism, hormones, and satiety.						fatty acids ↓ more after the high-fiber meal - glucose, insulin, norepinephrine , epinephrine, or gastrointestinal hormones ±0		
<b>Holt et al. 1995</b>  The aim of the study was to produce a validated satiety index (SI) of common foods	Isoenergetic 1000 kJ (240 kcal) servings of 38 foods separated into six food categories (fruits, bakery products, snack foods, carbohydrate-rich foods, protein-rich foods, breakfast cereals)	groups of 11–13 subjects	2 h  SI calculated by dividing the area under the satiety response curve (AUC) for test food by group mean satiety AUC for white bread (WB) and multiplying by 100. WB had SI of 100% and SI scores of other foods	Highest SI by boiled potatoes, lowest by croissant. Most foods (76%) had SI greater than or equal to WB.  SI correlated positively with serving weight of foods and negatively with palatability ratings.  Protein, fibre, and water contents of foods correlated			The amount of energy eaten immediatel y after 120 min correlated negatively with the mean satiety AUC responses	The results show that isoenergetic servings of different foods differ greatly in their satiating capacities. This is relevant to the treatment and prevention of overweight and obesity.

Reference Aim of the study	Fibre used / Fibre source	Subjects	Time scale	Satiety	Hunger	Biological responses	Food intake / <i>ad libitum</i>	Conclusions
			were expressed as a percentage of WB.	positively with SI, whereas fat content negatively associated				
<b>Silberbauer et al. 1996</b>  To examine the effects of equienergetic breakfasts with varying fiber and macronutrient contents on hunger and satiety ratings, on subsequent lunch intake, and on postprandial carbohydrate and fat metabolism	4 breakfasts: - commercially available high fiber cereal (HFC, 10% fiber) - medium fiber cereal (MFC, 7% fiber) - low fiber cereal (LFC, 3% fiber) - standard continental breakfast (0% fiber)	males, normal-weight		S $\pm$ 0	H $\pm$ 0	- glucose, lactate, and insulin $\uparrow$ more after LFC breakfast than other breakfasts  - plasma concentrations of fat metabolites (triglycerides, free fatty acids, beta-hydroxybutyrate) and of glucagon $\pm$ 0	size or microstructure of the subsequent lunch $\pm$ 0	The results are consistent with the assumption that energy content of a meal is the major determinant of subsequent energy intake in man and the fiber content and macronutrient composition have only a modulating effect.
<b>Gustafsson et al. 1995</b>  The effects of dose and structure of vegetables in mixed meals on satiety	- vegetables in mixed meals with varying doses (portions 150 and 250 g containing 4.3 and 7.2 g of dietary fibre, respectively) and structure (cut and minced) of microwaved spinach. - a control meal without spinach and the test	n = 10 m, healthy	3.5 h	S $\uparrow$ after largest spinach portions  S correlated positively with dietary fibre and water content in		glucose $\downarrow$ after largest spinach portions		

Reference Aim of the study	Fibre used / Fibre source	Subjects	Time scale	Satiety	Hunger	Biological responses	Food intake / <i>ad libitum</i>	Conclusions
	meals with spinach balanced regarding energy (2000 kJ) and digestible carbohydrates (59 g, 51 E%) and with protein and fat as far as possible			the vegetable.  differences in structure had no influence on satiety.				
<b>Liljeberg et al. 1999</b>  To study the effect of GI and indigestible carbohydrate-- resistant starch (RS) and dietary fiber (DF)-- content of cereal-based breakfasts on glucose tolerance at a second meal	7 breakfasts - WWB (white-wheat bread; control): fibre 2.0 g, resistant starch 0.1 g, GI 100 (high) - HAB (high-amylose barley bread baked under ordinary conditions): 10.0 g, 1.4 g, GI 99 (high) - HAB-long (HAB baked for a long time at a low temperature): 11.0 g, 5.1 g, GI 71 (low) - HAB-long+BF (HAB- long bread and barley flakes): 25 g, 11.2 g, GI 60 (low) - HAB-longp (HABlong made with preboiled flour): 12 g, 6.8 g, GI ~83 (mediate)	n = 10, 4 m, 6 f, healthy, normal- weight	4 h	S highest after barley breakfast with low GI and high RS + DF content.		Two of 4 low- GI breakfasts improved glucose tolerance at the second meal.  No measurable effect of fermentable carbohydrates on glucose tolerance at the second meal.		Glucose tolerance can improve in a single day. Slow absorption and digestion of starch from the breakfast meal, but not the content of indigestible carbohydrates in the breakfast meal, improved glucose tolerance at the second meal (lunch).
<b>Holt et al. 1999</b>	isoenergetic (2035 kJ) breakfasts, varying in macronutrient content (two fat-rich, two carbohydrate-rich (low- and high-fibre):	n = 14 (7 m, 7 f), healthy, normal- weight	12 h	F ↑ after HF, carbohydrate -rich breakfast  - post-	H ↓ after HF carbohydrate- rich breakfast vs. LF		- HF carbohydrate- rich breakfast associated with less	The results confirm the relatively weak satiating power of fat-rich meals observed in controlled laboratory-based studies and indicate that a high-fibre,

Reference Aim of the study	Fibre used / Fibre source	Subjects	Time scale	Satiety	Hunger	Biological responses	Food intake / <i>ad libitum</i>	Conclusions
	- high-fibre (HF) (sugar/starch/fibre: 40.9/36.6/19.1 g) - low-fibre (LF) (32.0/58.2/1.0 g)			breakfast alertness ratings ↑ after HF carbohydrate- rich meal  - alertness AUC values up until lunch correlated positively with fullness AUC	carbohydr.- rich meal.		food intake during the morning and at lunch.  - the total energy intake ↑ after fat- rich meal vs. HF carbohydrate- rich meal	carbohydrate-rich breakfast may assist weight control efforts by maintaining fullness. Further research is required to determine whether satiety directly enhances alertness and whether low-GI carbohydrate-rich meals enhance alertness to a greater degree than high-GI meals.
<b>Skrabanja et al. 2001</b>  To examine the nutritional characteristics of buckwheat starch to identify the possibility for reduced postmeal metabolic responses to various buckwheat products.	- Boiled buckwheat (BWG), total fibre 7.5%, soluble 2.4% - Buckwheat bread (50% buckwheat flour, BWG50%), 6.7%, 2.1% - White wheat bread (WWB, control) 3.8%, 1.0%  - each bread 50 g digestible carbohydrates, 1578 kJ	n = 10 (1 m, 9 f), healthy, normal- weight	3 h	S (AUC) ↑ after BWG vs. WWB		glucose and insulin ↓ after BWG and BWG50% vs. WWB		Buckwheat has potential use in the design of foods with lower GI properties.
<b>Holt et al. 2001</b>  To compare the effects of equal- energy portions of different	7 different eucaloric (238 kcal) breads: - control (fibre 1.8 g) - fruit (10.2 g) - high-protein (17.1 g) - coarse white (15.9 g)	n = 10 (3 m, 7 f), healthy, normal- weight	2 h	SI ranged from 100% to 561%, lowest SI score for regular white bread		The glycemic responses not associated with fullness responses	SI negatively correlated with energy intake at a	SI scores would be a useful addition to food labels to indicate which foods are less likely to be overeaten and could be used by dietitians to develop weight control plans

Reference Aim of the study	Fibre used / Fibre source	Subjects	Time scale	Satiety	Hunger	Biological responses	Food intake / <i>ad libitum</i>	Conclusions
bread on feelings on fullness and subsequent <i>ad libitum</i> food intake.	- protein-and-fibre-rich (19.9 g) - high-fibre (33.5 g) - low-fat high-moisture (23.9 g)		food by dividing the area under the 120- min satiety response curve (AUC) for the test bread by the satiety AUC for the control and multiplying by 100%.	The best predictor of SI portion size and energy density.			test meal and total day energy intakes	to help reduce energy intakes without increased hunger.
<b>Burton- Freeman et al. 2002</b>  To examine whether adding fiber or fat to a low-fat, low-fiber meal increases cholecystokinin release and enhances satiety and whether the cholecystokinin response correlates with satiety.	Three isoenergetic breakfast meals: - low fiber, low fat (fibre 7 g/4.2 MJ) LFLF - high fiber, low fat (20 g/4.2 MJ) HFLF - low fiber, high fat (8 g/4.2 MJ) LFHF	n = 16 (8 m, 8f), healthy, normal- weight / overweight	6 h	In women, F and S ↑ after meals higher in fiber or fat (HFLF; LFHF) vs. low-fat, low- fiber meal (LFLF).  In men, S ↑ after 2 low- fat meals (LFLF, HFLF) vs. high-fat meal (LFHF)	In women, H ↓ after LFHF, HFLF vs. LFLF  In men, H ↓ after HFLF, LFLF vs. LFHF	In women, CCK ↑ after HFLF, LFHFs vs. LFLFI.  In men, CCK ±0  Insulin ↑ more after LFLF vs. LFHF, HFLF  Glucose ↑ after LFLF vs. LFHF; and glucose ↑ after HFLF vs. LFHF  Triacylglycerol ↑ most after LFHF.	Food intake ±0	In women, the feeling of satiety caused by cholecystokinin release is enhanced by increasing either the fiber or fat content of a low-fat, low-fiber meal.

Reference Aim of the study	Fibre used / Fibre source	Subjects	Time scale	Satiety	Hunger	Biological responses	Food intake / <i>ad libitum</i>	Conclusions
<b>Pasman et al. 2003</b>  To study the effect of simple vs complex carbohydrates containing breakfasts on blood parameters, hunger and satiety and mood.	Breakfasts: - simple carbohydrates (433 kcal, fibre 2.1 g; SCHO) - complex carbohydrates (407 kcal, fibre 6.5 g; CCHO)	n = 26 m, healthy, normal-weight/overweight	4 h	S ↑ after CCHO vs. SCHO at 30, 60, 90 min	H ↑ after SCHO vs. CCHO at 60 and 180 min	Glucose and insulin ↑ after SCHO vs. CCHO at 30 min.  TG at 180 min, and FFA at 180 and 240 min ↑ after SCHO vs. CCHO.		Consumption of a CCHO breakfast is favourable in comparison to a SCHO breakfast, because of the lower perception of 'fatigue' and the higher degree of satiety after consumption.
<b>Warren et al. 2003</b>  The purpose of the study was to investigate the effect of 3 test breakfasts on ad libitum lunch intake, appetite, and satiety and to compare these with baseline values when habitual breakfast was consumed.	Breakfasts: - habitual (fibre 3.8 g, 1510 kJ) - low GI (fibre 5.9 g/portion, 1518 kJ) - low GI + 10% sugar (fibre 5.9 g, 1659 kJ) GIs - high GI (fibre 1.3 g, 1502 kJ)	n = 37 children (15 m, 22 f), normal-weight 70%, overweight 24%, obese 6%	from breakfast to lunch, 3 experimental days/meal type	S ±0  Prelunch S inversely related to subsequent food intake.	At lunchtime, H ↑ after high-GI breakfast vs. other 2 breakfasts on 2 of the 3 experimental days.		Lunch intake ↓ after low-GI and low-GIs vs. after high-GI and habitual breakfasts	Low-GI foods eaten at breakfast have a significant impact on food intake at lunch. This is the first study to observe such an effect in a group of normal and overweight children.
<b>Blom et al. 2005</b>  To examine the effects of amount and	liquid 578 ml breakfasts differing in energy content and carbohydrate structure: - water (control) (C)	n = 20 m, healthy, normal-weight/overweight	4 h	F ↑ after HC/SC and HC/CC vs. W  Ghrelin correlated	H ↓ after HC/SC, HC/CC vs. W  Ghrelin	glucose (AUC) ↑ after HC/SC, HC/CC vs. LC, C  insulin (AUC) ↑		The results support the hypothesis that ghrelin requires postgastric feedback, which may be regulated through insulin.



Reference Aim of the study	Fibre used / Fibre source	Subjects	Time scale	Satiety	Hunger	Biological responses	Food intake / <i>ad libitum</i>	Conclusions
type of carbohydrate on ghrelin concentrations and correlations among the variables ghrelin, glucose, insulin, leptin, and subjective measures of appetite.	- low-calorie, 736 kJ, fibre 14 g (LC) - high-calorie simple carbohydrate (incl. maltodextrin), 2674 kJ, fibre 12 g (HC-SC) - high-calorie complex carbohydrate (incl. exopolysaccharide), 2674 kJ, fibre 12 g (HC-CC)			negatively with F.	correlated positively with H.	after HC/SC, HC/CC vs. LC, C  ghrelin (negative AUC) ↑ after HC/SC vs. HC-CC, LC, C  ghrelin (negative AUC) ↑ after HC/CC vs. LC, C  leptin (AUC) ±0		
<b>Pai et al. 2005</b>  To determine the satiety values of six breakfast items commonly consumed in India	250 kcal portions of breakfast items: - white wheat bread (fibre 0.2 g) (control) - fermented rice-pulse preparation (fibre 0.3 g) - broken wheat preparation (fibre 0.9 g) - whole wheat flour flat bread (fibre 1.1 g) - semolina preparation (fibre 0.4 g) - rice flakes preparation (fibre 0.5 g)	n = 32 f, healthy, normal-weight	2 h	S ↑ in the order of: fermented rice-pulse preparation > broken wheat preparation > whole wheat flour flat bread > semolina preparation > rice flakes preparation > white bread.  Fibre content, energy density and				These data indicate that isoenergetic portions of various foods influence satiety to different extents. Thus consumption of high protein, high fibre and foods with greater water/volume leading to low energy density may be effective in delaying the return of hunger.

Reference Aim of the study	Fibre used / Fibre source	Subjects	Time scale	Satiety	Hunger	Biological responses	Food intake / <i>ad libitum</i>	Conclusions
				cooked weight of foods positively influenced satiety scores.				
<b>Johnson et al. 2005</b>  To determine the effect of adding chickpea flour or extruded chickpea flour to white bread on palatability and postprandial glycaemia, insulinaemia and satiety.	Four breakfasts (50 g available carbohydrate): - control (white) bread (WB) x 2 - chickpea bread (CHB) x 1 - extruded chickpea bread (EXB) x 1	n = 11 (9 m, 2 f), healthy, normalweight /overweight	175 min	S ±0		glucose: a trend towards ↓ incremental AUC after CHB compared to WB.  Insulin: ↑ IAUC and insulinaemic index after CHB than after WB  Glycaemic index (GI) ±0	food intake ±0	CHB demonstrated some hypoglycaemic effect compared to WB, but neither CHB nor EXB demonstrated effects on satiety or food intake. The hyperinsulinaemic effect of CHB observed requires further investigation.

S = satiety; F = fullness; H = hunger; D = desire to eat, PC = prospective consumption, *ad lib* = *ad libitum* meal, IAUC = incremental area under curve, GLP-1 = glucagon-like peptide 1, CCK = cholecystokinin, ↑ = increased response, ↓ = reduced response, ±0 = no difference, results in (parenthesis) = result not statistically significant, still a trend

## 6. Dietary composition in appetite and weight management

### 6.1 Low-fat diets

Low-fat diets are the best studied dietary approach to weight loss and several meta-analyses have been performed. In the first meta-analysis including 28 clinical trial by Bray and Popkin, a reduction of 10% in the proportion of energy from fat was associated with a reduction in weight of 16 g/d, which can be extrapolated to a weight loss of 8.8 kg over 18 months (Bray and Popkin 1998). Similarly, a decrease of 10 E% (% of total energy) from fat increased weight loss by 2.8 kg in another meta-analysis by Yu-Poth et al, including 37 intervention trials of 4 weeks – 4 year duration with the objective to evaluate the effect of a low fat diet on major CVD risk factors, (Yu-Poth et al. 1999). Astrup et al, have published two meta-analyses, the first with less restrictive inclusion criteria, finding a 2.6 greater weight loss on a low fat diet compared to a control diet, and every 1 E% reduction in fat was associated with a 0.37 kg weight loss (Astrup et al. 2000b). In the second meta-analysis, Astrup et al. (2000a) reported that a reduction of 10.2% in dietary fat can produce a greater reduction of 1138 kJ/d and a 3.2 kg greater weight loss compared to the control group. Furthermore, an initial pretreatment of 10 kg was found to be related to an additional weight loss of 2.6 kg (Astrup et al. 2000a). These four meta-analyses all conclude that dietary fat plays a role in obesity and a low fat diet is the best dietary strategy for weight loss, whereas this could not be concluded in the meta-analysis by Pirozzo et al. (Pirozzo et al. 2003). In this, the effectiveness of low-fat diets of 3–18 months duration and with 6–18 months follow-up in achieving sustained weight loss was investigated. A total of 594 subjects from 6 randomized controlled trials were included. It was concluded that low-fat diets are just as efficacious as other weight reducing diets for achieving sustained weight loss (Pirozzo et al. 2003).

In the Women's Health Initiative Dietary Modification Trial involving almost 50,000 comparing a low-fat diet with a control diet higher in fat it was suggest that an *ad libitum* reduced fat (24%–29% energy from fat) diet result in modest but greater weight loss during the first year of the trial and less weight gain over 7.5 years than the higher fat (35%–37% energy from fat) diet (Howard et al. 2006). This was seen, despite the fact that neither group was instructed to lose weight (Howard et al. 2006). After the first year the difference in weight loss between groups was 1.9 kg and 0.4 kg after 7.5 years. Compliance to the low-fat diet would be poor during such a long period, but post-hoc analysis of self-reported diet suggested that those who had reduced their fat intake had gained app. 2 kg less than the control group after 7 years.

Walter Willett and other researchers argue that dietary fat is not important in the development of obesity. The given explanations include the fact that the prevalence in obesity has increased in the United States despite the fact that fat intake has declined, and that other ecological studies have found no relations between dietary fat intake and body fatness. Furthermore a reduction in dietary fat has been found to have little effect on the reduction in body weight (Katan et al. 1997, Willett 1998).

## 6.2 Type of fat

Although all types of fat contain almost the same amount of energy, it seems that differences may exist in their potential to influence energy balance. In a recently published population-based, prospective cohort study (Nurses' Health Study) including more than 40,000 women, aged 41–68, found after 8-years follow-up a weak positive association between total fat intake and weight gain. Though, increases in vegetable oils (MUFA and PUFA) were not associated with weight gain, but increases in animal fat (SFA), and trans fat had a positive association with weight change (Field et al. 2007). Other studies also indicate that the intake of unsaturated fat does not lead to the same weight gain as an isocaloric saturated fat diet (Hill et al. 1991, van Marken Lichtenbelt et al. 1997, Couet et al. 1997).

It is known that both satiety and energy expenditure can be affected by the quality of dietary fat (Jeffcoat 2007) and in a cohort of women all lipids other than vegetable fat have been found to be positively related to BMI (Colditz et al. 1990). A cross sectional observational study showed that a higher intake of PUFA was not associated with adiposity as opposed to the total intake of fat, intake of SFA and MUFA (Doucet et al. 1998). MUFA also seems to increase body weight more than PUFA (Dulloo et al. 1995) and a study from Walter Willett's group further indicates that MUFA may be more fattening than other fats (van Dam et al. 2002). Furthermore, MUFA has been found to induce a lower level of post-ingestive satiety and a larger subsequent energy intake compared to PUFA and SFA in lean subjects of high-fat meals, differing in fatty acid composition (Lawton et al. 2000).

MUFA has also been found to be more favourable than SFA in changes in weight and body fat. In a 4 week crossover study substituting dietary saturated fat with unsaturated fat, predominantly MUFA, induced a small but significant loss of body weight and fat mass without a significant change in total energy intake or fat intake (Piers et al. 2003). The authors expect this as a result of a greater fat oxidation on the MUFA rich diet compared to a SFA rich diet as found in their previous study (Piers et al. 2002). Though the studies of Piers et al. were based on only 8 and 14 subjects, respectively and it could be interesting to test the differences in fatty acid composition in a larger and longer

study to verify these results and see if compensation in energy intake would take place. Further more, olive oil has been found to promote postprandial fat oxidation and stimulate DIT in abdominally obese postmenopausal women (Soares et al. 2004).

Animal studies have shown that rats fed a diet rich in safflower oil (PUFA) as opposed to a diet rich in beef tallow (SFA) accumulate less body fat (Shimomura et al. 1990, Dulloo et al. 1995). This is probably a result of a higher diet induced thermogenesis (DIT), an elevated fat oxidation and higher sympathetic activity (Shimomura et al. 1990, Matsuo et al. 1995). The dietary proportion of saturated to unsaturated fat possibly affects the contribution of fat to energy expenditure in humans (Jones et al. 1985), and it was demonstrated that a greater PUFA/SFA-ratio resulted in a greater DIT.

### **6.3 Low-carbohydrate diets**

Low-carbohydrate diets have been a very popular dietary strategy for weight loss and weight maintenance the last decade. Many versions of the low-carbohydrate diet exist (i.e., Atkins New Diet Revolution, South Beach diet), each with a unique interpretation of optimal low-carbohydrate eating. Low-carbohydrate focus on the restriction of carbohydrate containing foods based on refined carbohydrate (i.e., white bread, rice, pasta, cookies, and chips) and encourages consumption of controlled amounts of nutrient dense carbohydrate containing foods (i.e., low GI vegetables, fruits, and whole grain products). Although consumption of foods that do not contain carbohydrate (i.e., meats, poultry, fish, as well as butter and oil) is not restricted, the emphasis is on moderation and quality rather than quantity in most low-carbohydrate diets, with exception of the Atkins diet.

Five randomized studies conducted over 6–12 months have compared the effects of a low-carbohydrate diet and a calorie-controlled, low-fat diet on weight and body composition in obese adults (Brehm et al. 2003, Foster et al. 2003, Samaha et al. 2003, Stern et al. 2004, Yancy, Jr. et al. 2004, Dansinger et al. 2005). Two of the trials (Samaha et al. and Stern et al.) refer to the same study but report 6 month and 12 month data, respectively. The diet prescriptions in these five studies were comparable (e.g., a low-carbohydrate diet containing 20–60 grams of carbohydrate), body mass index (BMI) and ages ranged from 33–43 kg/m<sup>2</sup> and 43–54 years, respectively. Participants who consumed a low-carbohydrate diet lost significantly more weight than those who consumed a low-fat diet during the first 6 months of treatment in four of the five studies (Brehm et al. 2003, Foster et al. 2003, Samaha et al. 2003, Yancy, Jr. et al. 2004). Despite differences at 6 months, there were no differences in weight loss at 1 year (Foster et al. 2003, Samaha et al. 2003, Dansinger et al. 2005). In the studies by Foster et al. and Dansinger et al. a weight regain in both groups after 6 months was observed

with a greater regain in the low-carbohydrate group. While participants in the low-carbohydrate group did not regain weight in the third 1-year study, those in the low-fat group continued to lose weight after 6 months, resulting in similar weight losses at one year (Stern et al. 2004).

Another 12-month study compared four weight loss diets representing a wide range of carbohydrate composition (i.e., Atkins, Zone, Ornish, LEARN diets) in 311 overweight and obese, nondiabetic, premenopausal women (Gardner et al. 2007). Participants attended group treatment for 8 weeks and received specific dietary instruction, according to the guidelines of the assigned diet, as well as instruction on behavior modification. Unlike the previous studies, this study reported differences in weight loss between groups at one year. Compared with the Zone diet (i.e., -1.6 kg), women on the Atkins diet (i.e., -4.7 kg) lost more weight at 12 months; however, weight loss was not significantly different between the Atkins diet and any of the other diet groups at one year. Similarly, weight loss was not significantly different among the Zone, LEARN and Ornish groups.

Data from the studies described above suggest that although participants in the low-carbohydrate group were not instructed to limit their energy intake as were individuals in the conventional group, the low-carbohydrate group consumed fewer calories (Brehm et al. 2003, Yancy, Jr. et al. 2004). Thus, at 6 months, subjects who were instructed to count carbohydrate consumed fewer calories than those who were instructed to count calories. The reason for this is unknown but may include greater satiety on a higher protein, low GI diet.

## 7. Food structure

The effect of food on satiety and weight control is dependent on composition and energy content, but the physical properties of the food, like structure, are also important. Food structure affects e.g. rate and extent of digestion, and rate of absorption of nutrients. Usually solid foods with strong tissue structure like fresh whole fruits and vegetables, breads containing whole grains, and whole meat products are digested more slowly and are more satiating than foods that have soft, overripe or a highly processed structure (Porrini et al. 1995). Palatability of food is also an important factor determining the developments of satiety and amount of food ingested.

### 7.1 Macrostructure and rheological properties

#### 7.1.1 Foods containing tissue structures and large particles

Solid, large particles exit the stomach only after their size is reduced to below 2 mm in diameter. E.g. pasta requires extensive motoric activity from the stomach to reduce the particle size enough and exit the stomach. For spaghetti, the half time of emptying is about 75 minutes and for mashed potatoes about 35 minutes (Mourot et al. 1988). The speed with which food exits the stomach is correlated to blood glucose and insulin responses and can also affect feeling of satiety (Björck and Elmståhl, 2000). Independent of the form of food, the rate of stomach emptying and satiety are correlated (Bergmann et al. 1992).

#### Cereal products

By comparing the effect of milling extraction on physiological effects, intact whole grains were found to cause a lower glucose and insulin response and a higher feeling of satiety than crushed grains, which in turn was better than coarsely ground flour. A difference between coarsely and finely ground flours was also observed (Heaton et al. 1988; Jenkins et al. 1988; Holt and Brand Miller 1994). However, Behall et al. (1999) observed no difference in glucose and insulin responses between very finely ground and regular whole grain flour.

#### Fruit and vegetables

Similarly, effects on blood glucose, insulin responses, and satiety have also been observed with fresh fruit, juice and puree (Haber et al. 1977; Bolton et al. 1981). Whole apples (Haber et al. 1977), whole oranges and grape fruits (Bolton et al. 1981) caused a greater feeling of satiety than fruit puree. The satiating effect of the purees was in turn

higher than those of juice. The test portions contained the same amount of absorbable carbohydrates (60 g), but fibre had been removed from the juice, which made it different in composition. Different forms of fruit affected rate of eating: juice was ingested 11 times faster than the whole fruit and 4 times faster than puree. The blood glucose rose to the same level after each portion. However, the glucose level decreased very steeply after the juice ingestion, less steeply after the puree, and least after the whole fruit. Insulin level was higher after juice and puree than after whole fruit. Removal of fibre from the juice and breaking of the fibre structure in the puree made the fruit faster and easier to eat and thus changed its effect on satiety and glucose and insulin metabolism to a less favourable direction in respect of weight control.

Gustafsson et al. (1995a) studied the effect of processing and cooking on the metabolic response to carrots in mixed meals. Carrot portions containing 4.4 g and 6.6 g of dietary fibre were compared. Raw carrots elicited significantly lower glucose, insulin, and C-peptide responses and produced higher satiety scores than microwaved ones. Processed carrots with a higher dietary fibre intake had a significant effect on the glucose response only.

### Meat

French et al. (1991) studied the effects of meat type and particle size on satiety. At different times, before the main course, the subjects ate a bouillon, which contained pasta and small (2 mm) or large (4 mm) particles of beef or chicken. After the starter containing large particles, the subjects consumed a meal containing less energy than the meal consumed after the starter containing small particles. Both meals were ingested 30 minutes and 3 hours after the starter. In addition, the beef starter reduced energy intake more than the chicken starter. Toughness of the connective tissue as well as particle size were suggested to slow gastric emptying time and thus prolong satiety, measured as the energy content of the next meal.

### **7.1.2 Porous foods**

High porosity of bread promotes degradation of its structure in mouth and stomach. Starch in highly porous bread is more degraded prior to consumption, than the structure of more dense bread (Autio et al. 2003). In general, pasta and rye bread are swallowed as large particles, and the protein in them is not easily digested by the stomach. Protein of white bread is easily digested in the stomach, and separate starch granules are also easily transferred to the small intestine.

Organic acids or their salts in starchy foods lower the glucose response and especially the insulin response. The mechanisms suggested to be involved, are a slower gastric



emptying time or prevention of the action of amylases. Organic acids or their salts, e.g. lactic acid, ca-lactate, sodium propionate or acetic acid, can be added to products like bread dough or to food at meal. Acetic and lactic acids affect the structure of bread and it is possible that the dense structure of acid breads affects gastric emptying time. Acetic and lactic acids are also formed in sour dough fermentation or fermentation of vegetables. Breads containing sodium propionate (used in bakery industry to prevent growth of molds and bacteria) have been observed to increase feeling of satiety more than regular bread. Other organic acids or their salts in bread have not been shown to have the same effect (Todesco et al. 1991; Liljeberg et al. 1995; Liljeberg and Björck 1996).

## 8. Bioactive compounds

In addition to energy nutrients, food can contain a variety of bioactive compounds like vitamins, phenolic compounds, antioxidants, etc. Some of these have been proposed to decrease energy intake and increase satiety and/or energy expenditure and thus promote weight loss.

### 8.1 Caffeine

Caffeine is found in a large number of plants such as coffee, tea, cola nuts, and cacao beans and is widely consumed in many beverages and in chocolate. Caffeine has consistently been shown to possess thermogenic properties (Dulloo et al. 1989), and observational studies supports that a regular daily intake also produce a slight weight loss (Lopez-Garcia et al. 2006). Short-term thermogenetic effects of caffeine in a range of 100–600 mg have been reported in large number of studies in lean, obese and post-obese individuals (Acheson et al. 1980, Hollands et al. 1981, Jung et al. 1981, LeBlanc et al. 1985, Poehlman et al. 1985, Pasquali et al. 1987, Dulloo et al. 1989, Astrup et al. 1990, Koot and Deurenberg, 1995, Bracco et al. 1995). The effects have been shown to be dose dependent (Astrup et al. 1990) and may be different in caffeine users and non-users. There is also some evidence that caffeine stimulates lipolysis (Hetzler et al. 1990, Graham et al. 2000) and fat oxidation (Acheson et al. 1980, Bracco et al. 1995), but these results have been less consistent. Astrup et al. showed that an intake of caffeine ( $3 \times 200 \text{ mg day}^{-1}$ ) together with an energy-restricted diet did not result in a greater weight loss compared to placebo after 24 weeks (Astrup et al. 1992). The lack of long-term effect of caffeine on body weight may be attributed to development of tolerance to its thermogenetic effect. Although caffeine was found to increase thermogenesis in moderate caffeine users it is possible that the effect of caffeine disappears with concomitant consumption of other caffeine containing products, as is the case in free living conditions when daily caffeine intake may be large.

### 8.2 Green tea

Green tea is the non- and partly fermented/oxidized products in contrast to black tea that is fully fermented/oxidized. Green tea contains a mixture of catechins that enhances sympathetic activity slightly, and subsequently increase thermogenesis and fat oxidation (Dulloo et al. 1999). Dulloo et al. showed that green tea (caffeine:  $150 \text{ mg day}^{-1}$  and catechins:  $375 \text{ mg day}^{-1}$ ) stimulated 24-h thermogenesis in humans by 3.5% and fat oxidation by 27 g compared to placebo. The effect of green tea was greater than could be attributed to its caffeine content alone (which raised thermogenesis and fat oxidation

by 2.5% and 21 g, respectively). A number of studies have indicated that longer-term consumption of green tea components can have benefits for body weight or fat mass/distribution. In a non-placebo controlled trial a 12 week ingestion of green tea (caffeine: 150 mg day<sup>-1</sup> and catechins: 375 mg day<sup>-1</sup>) led to decreases of 4.6% in body weight and 4.5% in waist circumference (Chantre and Lairon 2002). In contrast, Kovacs et al. (Kovacs et al. 2004) found no evidence of long-term weight control benefits of green tea components. Green tea supplementation (caffeine: 104 mg day<sup>-1</sup> and catechins: 573 mg day<sup>-1</sup>) for 13 weeks following weight loss did not improve weight maintenance compared to placebo. In that study, among subjects given green tea, a higher habitual caffeine intake was associated with a higher weight regain, suggesting that background caffeine intake affects the effectiveness of green tea for weight maintenance. Although green tea has shown promising short-term effects on energy expenditure and fat oxidation, more data are needed to draw a conclusion on the long-term weight control effects.

### 8.3 Capsaicin

Capsaicin is the most pungent ingredients in hot spices like red pepper, tabasco sauce, mustard and ginger and has attracted interest because of the potential effect on thermogenesis and fat oxidation by enhancing sympathetic activity (Lejeune et al. 2003). In a short-term study, a 25% greater increase in metabolic rate over 150 minutes was observed with a meal containing 3 g of chilli sauce and 3 g of mustard compared to a non-spiced control meal (Henry and Emery 1986). An addition of 10 g red pepper with 30 mg capsaicin to a meal has been found to increase energy expenditure by 23% immediately after the meal (Yoshioka et al. 1995). Furthermore, the effect of red pepper on thermogenesis and fat oxidation was greater with a high-fat meal compared to a high-carbohydrate meal over 210 minutes (Yoshioka et al. 1998). Addition of red pepper to an appetizer has been found to reduce subsequent carbohydrate intake (36 g) and energy intake (791 kJ) at lunch and snack time (Yoshioka et al. 1999). Furthermore, a combination of red pepper added to two appetizers and caffeine as coffee reduced energy intake (3690 kJ equivalent to 17%) and increased energy expenditure (320 kJ equivalent to 3.2%) during 24-h in men, resulting in lower positive energy balance (Yoshioka et al. 2001). Data on the long-term of capsaicin are scarce. One study showed that red pepper supplementation in 3 months after a modest weight loss resulted in increased post-absorptive fat oxidation and resting energy expenditure (Lopez-Garcia et al. 2006). However, no improvement in weight maintenance or suppressed fat gain was found.

The search for natural foods ingredients that have a beneficial effect on energy balance is an interesting research topic. A combination of caffeine, catechins from green tea, and capsaicin may have a potential role in functional foods and dietary supplements for weight control (Belza and Jessen 2005, Belza et al. 2007).

## 8.4 Calcium

There is evidence that dairy calcium may play a role in body weight regulation (Zemel 2002, Teegarden and Zemel 2003, St Onge 2004), although meta-analyses of calcium consumption and weight loss has not shown any association between calcium consumption and a greater loss of body weight (Barr 2003, Trowman et al. 2006). The data reviewed by Parikh and Yanovski (2003) shows that in epidemiological studies the body weight is highest in the group with lowest intake of calcium. In intervention studies, high intake of calcium has promoted higher weight loss than low calcium low energy or normal energy meals. Calcium in milk products appears to be more effective than supplementary calcium, which has caused speculations that some other component in milk is promoting weight loss. Such compounds that have been proposed are whey proteins (Zemel 2003), conjugated linoleic acid (Belury 2003), and branched-chain amino acids (Layman 2003). However, a long-term study showed no effect of various conjugated linoleic acid isomers on body weight loss over a period of 18 wk (Malpuech-Brugere et al. 2004). A short-term increase in dietary calcium intake, together with a normal protein intake, has been found to increase fecal fat and energy excretion by approximately 350 kJ/day. This observation suggests that an interaction with dietary protein level may be important (Jacobsen et al. 2005). However, long-term studies are needed to see whether compensational mechanism in energy intake may take place (Jacobsen et al. 2005). Moreover, contradictory results showing no effect of milk/calcium on weight loss exist (Bowen et al. 2003, Macdonald et al. 2003).

## 9. Gut microbiota and obesity

### 9.1 Gut microbiota and its functions

Colon has an abundant microbiota dominated by anaerobically growing bacteria (Berg 1996). The number of bacteria in faeces typically is  $6-9 \times 10^{10}$  per gram (wet weight) (bacteria detected with molecular techniques) (Thiel and Blaut 2005). It is estimated that our intestinal tract contains as many as  $10^{14}$  microbes (which is about ten times more the total number of the host cells) (Bäckhed et al. 2005). Faecal microbiota is dominated by *Clostridium coccooides* – *Eubacterium rectale* group, *Clostridium leptum* group, and *Bacteroidetes* group (Franks et al. 1998, Suau et al. 1999, Sghir et al. 2000, Harmsen et al. 2002, Eckburg et al. 2005) which account for over 70% of the fecal bacteria (Sghir et al. 2000). The bacteria belonging to the *Clostridium coccooides* – *Eubacterium rectale* group (clostridial cluster XIVa) (Collins et al. 1994) comprise 10–45% of the total faecal bacteria as detected with hybridization based methods (Franks et al. 1998, Sghir et al. 2000, Harmsen et al. 2002, Maukonen et al. 2006) and 10–59% of the total faecal microbiota when analyzed with the 16S rRNA gene library method (Wilson and Blichington 1996, Suau et al. 1999, Eckburg et al. 2005). In total as many as 800 species and over 7000 strains are estimated to cohabit the human colon. Typically, gut microbial population is stable within an individual but varies between individuals. Host genotype seems to be an important factor in determining its composition (Bäckhed et al. 2005).

Gut microbiota contributes to various host processes such as defence against pathogens at the gut level, immunity, development of mammalian gut (development of intestinal microvilli and intestinal angiogenesis), transformation of bioactive molecules, fermentation of non-digestible food components, and recovery of metabolic energy for the host. It is also probable that human gastrointestinal microbiota contributes to the variability in host responses to various drugs and toxins (Hentschel et al. 2003, Nicholson et al. 2005).

### 9.2 Gut microbiota and the energy balance of the host

It can be postulated that gut microbiota influences the energy balance of the host. On one hand microbial fermentation in the colon generates short chain fatty acids (SCFA) which can be utilised by the host, but on the other hand gut microbiota is a substantial consumer of energy (which is needed to replace the bacteria that the host excretes) (Bäckhed et al. 2005). In humans on European diet 50–60 g of carbohydrate are fermented per day, yielding 0.5–0.6 mol of SCFA (total energy value 140–180 kcal, which is about 10% of the maintenance caloric requirement). The main SCFA acetate, propionate and butyrate are taken up by different organs and thus they have different metabolic fates. It is estimated that the colonic epithelium derives 60–70% of its energy

from butyrate, whereas propionate is transported to the liver and acetate is mainly consumed by muscles (Hooper et al. 2002).

Studies with germ-free mice have shown that gut microbiota can regulate fat storage: When germ-free animals were conventionalised with the cecal content of conventional mice, 60% increase in body fat content and insulin resistance development was observed, despite reduced chow consumption (Bäckhed et al. 2004). This study revealed that the gut microbiota promoted the absorption of monosaccharides from the gut lumen, which resulted in *de novo* hepatic lipogenesis. Microbiota was shown to suppress the intestinal expression of circulating lipoprotein lipase inhibitor Fiaf and thus to promote the storage of triglycerides in adipocytes (Bäckhed et al. 2004). Dumas et al. (2006) further revealed that gut microbiota contributes to fatty liver phenotype and plays an active role in the development of insulin resistance in mice. A later study of Bäckhed et al. (2007) investigated the mechanisms underlying the resistance to diet-induced obesity in germ-free mice. They concluded that germ-free mice were protected from diet-induced obesity by two mechanisms that increase fatty acid metabolism: by elevated levels of Fiaf and by increased activity of AMP-activated protein kinase, an enzyme involved in monitoring the cellular energy status.

Obesity has been shown to alter gut microbial ecology both in animals and humans. Studies with genetically obese and wild-type mice showed that obese mice had a 50% reduction in the abundance of Bacteroidetes and a proportional increase in Firmicutes (including e.g. clostridia and related species) (Ley et al. 2005). Later on this result was confirmed in a small number of human volunteers: 12 obese people were randomly assigned to either a fat-restricted or to a carbohydrate-restricted low-calorie diet and the composition of their gut microbiota was monitored for one year. The results showed that before diet therapy obese people had fewer Bacteroidetes and more Firmicutes than the lean controls and that over time the relative abundance of Bacteroidetes increased and the abundance of Firmicutes decreased. Furthermore, increased abundance of Bacteroidetes was shown to correlate with percentage loss of body weight (Ley et al. 2006). Based on metagenomic and biochemical studies performed with mice cecal samples Turnbaugh et al. (2006) suggested that “obese” microbiota has an increased capacity to harvest energy from the diet.

However, since the studies investigating the role of gut microbes in obesity were performed either in germ-free or genetically obese animals or in a small number of human volunteers on specific diets these results have to be considered to be preliminary. What kind of role gut microbiota could have in the obesity development of humans in a “normal” situation necessitates further studies. Since changes in diet can alter the gut microbiota composition (Mai et al. 2004) the hypothesis that gut microbiota could actually directly contribute to obesity will at the moment remain highly speculative.

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