13 Formulation Design to Change Food Habits

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13.1 INTRODUCTION

With increased prevalence of overweight and obesity it is important to identify properties of food that have the potential to promote reductions in energy intake and thus contribute to weight control. The literature demonstrates that foods that target within-meal satiation and post-meal satiety provide a potential approach to weight management. The effects of manipulating the macronutrient composition of the diet on appetite have been widely examined, with considerable research indicating that certain ingredients, consumed in food matrices, can produce significant effects on short-term appetite regulation. More recently, manipulating food structure has been identified as another valid mechanism for influencing appetite control with the potential to control the rate of release of macronutrients and slow the rate of stomach emptying in order to limit the amount of food consumed. To effectively intervene and alter energy intake through changes in food structure we must consider the nature of appetite expression, the structure of the appetite system, laboratory measures of appetite and finally the implications of these manipulations for weight management.

13.2 WEIGHT MANAGEMENT: THE CHALLENGE

The increasing prevalence of obesity in Europe and America poses a significant threat to public health. Obesity, and especially abdominal adiposity, is a risk factor for non-communicable diseases such as cardiovascular disease, non-insulin-dependent diabetes and various types of cancer (Bray, 2004). Given the complexity of the endogenous systems underpinning energy regulation (see Section 13.3) it may

Formulation Engineering of Foods, First Edition. Edited by Jennifer E. Norton, Peter J. Fryer, and Ian T. Norton.
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appear surprising that the obese state exists. This can be attributed to the combined impact of the modern obesogenic environment and an evolutionary-based appetite control system designed to increase food intake and storage during times of plenty, the so called "asymmetry" of appetite control. Although, in theory a small reduction in intake could produce significant weight loss, in practice many individuals experience great difficulty in achieving this small behavioural change and controlling their body weight.

The simple fact that not all individuals are obese despite the currently inappropriate combination of environment and asymmetrical appetite control demonstrates that important individual differences in vulnerability exist. Evidence indicates that a number of key behavioural traits are associated with overeating and the development of obesity. Elevated body mass index (BMI) is associated with a faster eating rate (Spiegel *et al*., 1991; Barkeling *et al*., 2007; Laessle *et al*., 2007; Halford *et al*., 2010a). Typically a failure to demonstrate the deceleration in eating rate normally associated with the development of satiation within a meal also occurs in the obese (Meyer and Pudel, 1972; Halford *et al*., 2010a). These characteristics are accompanied by weakened satiety responsiveness post consumption, such that ingested calories impact less on eating behaviour, hastening the onset of the next meal (Carnell and Wardle, 2008). The tendency for obese individuals to show a preference for energy-dense foods, usually high in fat and/or sugar, may contribute to this weakened satiety response (Bray *et al*., 2004).

However, overconsumption cannot be solely explained by a weakened regulatory control of eating behaviour. Eating is a sensory experience and a heightened hedonic response to ingestion in obese individuals can overwhelm regulatory control. The obese demonstrate a greater responsiveness to food cues, eating more than is required by physiological need (Mattes, 1997). This is associated with experiences of uncontrolled hunger and greater disinhibition of eating behaviour. Constant and excessive hunger and disinhibition both appear to have a genetic component linked to obesity and adiposity (Bauer *et al*., 2009).

In particular, the behavioural traits related to the meal-by-meal regulation of eating behaviour (inappropriate eating rate and weakened satiety) have all been linked to a lack of regulatory feedback from the gastrointestinal (GI) tract (see Section 13.3.2). Reduced release of satiety gut hormones, impaired response to gut hormones and enhanced gastric capacity all contribute to weakened appetite control (Blundell *et al*., 2008). As such, these deficiencies offer potential targets that can be exploited through manipulations of macronutrient composition and

food structure to enhance the impact of foods on appetite regulation. If such food formulation yields palatable products, behavioural traits associated with hedonic aspects of consumption may also be challenged.

13.3 THE APPETITE CONTROL SYSTEM

13.3.1 Appetite expression: Hunger, satiation and satiety

An increasingly adopted approach to the control of body weight is to exploit the regulatory mechanisms that control eating behaviour and which are encountered in our psychological experiences of hunger, satiety and satiation. Hunger is the motivation to seek and consume food. It initiates and sustains eating activity. Conversely, the act of consumption generates feedback to bring the resulting feeding episode to an end. The processes that terminate eating behaviour are termed satiation (Blundell *et al*., 2001). In turn, satiation processes ultimately lead to the state of satiety in which the hunger drive and eating behaviour are inhibited (Blundell, 1991). Whilst satiation determines meal duration and meal size, satiety determines the length of the post-meal interval. Feelings of fullness are key contributors to intrameal satiation. However, although fullness remains a powerful inhibitor of food intake immediately after a meal, alone it is insufficient to maintain intermeal satiety. The operation of these systems is influenced by many factors, including the physical and chemical properties (energy density, weight and volume, macronutrient composition, bulk, particle size and solidity) and the sensory impact (appearance, odour, taste and palatability) of food.

Despite the intimate link between these psychological events (experiences of hunger, satiation and satiety) and food intake, eating behaviour is also influenced by peripherally generated factors that arise from food consumption (nutrient absorption, utilisation and storage). There are three broad mechanisms via which such peripheral signals are generated:

1. *Digestion of food:* Neuronal and hormonal signals are generated in response to the physical and chemical properties of food and their presence and absorption in specific sections of the GI tract.
2. *Nutrient utilisation:* Transient declines in blood glucose may provide a signal for meal initiation. Similarly hormones such as ghrelin initiate hunger sensations in response to blood nutrient levels with concentrations peaking just before meal initiation and falling following intake.

3. Energy storage*:* Hormones such as leptin, insulin and glucagon are secreted by organs such as the liver, the pancreas and adipose tissue to indicate the status of the body's energy stores.

In turn this plethora of neuronal and hormonal factors provides input to the central nervous system (CNS) and specifically the hypothalamus and brainstem (see Section 13.3.3).

The satiety cascade (see Fig. 13.1) demonstrates the combination of behavioural, physiological and psychological factors that influence appetite control (Blundell *et al*., 2001). It also highlights the sensory and cognitive factors that contribute to eating behaviour, and illustrates how properties of a food (including macronutrient composition and physical structure) can modulate the processes underlying energy regulation. Pre-consumption physiological signals are generated by the sight and smell of the food, preparing the body for ingestion. Such signals stimulate hunger before eating and during consumption. During consumption, the CNS also receives post-ingestive sensory signals from the gut which reflect the amount and the nutritional content of the food eaten. Mechanoreceptors in the gut wall detect the stretch of the stomach and provide an indication of the amount of food consumed. Additionally, gut chemoreceptors detect the nutritional composition of the food consumed and release hormones that influence gastric emptying and transit (see Section 13.3.2). During and after consumption further appetite regulatory signals are generated through the metabolism of nutrients absorbed from the GI tract into the circulation, and the storage of energy in nutrient stores. In turn, this abundance of peripheral signals influences CNS functioning, either directly or through stimulation of afferent signal pathways.

13.3.2 Biomarkers of appetite

The satiety cascade clearly demonstrates that underpinning human appetite expression are various signals that provide potential targets for appetite control. These are predominantly generated by the GI tract in response to the physical and/or chemical presence of food. Of particular current interest are the gut hormones that influence the passage of food through the GI tract. Nutrients slow GI transit, enhancing and prolonging the secretion of gut hormones that inhibit eating behaviour. This can result in reduced meal intake, decreased between-meal snacking and a delay in the onset of the next major eating occasion. The hormones that have been recognised as having a significant role include cholecystokinin (CCK), glucagon-like-peptide-1 (GLP-1), peptide YY (PYY) and ghrelin.

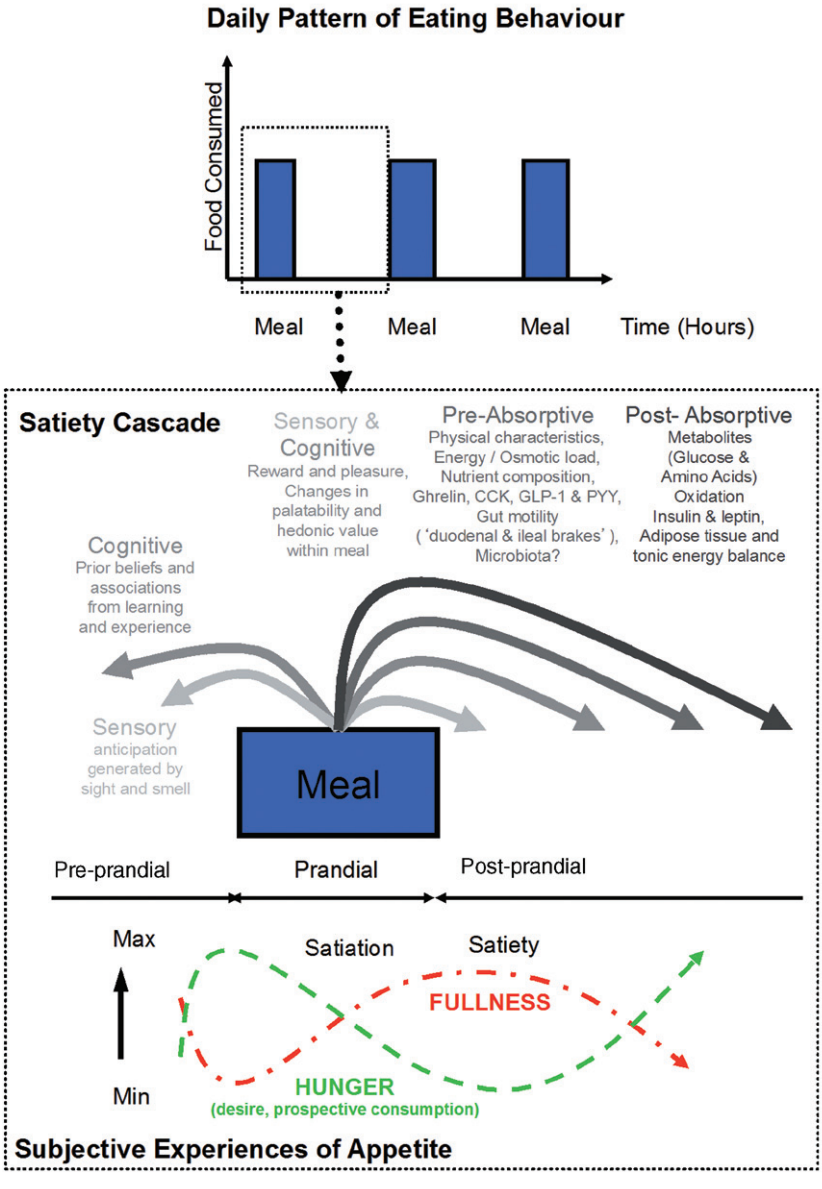

Fig. 13.1 The satiety cascade depicts the episodic behavioural, psychological and physiological signals arising prior to (pre-prandial), during (prandial) and after (post-prandial) food intake. These signals are involved in terminating a meal (satiation) and inhibiting further consumption (satiety). They act to co-ordinate the meal-by-meal pattern of eating by controlling the size and frequency of eating events. Reproduced with permission from Halford and Harrold (2012) Satiety-enhancing products for appetite control: science and regulation of functional foods for weight management. *Proceedings of the Nutrition Society* 71, 350–362. Cambridge University Press.

Endogenous CCK is released from I-cells in the duodenum and jejunum of the proximal intestinal tract upon detection of fat and protein from the diet. Infusions of CCK reduce food intake in animal studies (Gibbs *et al*., 1973; Figlewicz *et al*., 1992; Hirosue *et al*., 1993). Similarly, robust reductions of food intake, along with meal length, are observed in human subjects consistent with an involvement in satiation (Pi-Sunyer *et al*., 1982). These anorectic effects are mediated through CCK-induced reductions in gastric emptying rate (duodenal brake) and activation of CCK-1 receptors on vagal afferent neurones (Blackshaw and Grundy, 1990). There is also some evidence that CCK can communicate directly with appetite- regulating areas in the CNS (Blevins *et al*., 2000).

GLP-1 is released from L-cells in the ileum of the distal small intestine predominantly upon detection of carbohydrate, but also in response to fat. Its principle role is to release insulin and inhibit glucagon to achieve control of blood glucose levels. However, GLP-1 also delays gastric emptying (ileal brake – see Section 13.6.1; Naslund *et al*., 1999). Infusions of GLP-1 produce profound reductions in food intake via decreased hunger in both lean and obese humans (Verdich *et al*., 2001).

$PYY_{3\text{-}36}$ is also secreted from L-cells in the distal small intestine with its release occurring in response to fatty acids, fibre and bile in the gut. In a similar manner to GLP-1, $PYY_{3\text{-}36}$ causes a decrease in gastric empting and consequently a reduction in food intake (Batterham *et al*., 2002). When co-infused with GLP-1, an additive effect on energy intake is observed (Neary *et al*., 2005). Consistent with this, fermentation of dietary fibre in the small intestine, leading to the production of short-chain fatty acids (SCFA), has been shown to increase the release of both PYY and GLP-1 (Zhou *et al*., 2008; Tolhurst *et al*., 2012). As the release of $PYY_{3\text{-}36}$ appears to be confined to the very end of the meal or the period immediately thereafter, its release, and possibly that of GLP-1, may play a role in sustaining post-meal satiety and influencing intrameal satiation at the next eating event.

Ghrelin is unlike the gut hormones so far considered as it is produced higher up the GI tract, in the gastric fundus. Moreover, it stimulates rather than inhibits eating behaviour and stimulates gastric motility. Endogenous ghrelin levels peak just before meal initiation (Cummings *et al*., 2001) and fall following intake, particularly in response to high-energetic, high-osmotic loads (Callahan *et al*., 2004). Exogenous ghrelin infusions in lean participants increase food intake and appetite (pre-meal hunger and prospective consumption; Wren *et al*., 2001). Thus ingestion, through the inhibition of ghrelin signalling, delays gastric emptying and maintains fullness to contribute to satiation and early post-meal satiety.

13.3.3 Structure of the appetite control system

The regulation of food intake relies critically upon the CNS. The brain integrates the numerous signals that indicate the energy requirement of the body and in turn modifies the experience of hunger and initiates the relevant behavioural actions in response to this.

The CNS regions that control energy homeostasis are accessible to numerous circulating factors, including information generated by the sensory experience of eating and the physiological response to food ingestion. These signals enter the CNS by three main routes:

1. The peripheral signals briefly discussed above guide the central control of appetite by sending afferent vagal signals to the nucleus of the solitary tract/area postrema complex in the brainstem and from there upwards to the hypothalamus and other forebrain regions.
2. Regulatory signals are also derived from receptors within the CNS, particularly the brainstem. These detect circulating levels of nutrients, metabolites and other regulatory factors.
3. Specific substances e.g. glucose and neurotransmitter precursors, have the ability to cross the blood–brain barrier and alter neurochemical activity in key appetite-regulating sites of the brain.

Within the CNS itself are specific neuronal populations that recognise these signals and act in a network to integrate the multiple inputs, and help determine energy intake and expenditure. Primary locations involved in the regulation of food intake in mammals include the hypothalamus, and the amygdala and nucleus accumbens of the corticolimbic system. Structures in the brainstem also play an important role.

13.4 INGREDIENTS AND APPETITE CONTROL

13.4.1 Laboratory measures of appetite

Over the last 50 years the methodological platform necessary to develop protocols to measure the effect of a food on intrameal satiation and intermeal satiety has been established (Blundell *et al*., 2010). Whilst laboratory techniques are artificial in their nature, they are precise and reliable, they remove the confounds of the natural environment and they have been shown to have sufficient predictive validity to model real-world responses (Blundell *et al*., 2009, 2010).

The pre-load design represents the standard approach to examine the effects of a food on short-term appetite (Hill *et al*., 1995; Blundell *et al*., 2009, 2010). Pre-loads should take the intended form of the end product and should be matched for taste, appearance and other sensory

qualities to an equivalent control, such that only energy density and/or macronutrient composition are varied. A within-subject repeated-measures design allows for individual variations in appetite and eating style to be addressed. However, when food manipulations cannot be made covertly (thus removing the element of participant naivety as to the purpose of the study), a between-subjects design may be required.

The *ad libitum* meal (i.e. self-regulated intake) is the standard means of assessing the effect of a pre-load on short-term appetite (Hill *et al*., 1995; Blundell *et al*., 2009). The timing of meal administration is critical to ensure that it coincides with the product's maximal impact on appetite. If the pre-load meal interval is too short, any effects of the product on late inter-meal satiety will be missed. Conversely, if the interval is too long, any effects of the product on intra-meal satiation and early inter-meal satiety will be missed. Knowledge of potential mechanisms of action is also beneficial when determining the appropriate pre-load meal interval. The nature of the *ad libitum* meal is another important consideration (Hill *et al*., 1995; Blundell *et al*., 2009, 2010). Large buffet-style meals including foods that vary in sweetness, fat content and energy density provide the opportunity to examine the effect of a pre-load on food choice and macronutrient selection. However, such meals do not reflect typical real-world eating events (Blundell *et al*., 2010). Furthermore, the availability of excess amounts of foods, many with high hedonic value, has the potential to induce overconsumption in all experimental conditions (ceiling effect) and overpower any effect of the pre-load on appetite. By contrast single-item meals may artificially limit consumption through monotony providing an unrealistically low baseline intake in all conditions regardless of the satiety-enhancing potential of the product (floor effect).

Measures of *ad libitum* intake alone cannot demonstrate satiety-inducing effects of a food. Reductions in intake can equally occur as a consequence of nausea or malaise (Halford *et al*., 2010b). As a result, the measurement of subjective appetite sensations is required to provide insight into the driving forces behind changes in eating behaviour. Numerous appetite-related sensations can potentially be examined, but hunger, fullness, desire to eat and prospective consumption are those most consistently incorporated in research (Blundell *et al*., 2009, 2010). The Visual Analogue Scale (VAS), which is typically a 100 mm unbroken horizontal line anchored at either end with opposing extremes of appetite e.g. very full and not full, is the most common approach for measuring such sensations. The VAS is usually administered immediately before and after an eating occasion and at hourly intervals from the start of the eating event, with participants instructed to use a vertical line to divide the horizontal line and indicate their current experience (Hill *et al*., 1995). In this way the VAS is relatively easy for participants

to understand and complete, and as such can be applied both within and outside the laboratory. Furthermore, with regard to the researcher they provide easily administered tools that are relatively reliable and valid. VAS measures have been shown to be sensitive to changes in macronutrient composition (Blundell *et al*., 2010) and can predict subsequent *ad libitum* intake (Blundell *et al*., 2009, 2010). However, on occasions this predictive validity is lost which can potentially be attributed to design issues such as insufficient sample size or inappropriate pre-load meal interval.

13.4.2 Traditional ingredients (protein and fibre)

Reviewing the literature demonstrating the effects of ingredients on appetite and energy intake is beyond the scope of this chapter. The field is dynamic, with the impact of novel ingredients and alternative formulations of existing ingredients being frequently published. However, the effects of certain nutrients on short-term appetite regulation have been demonstrated extensively. Foods enriched with substantial amounts of protein or specific fibre types, given as pre-loads or supplements, have been shown to decrease hunger and/or strengthen processes of within-meal satiation and post-meal satiety. Larger doses of these nutrients slow GI transit, enhancing and prolonging the secretion of gut hormones that inhibit eating behavior, such as CCK, GLP-1 and PPY. This can result in reduced meal intake, decreased between meal snacking, and a delay in the onset of the next major eating occasion. However, only relatively small changes to nutrient composition are practicable and prototypes often fail to deliver tangible effects on appetite; the effects of functional ingredients are often masked by the food matrix.

13.4.2.1 *Effect of protein on appetite*

Protein is considered to be the most satiating of the macronutrients (Astrup, 2005), with this superior effect on appetite observed in single-meal studies (Latner and Schwartz, 1999) or over longer periods. A meta-analysis of 14 randomised trials examining the effects of high-protein diets found that in 11 a protein pre-load significantly increased subjective ratings of satiety (Halton and Hu, 2004). In one 24 h study the enhanced satiating potential of a fixed high-protein, high-carbohydrate diet was reported at both prandial and post-prandial periods compared to a high-fat diet (Westerterp-Plantenga *et al*., 1999). Such satiating effects are further supported by acute studies of differing design, with consumption of a high-protein snack delaying the request for dinner by 60 min, compared with a high-fat snack (25 min delay)

and high-carbohydrate snack (34 min delay; Marmonier *et al*., 2000). The literature relating to protein and energy intake is less consistent, but typically high-protein pre-loads also result in reduced energy intake at a subsequent *ad libitum* meal (Halton and Hu, 2004). Moreover, the effects of a high-protein diet on appetite (hunger and fullness) and energy intake typically translate into weight loss (Weigle *et al*., 2005).

There is evidence that the protein source employed may also impact on the observed effects. Whey protein has been reported to exert a stronger effect than casein on both appetite (Veldhorst *et al*., 2009) and energy intake (Hall *et al*., 2003). However, there are inconsistencies in the literature, with other studies reporting similar effects of both protein types (Bowen *et al*., 2006). The impact of plant-derived proteins has also been examined, with pea protein shown to produce a greater suppression of appetite in overweight participants than whey protein (Diepvens *et al*., 2008). However, the literature base remains limited at present.

With regard to potential mechanisms of action, protein-induced effects on satiation and satiety appear to be underpinned by increases in CCK, GLP-1 and PYY release. Beneficial effects of proteins on body weight also appear to be attributable to metabolic effects, such as dietary-induced thermogenesis (Halton and Hu, 2004).

Currently, the effects of differing proteins on appetite regulation remain poorly characterised and the relative contribution of key mechanisms underpinning protein-induced satiety remains poorly understood. However, with this knowledge, food structure could be manipulated through ingredient selection and processing techniques to enhance protein signalling. This has the potential to strengthen late within-meal satiation and early post-meal satiety though proximal small intestine chemoreception and later post-meal satiety by delaying absorption and thus prolonging the effects of protein on metabolism.

13.4.2.2 *Effect of fibre on appetite*

Fibre is a diverse group of ingredients that produce differing effects on appetite and energy intake via a variety of mechanisms (Wanders *et al*., 2011). The specific mechanism of action is dictated by the physicochemical properties of the fibre in question. The properties associated with appetite and energy intake include solubility, viscosity and fermentability. At present, viscosity appears to account for reductions in subjective appetite and acute energy intake to a greater extent than solubility and fermentability, and will be considered in more detail later in the chapter.

Soluble fibre types bind to water and swell, causing bulking which enhances satiety through gastric distension. Fibre, particularly soluble

forms and carbohydrate forms resistant to digestion, also generally delays gastric emptying, slows glucose absorption and/or promotes the release of satiety regulating gut hormones. The release of GLP-1 and PYY may in part be attributed to the release of SCFAs arising from colonic microbial fermentation. These are recognised by specific receptors that influence a variety of physiological responses, including the gut hormones known to affect satiety (Miyauchi *et al*., 2010; Sleeth *et al*., 2010). This provides a potentially key link between the fermentability of fibre and the control of food intake. Several recent reports have associated satiety effects with fermentable fibre sources in human dietary studies (Nilsson *et al*., 2008; Parnell and Reimer, 2009; Willis *et al*., 2009). However, the role of this mechanism in human appetite expression remains to be proven.

Novel fermentable fibres and resistant starch-based ingredients have been a recent focus of research. With regard to fermentable fibres, the data is inconsistent. Parnell and Reimer (2009) examined the effects of consumption of 21g of a fermentable fibre (oligofructose) per day for three months by overweight and obese participants. Significant reductions in plasma ghrelin and elevated PYY levels were associated with reduced body weight and self-reported reductions in food intake. However, when the direct effects of the same fibre on food intake were examined, either individually or in combination with β-glucans, no effects were observed (Peters *et al*., 2009). This may reflect the shorter duration of the trial, with the fibre consumed in morning and afternoon snack bars on two consecutive days, or the smaller fibre dose (8 g). In addition to these inconsistencies and as stated previously, there are little data to support the role of SCFAs in human appetite expression, one key potential mechanism underpinning the effects of these fibre types (Darzi *et al*., 2011).

The effects of the resistant-starch-containing product Hi-Maize 260 have been characterised in two studies. Bodinham *et al*. (2010) incorporated 80 g Hi-Maize 260 (containing 48 g resistant starch) into a mousse which was consumed in equal portions as part of a fixed-load breakfast and lunch. Food intake at a subsequent *ad libitum* evening meal was found to be significantly reduced. Similarly, Anderson *et al*. (2010) reported an effect of 50g Hi-Maize 260 combined into a soup on energy intake. However, significant reductions in energy intake at an *ad libitum* test meal were only observed if the meal was presented 2 h after the soup pre-load.

Although fibre produces many direct effects on satiety signalling systems in the gut, the impact of structure upon the signals produced by other nutrients has yet to be fully examined. The physical structure of non-soluble fibre and alginates can have potent effects on within-meal satiation (see Section 13.5). As such, using fibre ingredients to

delay the signals produces by lipids and protein, by slowing gastric empting, and/or protecting these ingredients from degradation and digestion, prior to reaching active signalling sites, may enhance and prolong post-meal satiety. However, a far better understanding of the physical properties of fibres and how these interact with other food components in the gut is required.

13.4.3 Novel ingredients

13.4.3.1 *Combinations*

As discussed above, foods supplemented with protein or fibre can, under certain experimental conditions, produce changes in appetite and energy intake consistent with enhanced satiation and satiety. Given that protein increases the release of the gut peptides CCK, GLP-1 and PYY, and fibre also increases the release of GLP-1, slows down gastric emptying and prolongs nutrient absorption, it is plausible that these two nutrients in combination will produce stronger effects. To this effect it has been shown that yoghurts enriched with milk protein and hydrolysed guar gum given as a mid-morning snack impact on appetite and energy intake (Lluch *et al*., 2010). Compared to an equicaloric low-energy yoghurt the supplemented yoghurt significantly reduced post-snack appetite (reductions in hunger, desire to eat and prospective consumption, and an increase in fullness). Compared to an equivolumetric low-energy yoghurt the supplemented yoghurt significantly reduced *ad libitum* lunch intake.

However, it cannot be assumed that ingredient combinations, including protein and fibre combinations, will necessarily produce additive effects. Other food ingredients, including other satiety-enhancing functional components, are equally as likely to diminish the effect of a satiety factor as enhance it (Harrold *et al*. unpublished results). In the case of combined ingredient approaches it often remains difficult to determine the relative contribution of different ingredient types, and the impact of their inclusion on food structure that drive any changes in subsequent eating behaviour or subjective experiences of appetite.

13.4.3.2 *Lipids*

A number of novel satiety ingredients exist, although the literature detailing their effects on appetite expression is limited. The largest body of literature probably relates to novel fats. Although the current level of understanding is that fats are the least satiating of the macronutrients, their effect on appetite have also been associated with

enhanced CCK, GLP-1 and PYY release, mechanisms that should delay gastric emptying and oral–cecal transit. As with fibre the different physico-chemical properties of fats influence their satiating properties. Fatty acid chain length is one characteristic that impacts on satiety, with chain lengths of 12 and above, in particular, associated with suppression of appetite and enhanced CCK and GLP-1 response (Feltrin *et al*., 2004). The degree of saturation also exerts an impact, with polyunsaturated fatty acids exerting the strongest effects on appetite (compared to monounsaturated and saturated fatty acids; Lawton *et al*., 2000).

Fat-based satiety functional ingredients include the oat- and palm-oil-based product Olibra (Fabuless). The effects of Olibra on appetite were established in early trials (e.g. Burns *et al*., 2002) with intake suppressant effects observed at 4 h, 12 h and 36 h post treatment. Additionally, the ability of Olibra to prolong the passage of food through the small intestine highlights a potential mechanism of action in terms of the effect of GLP-1 on gastric emptying through the ileal break (see later; Haenii *et al*., 2009). However, subsequent studies have not replicated these effects on appetite (Logan *et al*., 2006; Smit *et al*., 2011), with treatment dose and the processed nature of the product offered as explanations for the inconsistency. Despite these inconsistencies with regard to effects on appetite, longer-term trials have demonstrated improved maintenance of body weight (18-week trial following six-week weight loss; Diepvens *et al*., 2007) and reduced body fat mass (12-week trial following six-week weight loss; Olsson *et al*., 2011) following Olibra consumption.

Lipid-based approaches provide an intriguing possibility to modulate appetite control. Small doses of free fatty acids (FFAs) infused into the small intestine produce marked effects on biomarkers of satiety and suppress intake, possibly by slowing gastric emptying via the ileal brake (see Section 13.6.1). However, not only do these effects appear very dependent on the form and structure of the lipid, they also appear to be influenced by the nature of the food into which they are incorporated and the processing that food then receives. Ideally, changes in food structure or novel technologies such as encapsulation (see Section 13.6.1) could deliver bioactive lipids to their biological site of action intact and relatively free from the interference of other food components.

13.5 FOOD STRUCTURE

Changes in the structure of foods can produce a profound impact on appetite expression, but can also impede ingestion and reduce

palatability, making these approaches unappealing to consumers (Wolf, *et al*., 2002). Nonetheless, gelling in the stomach can produce robust effects on satiation without the negative sensory experience. Encapsulation and subtle changes to the microstructure of food can also be used to deliver small amounts of nutrients, for example novel lipids, to key sites along the length of the GI tract, defending these nutrients in transit from GI degradation. These may provide novel solutions to appetite control by strengthening between-meal satiety and reducing hunger prior to the next meal.

13.5.1 Viscosity and appetite

Systematic review of the literature relating to the impact of fibre on appetite (Kristensen and Jensen, 2011) indicates that clinical evidence for a role of viscosity in mediating physiological responses to appetite is somewhat limited. A major weakness is a lack of published information on the physical and chemical properties, particularly viscosity, of the fibre examined in individual studies. However, the majority of studies using fibre characterised as being more viscous (e.g. pectins, β-glucans and guar-gum), generally report reduced appetite and energy intake more often than less-viscous fibres. Furthermore, the studies which fail to demonstrate an effect of viscous fibres on appetite typically report the smallest differences in viscosity between control and active treatment, suggesting that a large increase in viscosity is required to achieve a significant response. Table 13.1 identifies a number of types of viscous fibre with potential applications in terms of targeting appetite and weight control.

Table 13.1 The properties of types of viscous fibre dictate their utility in the food industry. The differing chemical structures offer flexibility, enabling them to form gels at varying temperature and pH and in the presence of cations. High oral viscosity is associated with low palatability and acceptability of foods. However, with these properties viscous fibre does not need to be administered in gel form, but can gel spontaneously in the stomach, offering the potential to enhance satiety.

Fibre Type	Source	Properties
Alginate	Most large brown seaweeds	Forms gel without heating, yet heat stable; gels at low pH or high Ca^{2+} concentrations.
Pectin	Citrus fruits, apples, sugar beets, sunflowers	High-methoxy pectin: acid-stable gel; requires acid and sugar for gelling. Low-methoxy pectin: requires Ca^{2+} for gelling.
Guar gum	Cyamopsis tetragonolobus seeds	Soluble and gelling in cold water to form viscous solution; gels in the presence of other gums e.g. xanthan gum; gelling ability not dependent on pH.
Gum Arabic (Acacia gum)	Acacia sap	High solubility with low viscosity in cold water; viscous only at concentrations of 40–50%.

13.5.1.1 *Evidence from human interventions*

Vuksan and colleagues (2009) examined the impact of three beverage pre-loads containing fibre of differing viscosities on food intake and appetite in 31 normal-weight adolescents. Cellulose provided the low-viscosity fibre, glucomannan the medium-viscosity fibre and a novel viscous polysaccharide the high-viscosity fibre. The beverages were otherwise identical for taste, appearance, nutrient content and quality of fibre. The high-viscosity fibre beverage was found to reduce intake at an *ad libitum* meal consumed 90 mins after the pre-load, compared to both of the other beverages. However, appetite scores and 24 h intake did not differ between the three conditions, indicating that any satiety-inducing effects of the high viscosity fibre were short-lived.

In another study, the effects of beverages containing wheat bran, oat β-glucan and guar gum on appetite were compared to wheat bread and a control beverage lacking fibre (Lyly *et al*., 2009). The 19 normal and overweight participants reported higher satiety and lower desire-to-eat ratings following consumption of the guar gum beverage compared to the control. Additionally, the oat β-glucan beverage increased fullness and demonstrated trends for increased satiety and decreased desire to eat. However, the isocaloric wheat-bread load had the largest effects on appetite (increased perceived satiety and decreased desire to eat) compared to the control beverage, consistent with enhanced satiation potential of solid over liquid products.

The effects of β-glucan on appetite and intake were further examined individually and in combination with fructo-oligosaccharide by Peters *et al*. (2009). In this instance, the ingredients were combined in meal-replacement bars that were consumed for two consecutive days by 21 healthy participants. In contrast to the previous study, β-glucan was not found to exert any effects on appetite or intake. This may reflect the modest increases in viscosity induced by the β-glucan load in this study. Additionally, the use of a solid matrix rather than a liquid matrix may also contribute to the lack of observed effect.

Further contradictory evidence comes from a study examining the impact of two different oat-bran-containing beverages on appetite and satiety in 20 normal-weight participants (Juvonen *et al*., 2009). Both beverages contained the same amount of dietary fibre, but in one the oat bran was modified such that viscosity differed by more than 12-fold. In contrast to anticipated results, the low-viscosity beverage produced the larger increase in satiety. Additionally, it introduced the greater increases in CCK, GLP-1 and PYY, and the greater decreases in ghrelin levels. Furthermore, it yielded the faster gastric emptying rate. The authors suggest that enhanced viscosity may have prevented interaction between nutrients and hormone-secreting enteroendocrine cells of the

GI tract, yielding the observed reductions in biomarkers of appetite and associated appetite control. However, this rationale makes it difficult to explain the findings of studies in which enhanced viscosity was observed to impact on food intake and appetite (Lyly *et al*., 2009; Vuksan *et al*., 2009).

The studies cited above only address the acute impact of viscosity. As such, it is unclear whether sustained benefits may exist that will contribute to weight control. However, as the effects of non-viscous dietary fibre is generally more consistent in acute studies than long-term weight-control trials, this implies that the impact of viscous fibre on appetite and food intake may at best be transient. These studies also indicate that the food matrix may play an important role, with a liquid matrix being more frequently associated with enhanced satiety.

13.5.1.2 *Mechanisms of action*

With regard to potential mechanisms of action, viscous ingredients appear to exploit many of the regulatory mechanisms that control eating behaviour (see Section 13.3). As a consequence, their ability to enhance satiation and satiety has the potential to exceed that of protein, fibre and other individual ingredients. One probable means via which viscosity reduces intake is through a slowing of the rate of ingestion, with more time and effort required to chew viscous foods. Associated with this is a slowing of oral processing time such that the food is retained in the mouth longer. Consequently, there is a greater opportunity for sensory receptors to be exposed to and respond to taste, smell and texture, and for satiety-mediating signals to be relayed to the CNS (Zijlstra *et al*., 2008, 2009a). Additionally, as viscous fibres absorb large quantities of water this provides the potential to increase feelings of fullness through enhanced gastric distention, as observed using MRI techniques (Marciani *et al*., 2000, 2001). This effect may be prolonged through viscosity-induced delays in gastric emptying rate (Bergmann *et al*., 1992; Marciani *et al*., 2000, 2001). However, there is some inconsistency in the literature, as enhanced viscosity of elemental formula, through pectin addition, has been reported to accelerate the rate of gastric emptying (Shimoyama *et al*., 2007). Viscosity may also reduce intake by prolonging intestinal transit time, which in turn could alter the absorption rate of nutrients and facilitate meal-generated satiety signals. However, changes in CCK and GLP-1 levels were not identified following consumption of a semi-solid viscous product compared to a chocolate-flavoured milk drink matched for energy density and macronutrient composition (Zijlstra *et al*., 2009b). Small, but significant, increases in ghrelin levels were observed, however, but these conflicted with the reduced hunger and increased fullness reported in

the study (Zijlstra *et al*., 2008). Slower gastric emptying and intestinal absorption rates have also been suggested as mechanisms via which viscous fibre induces post-prandial delays in blood glucose responses, thus further impacting on satiety.

Despite the obvious potential for a role of viscosity in mediating physiological responses to appetite, limitations of this approach have been identified. Viscosity has been shown to profoundly reduce palatability (Hoad *et al*., 2004), and although this cephalic effect may be related to decreased feelings of hunger, the consumer is highly unlikely to accept unpleasant-tasting products as a means of appetite control. A study examining the effect of viscous-fibre-containing nutrition bars on satiety highlighted additional side effects. Consumption of the viscous fibre was associated with greater frequency and intensity of abdominal distension and flatulence, and a greater frequency of defecation (Chow *et al*., 2007). Enhanced GI intolerance will obviously also impact detrimentally on consumer acceptance.

13.5.2 Alginates: Gelling in the stomach

Appetite-orientated effects of alginates are entirely dependent on their unique chemical structure which allows them to form gels in the presence of Ca^{2+} or H^{+} ions at low temperature. Consequently, unlike other viscous ingredients that need to be consumed in a gel form, alginates can be administered in a low-viscosity form and are able to gel spontaneously at low temperatures in the acidic environment of the stomach. High viscosity in the mouth is associated with poor organoleptic properties of the food (Wolf *et al*., 2002). High viscosity in the stomach is linked to increased gastric distention and increased satiety (Hoad *et al*., 2004), suggesting that alginates are good candidates for food focusing on enhanced satiety and satiation.

The available literature on the alginates suggests this potential is real. Pelkman *et al*. (2007) demonstrated reductions in energy intake in non-dieting overweight and obese women following consumption of a post-ingestion calcium-gelling alginate-based beverage twice daily for seven days. However these reductions were not found to be accompanied by any meaningful change in appetite sensations.

Similar reductions in energy intake were also observed following seven-day daily ingestion of a post-ingestion strong-gelling sodium alginate beverage compared to control. (Paxman *et al*., 2008). On this occasion the population was less specific and included both males and females with BMIs in normal weight, overweight and obese categories. Despite this variation, no significant interactions between pre-load type, gender or BMI were observed.

Effects on appetite were also observed when a strong-gelling alginate was consumed by normal-weight males and females in a sweetened milk-based meal-replacement beverage. Compared to control and a weakly gelling alginate, consumption of the strong-gelling alginate beverage decreased hunger ratings and increased fullness ratings. However, it was noted that as a result of the viscosity of the strong-gelling beverage it was rated the least palatable and this may have contributed to the changes in appetite sensations observed (Hoad *et al*., 2004).

A liquid matrix was also employed when comparing the appetite-reducing effects of a high-viscosity alginate to a low-viscosity alginate and whey protein. When the viscosity of the drinks varied (but the protein content remained the same) hunger was found to be reduced in the high-viscosity product compared to the low-viscosity product (Solah *et al*., 2010). When protein varied in opposition to viscosity (i.e. low protein, high viscosity versus high protein, low viscosity), reductions in hunger were still observed in the high-viscosity beverage, suggesting that the effects of viscosity are greater than those of whey protein on satiety.

However, there are inconsistencies in the literature. Mattes (2007) reported no effect of alginate and guar gum combined in a breakfast bar on ratings of fullness, hunger, desire to eat and prospective consumption when consumed for five days by an overweight study population. Differences in daily energy intake were also not observed when compared to a matched control bar. The use of 24 h diet recalls to assess intake may explain the latter observation.

Interpretation of this literature is further hampered by poorly characterised ingredients and lack of details of their gelling properties (e.g. Mattes, 2007; Pelkman *et al*., 2007). Moreover, a number of ineffective consumer products are available on the market. Odunsi *et al*. (2010) reported no effect of 10 days ingestion of sodium (CM3) alginate in capsule form on energy intake or appetite. Similarly, no differences in gut hormone levels (ghrelin, CCK, PYY, GLP-1) or gastric motor function were detected in the 48 overweight and obese participants. However, despite these inconsistencies, recent data suggest that relatively small amounts of strong gelling alginates appear to suppress appetite. Peters *et al*. (2011) report reduced area under the curve (AUC) for hunger, desire to eat and prospective consumption, and increased AUC for fullness following consumption of a meal-replacer beverage matrix containing a post-ingestion calcium-gelling alginate on appetite. Effects on energy intake were deliberately not examined in this study as it was performed in the context of a meal replacer.

13.6 COMBINED APPROACH

Changes to food structure have largely been considered as an alternative approach to macronutrient manipulation for modifying appetite. When adopting this approach it is essential to ensure that changes in food structure don't undermine other nutrient-based satiety mechanisms. However, it may also be possible to utilise changes in food structure to enhance nutrient-derived signals. Encapsulation and changes to the microstructure of food could provide a means of delivering nutrient signals to key appetite-regulating receptors in the GI tract.

13.6.1 Ingredients and encapsulation

In order for enhanced satiety to be an effective approach to reduce energy intake, satiety signals need to be prolonged. One of the most effective endogenous mechanisms via which this can be achieved is activation of the "ileal brake". This is a distal to proximal feedback mechanism which delays gastric and intestinal transit time to enhance nutrient digestion and absorption.

A wealth of studies in both animals and humans show that activation of the ileal brake by local perfusion with fat, protein, carbohydrate and fibre influences gut function (motility, transit and gut hormone secretion). However, studies in humans demonstrating reductions in food intake and enhancement of satiety sensations are more scarce and have employed only fat infusions. Welch and colleagues conducted two studies (Welch *et al*.,1985; 1988) in which the effects of ileal infusion of 50% corn oil and 3% albumen on food intake and satiety were compared to control infusions of albumen and saline. Infusions were continued for 90 minutes with an *ad libitum* meal provided 30 minutes after the start of the infusion. Participants were found to eat for shorter periods of time and consume smaller amounts of food during the fat infusions (Welch *et al*.,1985; 1988). Whilst, ileal infusions did not reduce hunger sensations before the meal (Welch *et al*.,1988), fullness was found to increase significantly after the start of the meal (Welch *et al*.,1988). These results imply the need for a volume load within the GI tract before the satiating effects of the ileal brake are observed. However, a more recent study reports satiating effects of ileal perfusions of intralipid without a preceeding meal (Vu *et al*., 2006).

Although the satiating potential of the ileal brake has been recognised, it is uncertain whether it actually plays a physiological role in the regulation of gut function. In humans the percentage of nutrients

reaching the ileum after meal ingestion is dependent on the caloric load of the meal and meal composition. Generally, after a meal of normal size, only small amounts of undigested nutrients will reach the ileum (Keller *et al*., 1997). It is unclear whether these amounts are biologically relevant and will activate the feedback mechanism. However, encapsulating such materials in a manner that allows release at the appropriate location in the GI tract may overcome this limitation. Many encapsulation technologies currently exist. However, in the published scientific literature there is currently little, if any, evidence to demonstrate that these technologies have progressed beyond the developmental stage in terms of impacting on intrameal satiation and/or intermeal satiety.

13.6.2 Fats and emulsion

Fatty foods are both energy dense and palatable, but exert a relatively weak effect on satiation compared with protein- and carbohydrate-rich foods (Blundell and Macdiarmid, 1997). These characteristics may prompt overconsumption, justifying a low-fat approach to weight management. However, reduction of fat in or removal of fat from foods is often perceived to impact detrimentally on palatability, possibly through changes to texture. An alternative approach which may maintain consumer satisfaction is to attempt to utilise the satiating properties of fat-rich foods. One of the main mechanisms via which fat consumption impacts on satiety is through the release of CCK (Liddle, 2000). Delayed gastric emptying also contributes to satiety signalling (Boulby *et al*., 1999).

In the modern diet fat is commonly incorporated into foods in the form of an emulsion of lipid droplets. Emulsion stability in the acid environment of the GI tract has been shown to reduce the rate of gastric emptying, increase levels of circulating CCK and increase gallbladder contraction (Marciani *et al*., 2007). These changes were found to be accompanied by reduced prospective consumption (Marciani *et al*., 2007; 2009), increased fullness and reduced hunger ratings (Marciani *et al*., 2009). "Second meal" effects on appetite ratings were also observed despite, changes in the rate of gastric emptying having dissipated (Marciani *et al*., 2007). The proposed mechanism of action is increased release of FFA to the duodenum as a consequence of enhanced opportunity for lipolysis through emulsion stability. These results suggest that novel food-processing techniques offer the potential to design emulsions that provide all the eating pleasure of high-fat foods, but which target fat-mediated satiety mechanisms to help to reduce overconsumption.

13.7 IMPLICATIONS FOR WEIGHT MANAGEMENT

Over the past 50 years considerable research indicates that certain ingredients, combined in foods, can produce significant effects on short-term appetite regulation. Such changes in energy intake could translate into reductions in body weight if used in conjunction with necessary changes in diet and lifestyle. Proteins, fibre types and novel oils all have the potential to produce beneficial short-term changes in appetite (proof-of-concept). The challenge remains to demonstrate their enduring effects on appetite and energy intake, as well as the health and consumer benefits such effects provide in terms of optimising successful weight management.

Changes in the structure of foods can also produce a profound impact on appetite expression but this is often accompanied by impeded ingestion and reduced palatability making these approaches unappealing to consumers. Nonetheless, gelling in the stomach can produce robust effects on satiation without the negative sensory experience. Encapsulation and subtle changes to the microstructure of food also have the potential to deliver small amounts of nutrients, for example novel lipids, to key sites along the length of the GI tract, defending these nutrients in transit from GI degradation. These may provide novel solutions to appetite control by strengthening between-meal satiety and reducing hunger prior to the next meal. However, this research is in its relative infancy and requires collaboration to allow the contribution of food production, physiology and behaviour to be optimised.

Another important aspect is that the foods produced as a result of altered composition and/or structure need to be appealing, desirable and affordable in order for consumers to accept the products and incorporate them into their daily diet. It should also be noted that such products are likely to have at best a modest impact on energy intake when used in isolation. However, if incorporated into a diet containing multiple satiety-enhancing products targeted at different regions of the GI tract they could help individuals maintain an effective and sustainable weight-control strategy.

13.8 CONCLUSION

In conclusion, it is not only the macronutrient composition of food that influences appetite via GI physiological responses. Radical changes in food structure can also be used to produce changes in appetite expression equivalent to substantial protein or fibre enrichment. Furthermore, alterations in microstructure have the potential to provide a means to boost the effects of small nutritional manipulations by delivering

functional ingredients to their site of action within the GI tract. However, the means via which food structure interacts with the GI tract is not well understood. Moreover, research has concentrated on the changes to structure that are likely to enhance within-meal satiation, and produce transient rather than sustained post-meal satiety. Crossdisciplinary research is required to target key nutrient-sensing mechanisms to develop food products through novel processing to produce enduring effects on appetite and provide the potential to combat excessive body weight. It is only by understanding how food structure can both enhance and inhibit nutrient-based satiety signals that we can hope to optimise the development of products designed to enhance satiety and enable consumers to successfully engage with the energy intake restriction required to lose weight and prevent weight regain.

13.9 REFERENCES

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