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Satellite Symposium: Industry and academic partnerships for developing health-improving products*

Satiety-enhancing products for appetite control: science and regulation of functional foods for weight management†

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The current review considers satiety-based approaches to weight management in the context of health claims. Health benefits, defined as beneficial physiological effects, are what the European Food Safety Authority bases their recommendations on for claim approval. The literature demonstrates that foods that target within-meal satiation and post-meal satiety provide a plausible approach to weight management. However, few ingredient types tested produce the sustainable and enduring effects on appetite accompanied by the necessary reductions in energy intake required to claim satiety/reduction in hunger as a health benefit. Proteins, fibre types, novel oils and carbohydrates resistant to digestion 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. Currently, the benefits of satiety-enhancing ingredients to both consumers and their health are under researched. It is possible that such ingredients help consumers gain control over their eating behaviour and may also help reduce the negative psychological impact of dieting and the physiological consequences of energy restriction that ultimately undermine weight management. In conclusion, industry needs to demonstrate that a satiety-based approach to weight management, based on single-manipulated food items, is sufficient to help consumers resist the situational and personal factors that drive overconsumption. Nonetheless, we possess the methodological tools, which when employed in appropriate designs, are sufficient to support health claims.

Satiety: Satiation: Health Benefit: Consumer: European Food Safety Authority

Over the last 40 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. Nonetheless, despite a considerable number of appetite-control health claim submissions to the European Food Safety Authority (EFSA), few products have had their claims approved. It is apparent that much of the existing literature is insufficient to substantiate appetite-related health claims, falling short of EFSA requirements to demonstrate sustained and enduring effects of these foods on appetite. Specifically, many studies fail to include the significant reductions in energy intake required to produce meaningful changes in body weight. Nonetheless, over the last 40 years, the methodological platform necessary to develop protocols capable of substantiating appetite health claims has been established. The current review considers the context of weight management from the perspective of the consumer, discusses the

Abbreviations: CCK, cholecystokinin; CNS, central nervous system; EFSA, European Food Safety Authority; GLP-1, glucagon-like peptide-1; PYY, peptide YY; VAS, Visual Analogue Scale.

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regulatory and commercial context of appetite in weight management, the potential consumer benefits of satiety, and also details recently published EFSA evaluations of certain ingredients.

Weight management: consumer context

Within Europe and North America the prevalence of overweight and obesity in adulthood has increased to such a point that carrying excess body weight is now the norm[1]. Globally, in urban populations excessive weight gain is now a major health care issue[2]. This weight gain, a consequence of energy imbalance between energy intake and energy expenditure, can be viewed as a consequence of a modern obesogenic environment. Certainly, the contribution of energy-dense high-fat sugar salt foods to weight gain is well recognised[3]. The individual's inability to adapt to an environment rich in energy is a distinct issue. Clearly the human appetite system cannot adequately prevent the consumption of excess energy in situations where energy-dense high-fat and/or sugar foods are freely available and heavily promoted. From a general health perspective, consumers require healthier low energy, low-fat energy-dilute foods that are affordable, attractive and convenient, and – importantly – as tasty and gratifying as the unhealthier items they are intended to replace. This is, in itself, a considerable food reformulation challenge. However, consumers also seek products that directly address weight control (i.e. induce weight loss and/or prevent weight gain/regain) and as such provide distinct health benefits (reduced risk of weight-related illness) and improved quality of life (better well-being). Such products need to provide the clear and enduring effects on experience of appetite and energy intake necessary to combat the physiological consequences of energy restriction and the psychology of deprivation that accompany energetic restriction. This should enable consumers to resist the situational cues to over-consume and meet the demands of self-control required for successful weight management.

Key behavioural phenomena such as weaknesses in within-meal satiation and post-meal satiety, and an inability to resist external food cues, are associated with adiposity and weight gain[4]. Although these are predominantly observed in the obese, it is likely that these operate in many individuals experiencing difficulty in controlling their own body weight. Certainly, similar behavioural traits can be found in those engaged in repeated attempts to control their weight, including at the extreme, and those with disordered eating[5–7]. Given the prevalence of both dieting and consumption of diet-related products, and of overweight and obesity within the population, these behavioural traits represent a continuum between successful and unsuccessful weight control[8]. Precursors of some of these traits can be observed in young children prior to any apparent differences in weight status[9,10]. These traits appear heritable[4,10] and are related to at least one genetic marker for obesity, suggesting that such traits are in part predetermined and distributed across the population.

Some of these traits clearly relate to the meal-by-meal control of energy intake and deficiencies in operation of satiety (see later)[4]. An inadequate behavioural response during ingestion allows over-consumption during a meal. Rapid consumption (i.e. increased eating rate) and failure to decelerate eating prior to meal termination have become the subject of intense research activity[4]. Similarly, an inadequate suppression of appetite after a meal hastens the onset of the next eating episode[4]. Certainly, those with excessive weight or a history of over-consuming lack crucial feedback from the gastrointestinal tract normally associated with meal-to-meal appetite control[11]. Increased gastric capacity, reduced satiety gut hormone levels and impaired gut hormone response to ingestion all contribute to reduced behavioural response to ingestion[4]. Such deficiencies could be challenged by strengthening the impact of foods on appetite regulation, and this has generated product development focused around sensory impact, macronutrient composition, functional ingredients and food structure. The benefits of such manipulations on short-term appetite regulation have been demonstrated in numerous studies. However, the sustainability of these effects remains the critical issue in determining their usefulness in weight management. Moreover, the more radical the dysfunction, the greater the potential nutritional manipulation required, a factor that poses considerable technical challenges, and is likely to impact on the commercial viability of any product.

Other behavioural traits relate to control and the individual's ability to resist[4]. Adiposity is associated with a heightened responsiveness to food cues, a response largely undiminished by prior ingestion. Similarly, individuals also demonstrate a heightened hedonic response to palatable food[12]. This enjoyment does not appear to derive from differences in taste perception such as enhanced or diminished flavour detection[13]. The enjoyment of the food appears largely derived from the gratification of consumption rather than savouring of flavour[4,12]. It is difficult to conceptualise how to directly address such issues through product development and it may be more useful for the food industry to reflect on how their food promotion practices (marketing, branding and pricing) contribute to such maladaptive consumption patterns. Nonetheless, food formulation may produce benefits. If the foods produced are pleasing and palatable they may prove gratifying without provoking excessive consumption. Similarly, foods that have a greater impact on the physiological processes of appetite may lessen the impact of such external food cue stimuli, preventing eating in the absence of hunger. Such benefits remain to be demonstrated but would appear to be of value to those trying to control weight. Factors such as feelings of uncontrolled and excessive hunger, disinhibited and binge eating, and eating in response to negative emotions and stress all mediate long-term success and failure in weight control[14,15].

Commercial and regulatory context

The range of consumer weight management products available within national markets is phenomenal and the value of this market is enormous and growing[16,17]. Through the internet the availability of the latest

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'promising' weight loss solutions is unlimited. The evidence base underpinning most of these products is weak and certainly fails to sustain the veracity of the claims made for them. Versions of these products may produce *in vitro* effects or significant changes in key parameters in *in vivo* animal models. However, these products have seldom been tested adequately in human subjects and rarely with the intended users or in the final form marketed. The regulation of marketing across many forms of advertising in many national jurisdictions offers consumers some form of protection against misleading claims. However, this fails to offer a commercially level playing field, which poses a considerable challenge for those trying to devise, develop and market legitimate science-based approaches to weight management. Notably, levels of proof required for food and supplements, medical devices and herbal approaches differ. Nonetheless, within Europe health claims made for food products are now systematically evaluated and regulated.

In 2006, the European Commission adopted regulation 1924/2006 on the use of nutrition and health claims made on foods and non-alcoholic beverages[18]. These rules were designed to (i) ensure claims were based on the nutritional profiles of products, (ii) harmonise the use of nutrition and health claims across the single market, and critically (iii) to ensure any claim is clear, i.e. comprehensible and not misleading, and (iv) is substantiated by scientific evidence. The regulation covers both new and existing claims made on new or existing products in all commercial communications, including in promotional campaigns and adverts, brand names and trademarks, as well as on product packaging. The primary drive of the regulation was to ensure that consumers were protected, enabling them to reliably choose from safe and adequately labelled products, with scientifically substantiated health benefits. The regulation is also meant to benefit the food industry by (i) supporting innovation by encouraging manufacturers to develop products for which health and nutrition claims can be genuinely made, (ii) regulating the market consistently across Europe, and critically (iii) preventing unfair competition from competitors making false or misleading claims. However, out of the 2758 claims EFSA evaluated by June 2011, the vast majority have been rejected.

With regard to appetite control, current draft guidance from EFSA[19] suggests that effects on appetite should be accompanied by corresponding reductions in energy intake. These effects on appetite should be sustainable. Sustainability is in part demonstrated by the absence of compensation. It is not sufficient for a food to reduce energy intake at a subsequent *ad libitum* meal if overconsumption then occurs at later eating opportunities. However, sustainability also relies on demonstrating continuous effects of the products during repeated dosing over a minimum of 28 d. With regard to weight loss, significant changes in body weight need to be of an appropriate duration (e.g. 3 months minimum) under specified conditions (e.g. as part of a reduced energy diet). Although it is assumed that this will also result in a decrease in fat mass, to make a health claim on fat mass reduction requires body composition analysis by methods with appropriate validity and precision. Specifically this means direct measures of body composition derived from scanning and imaging (e.g. Dual-energy X-ray Absorptiometry or MRI). Simple measures of waist circumference are not sufficient as these could result from effects other than reductions in abdominal fat. For claims on weight maintenance, prevention of significant weight regains needs to be demonstrated over at least a 6-month follow-up after weight loss.

The purpose of this review is to detail methodology underpinning claims substantiation. It is not intended to provide a critique of the current regulatory environment or the standard of evidence required but rather to consider the challenges of weight management and appetite control and consider the evidence that can support health claims in this area.

Appetite: satiation and satiety

In classic motivational terms, hunger is the conscious experience associated with the drive to eat. As Blundell *et al.*[20] comment, while it is difficult to gauge the strength of this drive, it can be inferred from the behaviour it motivates. Specifically, in this case a simple measure of food intake provides an indication of the strength of the drive to consume. However, it is the mental urge to consume experienced by individuals (motivation), and the sensation itself (hunger) to which they attribute control of their eating behaviour that is the primary focus of scientific study[20]. Sensations of hunger and also of cravings are often linked to physical experiences such as feelings of emptiness, light headedness or weakness and it is these sensations to which the measurement of appetite described in this review refer.

Hunger initiates and sustains eating activity, but simultaneously the act of consumption stimulates feedback to bring a meal to an end. The intra-meal processes generated by ingestion that terminate a meal are collectively referred to as satiation. It is intra-meal satiation that determines the duration and the size of a meal and also the rate of consumption within it[21]. Feelings of fullness are particularly potent at reducing further eating behaviour and are a critical component of intra-meal satiation. Satiety is the end state that occurs at the meal's end to inhibit further eating behaviour. Inter-meal satiety prevents consumption between eating episodes and delays the onset of the next substantive meal[21]. Although fullness remains a potent inhibitor of food intake immediately after consumption, other processes are required to sustain inter-meal satiety. The operation of these systems is influenced by the physical and chemical properties of food such as the bulk, solidity and macronutrient composition, but is also influenced by the sensory impact of food. For instance, palatability can stimulate hunger and delay intra-meal satiation even though the latter is driven largely by fullness (Fig. 1).

The satiety cascade is often used as a conceptual framework to examine the impact of foods on satiation and satiety[21]. The cascade maps the biological systems underpinning the control of appetite onto the behavioural events and psychological experiences that determine meal-by-meal appetite control. The cascade demonstrates how properties of a meal such as its sensory qualities, physical

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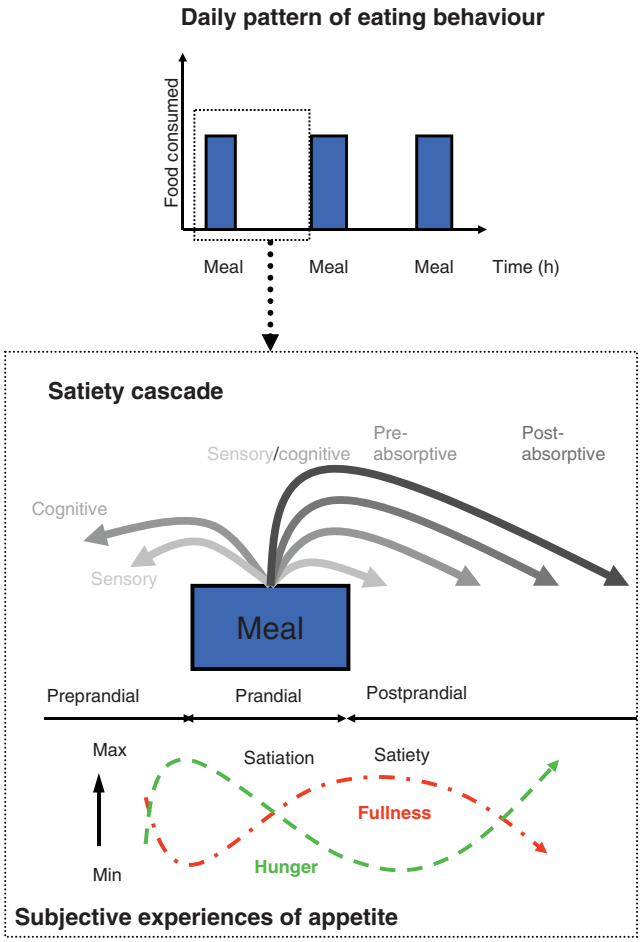

Fig. 1 The satiety cascade. CCK, cholecystokinin; GLP-1, glucagon-like peptide-1; PYY, peptide YY.

structure (both macro and micro), macronutrient composition and energy density influence peripheral physiology and metabolism and central nervous system (CNS) processes critical to energy regulation. As such the system details mechanisms that could be targeted by foods designed to strengthen intra-meal satiation and/or sustain inter-meal satiety. The cascade also highlights the crucial sensory and cognitive factors that determine eating behaviour[21]. Familiarity with the food triggers associations that generate expectations of the likely pleasure derived from and estimated satiating potential of the meal, factors that influence the amount consumed. In turn, meal size is a critical post-ingestive factor influencing satiation. The stretch of the stomach detected by mechanoreceptors in the gut wall, along with early indications of osmotic load, provides an early physical indication of meal size and likely energy load. Other post-ingestive signals stimulated by the products of digestion within the gut trigger the release of hormones that influence stomach emptying and gastric transit. These act as potent signals for satiation and satiety through their impact on stomach emptying, by stimulating afferent signals to the CNS or directly influencing CNS function. The post-absorptive impact of circulating nutrients and hormones designed to control their circulating levels also produce a profound impact on appetite. The oxidation and metabolism of nutrients and the storage of energy also produce potent post-absorptive effects on energy regulation[21].

With regard to developing foods with enhanced appetite-suppressing properties, the satiety cascade clearly indicates a number of biological targets. Of particular interest are peptides released in the gastrointestinal tract that modulate the passage of food through the tract and regulate blood glucose levels. These hormones include ghrelin, produced by the P/D1 cells of the gastric fundus, which is associated with hunger. Physiological studies demonstrate that endogenous ghrelin levels peak prior to a meal and are suppressed by meal intake, and exogenous ghrelin infusions stimulate appetite and increase food intake. Endogenous ghrelin stimulates gastric motility, and its circulating levels appear particularly sensitive to high-energetic, high-osmotic loads. Thus ingestion, particularly of carbohydrate, delays gastric emptying, sustaining fullness, which contributes to both satiation and early post-meal satiety[21].

Similarly, hormones are released lower down the gastrointestinal tract in response to food consumption. These hormones include cholecystokinin (CCK), glucagon-like peptide-1 (GLP-1) and peptide YY (PYY)[4,11,21]. CCK is released in the I-cells of the proximal small intestine (duodenum and jejunum) in response to dietary protein and NEFA, particularly those with a C chain length of 12 or greater. CCK promotes digestion through bile and enzyme release and also slows gastric emptying (the so-called ‘duodenal brake’). In physiological studies, exogenous administration of CCK produces robust effects on human appetite and food intake. These effects are in part mediated by gastrointestinal CCK receptors on vagal afferents. Therefore, through a direct effect on gastric emptying and vagal signals, endogenous CCK release contributes to satiation and early post-meal satiety[22,23,24].

GLP-1 is released from the L-cells of the distal small intestine (ileum) and the large intestine in response to carbohydrate and fat. It is an incretin hormone that lowers blood glucose by triggering insulin release and inhibits gastric emptying (‘ileal brake’)[11,25,26]. An extensive literature demonstrates that in human subjects GLP-1 infusions inhibit pre-meal appetite producing robust effects on food intake[4,11,26]. Similarly PYY, also released by the L-cells in the distal small intestine and the large intestine in response to dietary fat, protein and carbohydrate, also inhibits appetite and produces robust effects on food intake in human studies[4,11,27,28]. PYY also reduces gastric motility, slowing oral–cecal transit time. Notably, microbial production of SCFA, resulting from the fermentation of dietary fibre in the colon, also triggers GLP-1 and PYY release[29] an effect that may also influence appetite expression. Therefore, endogenous GLP-1 and PYY responses to ingestion may play a particular role in sustaining post-meal satiety and influencing intra-meal satiation at the next eating event.

Benefits of satiation and satiety

The range of weight control products available to consumers is vast, the largest category comprising herbal

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products such as teas, caffeine-based products and culinary herbs. Most of these make no specific claims on appetite and are generally used as supplements. Similarly, fatty acid-based products specifically marketed as abdominal fat mass reducers and fibre-based medical devices reported to prevent fat absorption are available for weight control. None of these make any appetite-specific claims either. However, fibres (carbohydrates resistant to digestion), certain fats and various proteins have been commonly used as ingredients in foods and beverages purported to enhance satiety.

Such products often make specific health claims promising consumers that these products will (i) keep them fuller for longer, (ii) help them stay satisfied, (iii) provide lasting satisfaction, (iv) reduce hunger and cravings and (v) help them want to eat less, and so forth. The link with weight control is not always made in the form of a claim, on a number of products it is implied by imagery on product packaging (images of tape measures, weighing scales or emphasised waistlines) or in the product name (terms such as slim, svelte or light). Consequently, consumers are left to infer whether these products produce the long-term benefits they desire. The benefits of satiety to the consumer remain an under researched area, and it also remains uncertain what consumers understand about and expect from satiety-enhancing products[30]. From a regulatory perspective, protection aims to prevent the consumer overestimating the potential benefits of satiety-enhancing products[19].

The management of appetite *per se*, without the specific goal of weight management, may be a legitimate benefit to certain consumers, as some would argue[30]. Consumers, who find it difficult to control their appetite, and respond to demands of the food environment by eating unhealthily, may wish to use satiety-enhancing foods to help them resist these temptations and improve the quality of their diet. If a food can prolong post-meal feelings of satisfaction these consumers should be less likely to be distracted by cues to consume and more able to maintain regular eating habits[30]. This leaves the consumer free to devote cognitive resources to other issues. Additionally, the ability to manage eating behaviour over the course of the day should enhance feelings of self-control and well-being. Giving the consumer mastery over their eating behaviour may prove beneficial in increasing general self-efficacy (belief in one's own ability to succeed), increasing the likelihood of trying and achieving behavioural change in other spheres of their life[30]. An increase in self-efficacy would support other healthy behaviour changes around diet and exercise, and the pursuit of personal goals. However, such consumer benefits remain largely speculative and, from a regulatory perspective, their benefits to health remain tangential.

For other consumers, the benefit of satiety-enhancing foods is clearly for weight control. Most of these products have acute human appetite studies (proof of concept), but as these largely fail to support direct appetite-related health claims their weight management potential remain largely unproven[29,30]. It is assumed that changes in appetite observed in acute dosing studies would translate into more general behavioural benefits in long-term weight management[20,30]. This does not necessarily mean that such products will not provide any weight management benefits. Indeed, more radical nutritional and pharmacological methods that enhance satiety have been demonstrated to produce weight loss, validating a satiety-based approach[4,30]. However, without supporting weight management data the real-world long-term benefit remains supposed at best and certainly cannot be generalised from laboratories examining the acute effects of specific products on ratings of appetite and/or *ad libitum* meal intake.

The negative physiological and psychological consequences of restricting food intake make dieting difficult[4,14,15,30]. Uncontrolled hunger is a predictor of difficult and ultimate failure in weight management[4,31,32]. Targeting appetite using specific foods may provide a means of managing hunger and overcoming the physiological mechanisms that defend current body weight. Surprisingly, the impact of dieting on the mechanisms underpinning appetite regulation remains poorly understood. However, changes in gut function and the release of ghrelin, CCK, GLP-1 and PYY could potentiate hunger, and weaken satiation and post-meal satiety during periods of weight loss[30,33,34]. Heightened pre-meal ghrelin could stimulate hunger and delay the onset of intra-meal satiation. Similarly, post-prandial reductions in CCK, GLP-1 or PYY associated with weight loss and/or dietary restraint could weaken intra-meal satiation and post-meal satiety[30,33,34]. Furthermore, changes in the function of these peptides post weight loss may pose a significant risk of weight regain. Could satiating and satiety-enhancing foods suppress ghrelin and boost levels of CCK, PYY and GLP-1 release to normalise appetite regulation during and after weight loss[34]? Weight loss-induced reductions in circulating levels of the adipose tissue hormone leptin, known to suppress appetite, may also stimulate feelings of hunger and weaken satiation and satiety[30,33,34]. Although satiety-enhancing foods will not alter diet-induced changes in leptin secretion, a diet enriched with satiety-enhancing foods may lessen some of its impact on appetite.

The impact of weight loss on appetite is associated with distinct psychological phenomena such as cravings, feelings of deprivation, increased subjective appeal of high-energetic foods, increased reinforcing value of food, and an increased CNS reward system response to high-energetic foods[4,30,35,36]. Studies demonstrate that restriction of energy intake can produce profound effects, including a preoccupation with food, unrelenting thoughts of eating, distraction and limited concentration, analogous to the effects of dieting[37,38]. This is associated with increased emotional responsiveness, irritability and dysphoria along with fatigue. Consequently, reducing energy intake sufficiently to lose weight has the potential to produce detrimental effects on mood as well as appetite[39]. Preoccupation with thoughts of food, avoiding specific foods and the experience of unrelenting food cravings all bear a cognitive cost[40]. Dieting is associated with deficits in attention, preoccupation with food associated with dieting impairs cognitive function and dieters perform poorly on cognitive tasks because of preoccupying thoughts of dieting[41]. In particular, cravings appear to limit cognitive resources[42].

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Individual psychological state (mood and feelings of well-being) is critical to successful weight loss and prevention of weight regain[11,30,40]. Feelings of deprivation resulting from cravings and pre-occupation with food are likely to undermine dietary compliance[43]. Moreover, the impact of dieting on mood and cognition can be profound[40,44]. The evidence that satiety-enhancing foods provide some benefit in managing these psychological phenomena remains limited. In the context of prolonged energy restriction associated with weight loss, do satiety enhancing products (1) reduce feelings of deprivation and increase dietary compliance? (2) satisfy hunger or reduce reactivity to food cues? and (3) lessen the intensity of cravings or dysphoria? Such benefits would be of real value to consumers engaging in active weight loss through dietary restraint.

Proving an effect on appetite

Fundamental to proving an effect of a food on appetite is the measurement of satiation within meals and inter-meal satiety[4,11,20]. Self-report measures such as food diaries, short-term recalls and food frequency questions are suited to large population samples and studying the impact of products as they are actually used by consumers. However, they lack the precision and reliability of laboratory-based observations[45]. Laboratory-based techniques have been used for nearly 50 years to characterise psychological, nutritional and pharmacological effects on human appetite expression[4,11]. They have successfully captured the effects of numerous nutritional manipulations on appetite. Despite the artificiality of the laboratory situation, such studies are held to have predictive validity sufficient to model real-world responses. It also enables researchers to assess the effects of foods on various aspects of appetite free from the turbulence of the natural environment[20,45]. Laboratory-based study is also an essential element in substantiating health claims around appetite[20].

The standard laboratory technique to study the effects of food intake on short-term appetite is the preload study design[20,45,46]. The preload should take the form of the food item intended for end use, for instance yoghurts, snack bars, breakfast items, soups or beverages. These test items may vary in energy density and macronutrient composition, but in other aspects, such as taste and appearance, should be well matched to an equivalent control item. For instance, yoghurt enriched with protein and fibre may be compared to a similar low-energy yoghurt product, or a snack bar enriched with added fibres may be compared to a similar non-enriched bar. Standardisation here is critical[20]. Other than the changes in the product that result directly from the satiety-enhancing manipulations, test and control preloads should, wherever possible, be matched in energy content, dilution and macronutrient composition[45]. Wide variations in the physical, nutritional and sensory characteristics of preloads produce effects on appetite that are difficult to interpret. If these factors are not adequately controlled for within a study design it remains difficult to attribute any observed effects on appetite to the purported satiety mechanism[20]. The close matching of control and test preloads allows the experimenter to precisely study the impact of manipulated foods on appetite expression[45]. This is essential when assessing if discrete changes to food structure or the addition of a key functional ingredient trigger distinct changes in sensory characteristics, cognitive impact, gut function or hormone release underpinning the timeline of satiation and satiety.

Variations in habitual eating styles and individual idiosyncrasies in reporting changes in appetite generally necessitate within-subject repeated measures designs in preload studies, usually double-blind designs[20]. However, not all changes to foods can be made covertly or easily disguised. Indeed, certain satiety-enhancing manipulations may actively pursue overt changes in the sensory and physical properties of foods to enhance their impact on appetite. Differences in the cognitive impact, participant experience of the preloads and the expectations of their likely satiating impact are important. However, this can introduce confounding demand characteristics, the participant guessing the purpose of the study and adjusting their behaviour accordingly. Participant naivety over the purpose of the study may not suffice and a between-subjects design may be required. Pilot testing is recommended.

The *ad libitum* test meal is a standard means of assessing the impact of a preload on appetite[45,46]. The size, energy content and duration of this meal should be inversely proportionate to the effect of the preload on appetite. Regulations within Europe now demand that the effects of a food on appetite are sustainable, and the effects of single or multiple preloads need to be observed across the day, to determine if energetic compensation (over-consumption at later eating opportunities) negates the benefits of reduced energy intake earlier in the day[19]. The timing and nature of these test meals are critical. It is essential to ensure that the product's maximal impact on appetite coincides with the next eating opportunity. Long intervals between preload and test meal will miss effects on satiation and early post-meal satiety. Similarly, shorter preload test meal intervals will miss later post-meal satiety effects. Successful outcomes potentially depend as much on consideration of the supposed mechanism of action of the preload as they do on the actual efficacy of the ingredient. Negative findings resulting from inappropriately timed measures of *ad libitum* intake have the potential to lead to substantive discrepancies within the published literature. Piloting is essential for optimising timings within the protocol. Products must be designed for real-world application, therefore the length of the pre load to test-meal interval will also impact on the nature of preload chosen. Soups are more likely to be given immediately prior to a meal, with snack bars and dairy products mostly given at least 2 h, and cereals at least 4 h, before a meal.

The nature of the meal is also important[20,45,46]. It is difficult to determine the optimal *ad libitum* test meal composition. Large buffet style meals allow researchers to determine the effects of a preload on food choice and macronutrient selection. Given the relationship between fat, sugar, energy density and overconsumption, the impact of satiety-enhancing products on food choice is a critical question. Thus, often researchers aim to include food items varying in sweetness, fat content and energy density

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in *ad libitum* meals and the number of items offered can vary from four to twenty-four within a single meal. However, in the real-world individuals seldom face such a variety of foods from which they can freely choose in one sitting[20]. The high hedonic value of many of the foods offered in excess may induce over consumption in all conditions (ceiling effect), overwhelming the satiating effects of preload manipulations. Conversely, single-item meals are often monotonous, an attribute likely to limit consumption within the study as a whole (floor effect), irrespective of the enhanced satiating potential of one of the preloads[20]. Dietary monotony may well curb excessive intake but is equally unrepresentative of a normal meal and is also unlikely to be commercially viable as a solution to weight management. Consumers are not likely to adhere to and economically commit to a monotonous dietary regime for any prolonged period of time. Surprisingly, the effect of the number of *ad libitum* meal items on overall energy intake has not been systematically evaluated. Nor does examination of the literature provide any clear indication that increasing the number of food items *per se* increases intake at test meals. The potential for the number of food items offered to decrease the likelihood of observing significant changes in energy intake through ceiling and floor effects remains to be quantified.

Changes in *ad libitum* intake of a food generally result from and are indicative of the effects of foods on appetite[20,45,46]. However, reduction in gram and kJ (kcal) intake cannot confirm satiety-specific effects and suppression of eating behaviour can equally result from feelings of nausea or malaise, or changes in the perceived quality of food[4]. The measurement of subjective appetite sensations is required[20]. These measures provide great insight into the motivational determinants of volitional changes in directly observable eating behaviour. Appetite has many dimensions[20]. Early studies focused on feelings of hunger and fullness[45,46]. But satiety is more than the physical impact of food and the suppression of the motivation to ingest, such that desire to eat and prospective consumption (how much could you eat at this time?) have generally been incorporated into results. Other aspects of appetite such as satisfaction, cravings, urges to eat (controllable or otherwise), persistent thoughts about food and desire for specific foods (healthy *v.* unhealthy) may well tap into aspects of appetite control relevant to consumers. Of all of these appetite-related dimensions, hunger, fullness, prospective consumption and desire to eat are most consistently used in research[45,47].

Subjective states of hunger, fullness, prospective consumption and desire to eat can be rated in a number of ways; however, the most common format is the Visual Analogue Scale (VAS)[45,47]. The standard VAS, a 100 mm horizontal line, anchored at each end with opposing extremes of appetite ('very hungry' and 'not hungry at all'), provides a means of quantitatively measuring the intensity of subjective experience. Variations of the VAS exist[45]. The line can vary in length and intermediate anchor statements (e.g. 'slightly hungry' or 'fairly hungry') can be included along its length. VAS are usually administrated from the start of the experimental day, before and after fixed-load meals, preloads, and *ad libitum* meals and snacks (usually within the laboratory), and at hourly intervals after the start of each eating event (sometimes completed outside the laboratory). At each time participants are instructed to mark the VAS with a vertical line that transects the horizontal line, depicting their current appetite experience[46,47]. Although most data collection relies on traditional paper-and-pencil VAS techniques, electronic collection of VAS at set times can be combined with techniques to capture other real-time changes in behaviour outside the laboratory to increase the validity of the experimental protocol[45]. With regard to the validity of VAS measures, subjective changes in appetite measured by VAS are sensitive to dietary manipulations[20,45]. Moreover, changes in VAS (i.e. reductions in hunger or increases in fullness) can predict subsequent *ad libitum* energy intake[20,45], and are certainly superior to any 'biomarker' of appetite in this respect[48]. Nonetheless, many well-controlled studies can be cited in which changes in VAS failed to predict subsequent reductions in intake. Here the appetising potential of the *ad libitum* test meal may be a critical factor. However, as stated previously, methodological issues around test meals are yet to be systematically studied. In contrast, a failure to detect changes in appetite prior to a significant reduction in energy intake can be attributed to insufficient sample size (statistically underpowered design) or preload test-meal interval.

Researchers often seek 'objective' biological markers (changes in gut hormones or CNS function) to validate an authentic appetite effect. Such measures demonstrate proof-of-concept for potential mechanisms and also indicate strength of a particular signal. But their fluctuations illustrate operation of only one of many components underpinning the experience of appetite ultimately driving eating behaviour. From a regulatory perspective, biomarkers underpinning changes are insufficient to substantiate a claim and changes in physiological systems are hard to achieve with single foods[19]. VAS offer researchers a reasonably reliable and valid, easy to administer and inexpensive measure of appetite. For participants, VAS are non-invasive, easy to comprehend and straightforward to use within or outside the laboratory.

Ingredients, foods and appetite

The literature on the effects of foods and functional ingredients on appetite is beyond the scope of the current review. The field moves forward at a rapid pace with new ingredients, formulated in new products given in a variety of manners, entering the published domain frequently. Nonetheless, we can consider the evidence around certain ingredients groups in relation to satiety and claims. There are 40 years of literature on the effects of proteins[49,50] and fibres[29] on appetite and energy intake. The quality of early study designs, the adequacy of controls and the suitability of the measures do not always reach current standards of research practice[20,29]. Moreover, the ingredient manipulations are crude and of a magnitude commercially unviable for a consumer application. However, the satiating potential of these ingredients remains widely accepted[51].

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Protein-induced effects on satiation and satiety appear to be underpinned by pre-absorptive increases in CCK, GLP-1 and PYY release, post-prandial amino acid concentrations and metabolic effects such as dietary-induced thermogenesis[49,50]. Moreover, the effects of a high-protein diet on appetite, both on total kJ (kcal) intake and on hunger and fullness, appear to translate into radical weight loss[52]. However, with regard to claims approval for generic proteins and energy intake or body weight, the study designs did not allow conclusions to be drawn on whether the effects observed were due to dietary protein *per se* or to the concomitant modification of carbohydrate and fat intakes (impossible to vary protein, carbohydrate and fat with a single control pre load)[53].

Currently, the literature on the effects of differing protein sources and differing protein ingredients on satiety remains comparatively limited and certainly insufficient to demonstrate enduring effects on appetite. Therefore, with regard to individual protein sources, published opinions have been largely negative. A cause-and-effect relationship between soya protein and the maintenance of a normal body weight was rejected because the only study that allowed conclusions to be drawn for the scientific substantiation of the claimed effect showed no effect on body weight when compared with other protein sources[54]. Similarly, a cause-and-effect relationship between whey protein and the maintenance of a normal body weight was rejected due to the failure to provide references from which conclusions could be drawn for the scientific substantiation of the effect[55]. Recent evidence does suggest that whey protein may be more effective at inducing changes in body weight than soya over 23 weeks in overweight and obese adults[56]. Additionally, an effect of whey protein on satiety was rejected due to the failure to demonstrate the sustainability of an effect on measures of satiety and subsequent intake[55]. Finally, for the effects of mycoprotein on appetite, no references were provided from which conclusions could be drawn for substantiation of an effect[57].

Fibres, a heterogeneous group of ingredients, produce diverse effects on differing mechanisms underpinning appetite control[29]. Certain fibre types bind to water and swell causing bulking, and others increase viscosity. Fibres, particularly soluble forms and carbohydrate forms resistant to digestion generally delay gastric emptying, slow glucose absorption, and/or promote release of CCK, GLP-1 and PYY. The release of GLP-1 and PYY may in part be mediated by the release of SCFA that result from colonic microbial fermentation. The role of this in human appetite expression remains to be proven. Generic fibre-based claims for appetite and weight management have been rejected because the ingredients category was diverse and 'the food constituent, dietary fibre, is not sufficiently characterised in relation to the claimed effects considered in the opinions'[58].

With regard to specific fibre ingredients, for β-glucans no studies testing the sustainability of an effect on appetite ratings and subsequent energy intake were submitted[59]. Additionally, inulin-type fructans and xanthan gum were not sufficiently characterised to substantiate a claimed effect on satiety[60,61]. For guar gum, no controlled studies assessing effects on appetite ratings and subsequent energy intake were presented[62]. For partially hydrolysed guar gum, the two studies presented showed no effects on appetite ratings leading to a reduction in energy intake when the energy content of the test meal was taken into account[63]. These negative opinions reflect the fact that any observed effects of fibres on energy intake have been relatively small[29] and often demonstrated in studies lacking adequate control, not measuring energy intake and/or measuring appetite over insufficient duration.

Combining relatively small amounts of protein and fibre has the potential to induce satiation. Yoghurt enriched with whey protein and hydrolysed guar gum given as a mid-morning snack significantly reduced post-snack appetite (reductions in hunger, desire to eat and prospective consumption, and an increase in fullness) and *ad libitum* lunch intake by 6% compared to equivalent low energy yoghurt ($P<0{\cdot}05$)[64]. However, in this study, the effects were observed at only one test meal. A claim for another milk product rich in fibre and protein was rejected on the basis that the product's effect on hunger did not endure over 6 weeks dosing[65]. More generally, with regard to protein–fibre mixes it cannot be assumed that ingredient combinations necessarily produce additive effects. As rigorous pilot studies often demonstrate, other food ingredients, including other satiety-enhancing functional components, are equally as likely to diminish the effect of a satiety factor (JA Harrold, GM Hughes, EJ Boyland, N Williams and JCG Halford, unpublished results).

A number of novel satiety ingredients exist, although the published literature detailing their effects on appetite expression is limited[66]. The effects of novel fats on appetite have also been associated with enhanced CCK, GLP-1 and PYY release, mechanisms that should delay gastric emptying and oral–cecal transit. NEFA with chain lengths of twelve and above in particular are associated with suppression of appetite and enhanced CCK and GLP-1 response, effects likely to underpin both satiation and early post-meal satiety. Fat-based satiety functional ingredients include the oat- and palm oil-based product Olibra (Fabuless) and the pine nut oil-based product Pinnothin. The effects of Olibra on appetite were established in early trials[67] and a potential mechanism of action in terms of the effect of GLP-1 on gastric emptying through the ileal brake appears entirely plausible[68]. However, subsequent studies have not replicated these effects on appetite[69,70]. No satiety claims have been approved. A weight control claim for oat and palm oil was submitted, but not approved because no references were provided from which conclusions could be drawn for the scientific substantiation of the claim[71]. The one human intervention study from which conclusions could be drawn for an effect on maintenance of body weight after weight loss had methodological limitations and did not show a statistically significant effect[72]. With regard to appetite, a claim submitted on pine nut oil was rejected[73] as no studies submitted substantiated the claim[74].

Novel fermentable fibres and resistant starch-based ingredients have been a recent focus of research. Significant effects of fermentable fibres on body weight in the overweight and obese have also been reported. In this 12-week study, oligofructose significantly reduced ghrelin

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and increased PYY secretion (lower area under the curve for ghrelin ($P = 0{\cdot}004$) and higher area under the curve for PYY ($P = 0{\cdot}03$), an effect associated with self-reported reductions in food intake[75]. However, in a direct examination of eating behaviour, smaller doses of the same fibre given in morning and afternoon snack bars (8 g per bar) on two consecutive days failed to significantly reduce appetite or *ad libitum* intake[76]. There are also little data to support the role of SCFA in human subjects, one key potential mechanism underpinning the effects of fermentable fibres on appetite[77]. The effects of the resistant starch-containing product Hi-Maize-260 have been characterised in two studies. In the first, Hi-Maize (80 g containing 48 g resistant starch) added to a fixed-load breakfast and lunch produced a significant reduction in energy intake at the *ad libitum* meal ($P = 0{\cdot}003$)[78]. In the second, 50 g Hi-Maize combined into a soup significantly reduced intake at an *ad libitum* test meal, but only if the meal was presented 2 h after the soup preload ($P<0{\cdot}0001$)[79]. No claims for effects of general fructooligosaccharides or resistant starch on energy intake or body weight have been evaluated and the published data appear too limited to substantiate any appetite-related claims.

Summary and discussion

The current regulatory environment poses a fundamental challenge to industry. There is a clear demand for products that help consumers manage their own body weight (induce weight loss and/or prevent weight gain or regain). Such products need to make a direct contribution to effective appetite control and should be used in addition to the general reformation of processed foods and the adequate provision of low-energy options to replace energy-dense equivalents to promote healthier consumer choices. These foods should demonstrably strengthen within-meal satiation, thereby reducing meal size and post-meal satiety, thus reducing between-meal consumption. Deficits in appetite control are related to weight gain and/or current levels of adiposity. However, are small modifications in subjective experiences of appetite sufficient to help consumers resist the external and individual factors that drive overconsumption in real-world food environments? Can satiety-enhancing products actually help consumers resist the cues to overeat that overwhelm appetite control? The benefit of satiety enhancement has recently been questioned[80–85] and this detailed debate will not be reproduced here. However, ultimately these questions can only be resolved when we better understand the problems consumers face around managing their diet and eating behaviour, and how exactly satiety-enhancing foods benefit consumers. These are substantial scientific questions that will take a considerable investment in time and resources to resolve.

With regard to claims, few approaches, with the exception of meal replacements[86] and very low-energy diets[87], have been approved for either appetite control or weight management (very low-energy diet for both weight control and appetite). Most failures (excluding claims lacking any direct evidence, not conducted in the relevant population or with the product as intended) were due to an absence of measures of energy intake or a failure to measure reductions in energy intake over more than one *ad libitum* meal. Preloads, measures of *ad libitum* intake and VAS measures of appetite provide the basic elements within a researcher's tool kit to prove an effect on appetite. They do present a valid platform recognised by regulators as sufficient to build evidence to support product claims. The inclusion of biomarkers provides additional mechanistic proof-of-concept but cannot substantiate appetite claims. Biomarkers are important in product development. For food formulators, the challenge remains to prevent the food or beverage matrix diminishing the functional ingredients' effect and ensuring it reaches its intended site of action intact. Modifications to food structure may provide opportunities for innovation and this can be tested with biomarkers *in vitro* and *in vivo*. However, despite having this platform of behavioural measures, current study designs and protocols are largely inadequate to demonstrate a clear health benefit. From the published opinions and EFSA draft guidance[19] it is clear that the scientific panels are looking for clear sustainable effects on appetite across multiple meals across the day in experimental studies, and a durability of effect that is apparent for at least 28 d of product use. These changes in appetite must be accompanied by significant reductions in food intake. Claims on weight loss and weight regain demand longer treatments (12 and 26 weeks respectively). For all claims, replication of significant findings in more than one independent study, preferably from differing laboratories, is required.

Despite the vast literature on the impact of nutrients and foods on appetite and energy intake, there are insufficient data on virtually all products and ingredients to satisfy such rigorous criteria. It remains to be demonstrated that marginal changes in energy intake by acute preloads of products within the laboratory can translate to sustained effects on appetite sufficient to significantly impact upon weight management. With regard to specific ingredient types, while the appetite suppressing potential of protein enrichment is apparent in the literature, to substantiate a health claim the effects of protein enrichment *per se* need to be compared against adequate controls that manipulate both fat and carbohydrate content. For specific ingredients, research directly comparing individual proteins and protein sources against equivalent alternative proteins and protein sources are required. For fibres, the category is so diverse that generic claims are inappropriate. Currently, many claims fail because the fibre type is insufficiently characterised. For individual fibre and protein types and for novel ingredients (e.g. oils, fructooligosaccarides and resistant starches) substantially more data are required before any health claim can be substantiated.

The consumer and health benefits of satiety-enhancing products need to be better defined. It is not clear as to what the consumer understands by satiety or whether consumers know how satiety products should be incorporated into the daily diet. This gap in understanding is matched by a gap in scientific understanding of how satiety-enhancing products can be used for optimum effect, who they are most likely to benefit, and perhaps most critically what behavioural changes in real-world consumer behaviour

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they support? Nonetheless, helping the consumer achieve control over their own eating behaviour remains a worthy goal, as is decreasing the negative psychological consequences of deprivation and the physiological consequences of energy restriction associated with dieting.

Conclusion

The EFSA currently demands that appetite-based health claims are supported by studies that show sustainable changes in appetite, accompanied by corresponding reductions in energy intake that are sustained across the day, and endure over repeated exposure, i.e. are still observable after at least 4-weeks of administration. However, published studies more often than not are too short, have inadequate measures of food intake, fail to detect energetic compensation and do not demonstrate product effects beyond a few occasions of use. The choice of controls used in claim substantiating studies has to recognise that the cognitive and sensory impact of these foods may be critical for satiating effects and this has implications for the blinding of conditions within controlled studies. It is particularly critical that experimental findings should also be replicated in independent laboratories and clinical trials. However, the existing methodological platforms consisting of preload designs, *ad libitum* test meals and VAS measures of subjective changes in appetite are both acceptable and approved methods, and considered sufficient to substantiate appetite-related health claims.

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