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The impact of dietary fibre intake on the physiology and health of the stomach and upper gastrointestinal tract

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Abstract

This review is the first in a series of three articles considering how different types of dietary fibre may affect how the gut functions and gut health. This first review will focus on the impact of dietary fibre intake on the upper gastrointestinal tract (i.e. the mouth, oesophagus and stomach). While a larger body of evidence links fibre intake to bowel health and disease, it is apparent that the presence of fibre, whether as an added ingredient in foods, or as an integral part of the structure of plant foods, also plays key roles on oral and gastric secretions and upper gut motility. These actions are possibly modulated through fibre's effects on the physicochemical properties of luminal contents in the gut.

The major physiological functions of the mouth, oesophagus and stomach are discussed and recent evidence relating dietary fibre intake to these actions is introduced. A summary of evidence linking habitual dietary fibre consumption to major mucosal diseases of the upper gastrointestinal tract is also provided.

Keywords: Dietary fibre; Mastication; Swallowing; Saliva; Gastric juice; Upper gastrointestinal ~~cancer~~cancer

1 Introduction

An updated definition of dietary fibre was recently presented by Codex (Jones, 2014). This newer iteration has, within the long-standing definition of dietary fibre as indigestible carbohydrates of dietary origin, included resistant starches clearly within the definition while omitting lower chain-length saccharides (i.e. those between three and nine units long). Some countries still retain the shorter saccharide chains within their definition of dietary fibre (De Menezes, Giuntini, Dan, Sardá, & Lajolo, 2013). Regardless of these solidifications the consensus definition, it is important to note that the term dietary fibre represents a wide spectrum of different compounds, with divergent molecular structures and physicochemical properties. While dietary fibre intake is generally accepted as part of a positive dietary template with regards to improved health outcomes in many major, non-communicable diseases (European Heart Network, 2011; World Cancer Research Fund/American Institute for Cancer Research, 2007), the exact action through which fibre may have such effects is not well characterised. The association with higher fibre intake and improved health comes as a result of findings from large observational studies (Bingham et al., 2003; Howe et al., 1992; Hu et al., 2001; Rimm et al., 1996). Even with meticulous consideration of other confounding lifestyle factors (Kratz, Baars, & Guyenet, 2013), such evidence cannot separate the impact of dietary fibre intake from the intake of its major dietary sources (i.e. fruits, vegetables and cereal products) from other putatively beneficial components within these foods (Mellen et al., 2007), or the broader effect that inclusion of high amounts of these foods within the diet may have to displace other less optimal food choices (Bogart et al., 2014; Lazzeri et al., 2013).

Recent research on dietary fibre has tended to focus on how different types of fibre might interact with the large bowel microflora (e.g. Flint, 2012; Kaoutari, Armougom, Gordon, Raoult, & Henrissat, 2013; Kumar, Sinha, Makkar, de Boeck, & Becker, 2012; Shen, Zhao, & Tuohy, 2012). The mouth and stomach play crucial roles in mechanical, chemical and enzymatic digestion of food and are also thought to be key roles in appetite regulation and microbial defence (Jolliffe, 2009; van der Bilt, Engelen, Pereira, van der Glas, & Abbink, 2006). Aside from this, the sensing of texture and chemical composition of ingested foods results in neurohumoral signals being sent to other parts of the body, which can result in acute and long-term changes to whole body metabolism (Côté, Zadeh-Tahmasebi, Rasmussen, Duca, & Lam, 2014; Depoortere, 2014; Chen, ~~2011~~2011).

The current review is the first of a series of reviews within this journal that aim to update a previous, broader work considering the physiological roles of dietary fibres (Brownlee, 2011). Each review will focus on the actions of dietary fibre on a section of the gastrointestinal tract and critically consider the recent evidence in this field and highlight potential areas for future research. This review series will also highlight how inclusion of increasing amounts of fibre-rich food in the diet could relate to longer-term health consequences within the gut. As the first article in this series, it seems relevant to start with the mouth, oesophagus and stomach and work aborally in the future reviews (focused at the small intestine and large intestine).

2 Bolus production in the mouth

The mouth's major role in digestion is to grind food into more homogenous, softer entities (boluses) that can be swallowed and pass through the oesophagus to the stomach. Only minor digestion of macronutrients is believed to occur as a result of oral secretions (Pedersen, Bardow, Jensen, & Nauntofte, 2002). The main effectors of this homogenising process (known as mastication) are the teeth and a complex arrangement of the major facial muscle groups, namely the masseter, temporalis, lateral and medial pterygoid, digastric, milohyoid and geniohyoid muscles (Le Révérend, Edelson, & Loret, 2014). The action of mastication results in texture analysis of the ingested food in two ways. **Firstly, First**, the amount of force that the muscles of mastication produce appears to provide signals (possibly generated in the muscle spindle) back to the medial division of the central nucleus of the amygdala, a structure well-linked to the development of conditioned responses (Lund & Kolta, 2006; Van Daele, Fazan, Agassandian, & Cassell, 2011). **Secondly, Second**, the periodontal ligament that attaches teeth to the surrounding bone tissue is momentarily deformed by the deflection of the inset tooth as a result of chewing. The deformation leads to signal production from mechanoreceptors within the periodontal ligament. This signal is conveyed to the trigeminal nucleus area that occurs across the entire brainstem (Yamaguchi, Nakajima, & Kasai, 2012). It could be hypothesised that the hardwiring of these receptors to the brain allows development of conditioned food choice based on previous experience of texture analysis of foods. In other words, our previous feeling of pleasure or enjoyment associated with prior eating experiences could become linked to specific textures. Subsequent eating experiences that match that specific texture may therefore also be seen as positive, whereas subsequent eating experiences that do not match previous texture expectations may be viewed negatively. It must be noted that this would be extremely difficult to evidence experimentally.

Dietary fibre plays a key role in the texture of both plant-based foods and foods with added dietary fibre. In fruits and vegetables, the process of ripening is particularly important in the oral sensation of food. This process is perhaps primarily governed by the rate at which pectin (a highly branched polysaccharide mainly made up of uronic acid monomers) is degraded (Champa, Gill, Mahajan, & Arora, 2014; Guzmán, Sánchez, Salas, Del Moral, & Valenzuela, 2012). Pectin binds to water in the cell wall structure of plants, thereby exerting hydrostatic pressure onto the cellulose and hemicellulose lattice surrounding it (Jarvis, 2011). This increases the turgidity of plant tissues and thereby is a major factor in the perceived firmness, crunchiness and other organoleptic properties of plant foods, particularly those frequently consumed uncooked or with minimal processing (e.g. Billy et al., 2008; Makkumrai et al., 2014). Similarly, loss of the cellulose/hemicellulose meshwork around the pectin matrix is also likely to lead to changes in organoleptic characteristics. The mechanical breakdown of the cell wall during mastication also plays a crucial role in improving the bioaccessibility of plant nutrients (e.g. Ellis et al., 2004) and is likely to affect the taste perception of these foods (Tarascou et al., 2010).

Recent work (Koç et al., 2014), suggested that increasing the concentration of agar (which the authors equated to increasing in the hardness of food gels) and **carrageenan-locustcarrageenan-locust** bean gum mixture (equated to increasing gel rubberiness) resulted in a significant increase in the number of times the food was chewed, as well as the amount of time before the food was swallowed (although the time taken to complete each individual mastication cycle did not differ) in both cases. Within these studies, there appeared to be a difference in jaw movement to chew the different products, suggesting that the muscular effort behind chewing was altered as a result of the texture of the food. Comparison of the total oral processing time (i.e. time to swallow after first bite) for food items that looked the same but differed only in hardness (which could equate to fibre content and processing among other factors) highlighted that the feedback from the oral sensory organ rapidly results reduced energy intake and increased oral processing time (Bolhuis et al., 2014).

3 Swallowing and the oesophagus

Alongside taste, this initial analysis of the morsel of food consumed provides initial feedback on whether or not to swallow (**Alsanei & Chen, 2014** Alsanei & Chen, 2014; Chen, 2009; Ertekin et al., 2001; Nishino, 2013). Swallowing is a complex and sequential series of organised events that is believed to be initiated by conscious choice, leading to a series of organised movements, including those of the tongue and soft palate to move a food bolus into the pharynx. It also appears that a single mouthful of food requires at least two different swallows in order to clear it into the oesophagus for passage to the stomach (Chen, 2009). Secretion of saliva is important in the formation of a soft, lubricated bolus that is easy to swallow. The lubricative action of saliva is dependent on the high water content and presence of high molecular weight mucins (Veeregowda et al., 2012). Saliva also contains a wide spectrum of antimicrobial factors that help to entrap, neutralise or precipitate microbes in the mouth, thereby benefiting oral health (Schulz, Cooper-White, & Punyadeera, 2013). The presence of saliva also results in very different properties of the bolus within the mouth, pharynx and oesophagus. As saliva effectively coats the mucosal surfaces in the upper gut, the movement of the bolus is affected greatly by the shear characteristics of this thin, unstirred layer of watery and lubricative saliva and perhaps less by the interaction of the bolus and mucosal surface than had classically been considered (Chen, Liu, & Prakash, 2014).

For gelled structures, the process of mastication is necessary to break down the macrostructure of the gel and/or give an overall more liquid-like consistency to the bolus (partly through the addition of saliva) in order for the bolus to be swallowed (Inoue, Sasai, Shiga, & Moritaka, 2009). In rheologically thick liquids, large inter-individual differences were noted between the initiation movements for swallowing (the tongue moving the bolus into the pharyngeal area) but that increasing bolus viscosity correlated with increasing time to complete each swallow, even though higher viscosity was also associated with lower fluid intake at each sip (Steele & Van Lieshout, 2004).

Reduced production of saliva is one of a number of key factors that could drive dysphagia (a difficulty with swallowing food). One of the main routes for dietary modulation to improve swallowing in dysphagic patients is addition of dietary fibres and other hydrocolloids in order to change the rheological properties of supplements or food (Cichero, 2013; Popa Nita, Murith, Chisholm, & Engmann, 2013; Wendin et al., 2010; Yamagata, Izumi, Egashira, Miyamoto, & Kayashita, 2012), as formulating fluids/gels with different rheological properties is believed to benefit swallowing (Sworn, Keravid & Fayos, 2008). There does not seem to be a "one-size-fits-all" approach to providing a set rheological template to foods to make them easier to swallow but the broad spectrum of viscous and gel-forming polysaccharides available does allow design of products tailored to patient needs.

Previous studies on the oesophageal handling of boluses of varying consistency has highlighted that gel boluses (cubic bean curd) pass from the pharynx into the stomach at a significantly slower rate than viscous boluses of a texture-

modified viscous liquid (approximately 8 versus 7 ~~seconds~~, respectively) when tested in healthy participants ~~(G.L. (Chen, Yi, Chou, & Liu, 2013).~~ This suggests that dietary fibre added to food or beverage preparations is also likely to affect oesophageal handling of boluses. It must be noted however that the impact of such inclusion is unlikely to have major physiological ramifications on the digestion or handling of a single meal due to the minimal amount of time that a food bolus spends within the oesophagus. While oesophageal exposure to potentially positive or negative nutrients could be extended in fibre-rich foods, it is currently believed that retrograde movement of gastric contents is the major factor involved in oesophageal disease and this will be discussed below.

4 Gastric motility

~~Three distinct layers of muscle control motility within the stomach (i) the outer, longitudinal layer covers the distal two thirds of the stomach (ii) the circular layer that is present across the entire stomach and (iii) the internal oblique layer that occurs in the proximal half of~~The stomach is classically represented as a mixing and digestion chamber that is closed at either end to allow these two aforementioned processes to occur. More evidence now suggests that certain meals may spend a very limited amount of time in the stomach prior to passage to the ~~stomach (small intestine, Shafik, El Sibai, Shafik, & Shafik, 2007). For example ...~~

Three distinct layers of muscle control motility within the stomach (i) the outer, longitudinal layer covers the distal two thirds of the stomach (ii) the circular layer that is present across the entire stomach and (iii) the internal oblique layer that occurs in the proximal half of the stomach (Shafik, El Sibai, Shafik, & Shafik, 2007).

As a bolus of food enters the stomach, the gastric phase of digestion commences. At this point, the stomach, the three muscle layers relax isotonicly (receptive relaxation). This process increases the intraluminal volume within the stomach, thereby allowing a larger intake of food. As food boluses continue to enter the stomach, the gastric distension drives a further relaxation within the proximal gastric smooth muscle, known as gastric accommodation (Pauwels, Altan, & Tack, 2014; Vijayvargiya, Camilleri, Shin, Breen, & Burton, 2013) although this action does not seem to occur in the absence of nutrients (e.g. in gastric balloon distension) and may also be driven by enteroendocrine cells sensing of the chemical milieu (Janssen et al., 2011). This relaxation results in an immediate reduction in intragastric pressure following ingestion of a meal compared to the preprandial phase in healthy individuals (Pauwels ~~et al.~~ et al., 2014) followed by an increase in pressure as the meal continues.

Gastric distension is sensed by stretch receptors within the myenteric plexus (the layer that lies between the longitudinal and circular muscle layers), and the submucosal plexus (Furness, 2000). As distension of the smooth muscle by luminal content appears to play an important role in driving receptive relaxation and gastric accommodation, the presence of fibre in plant food structures, or the inclusion of isolated fibres that could form strong gels within stomach conditions (e.g. some alginates and pectins) are likely to affect these processes, although no direct experimental evidence of this effect currently exists. Previous studies in a small cohort of healthy participants have suggested that while food intake is not governed by a set-point cut-off for intragastric pressure, the steady increase in pressure experienced during a meal results in a reduced desire to continue eating (Janssen, Verschueren, & Tack, 2012). It is postulated that a more rapid increase in pressure would result in stopping reaching a state of satiation more rapidly at a single meal compared to the same meal without the volume occupied by ~~fibre-water~~~~fibre-water~~ matrices.

During the course of a meal and directly following it, the gastric pacemaker (situated at the upper part of the greater curvature) produces a pattern of slow, contractile waves to help mix the food boluses into a homogenous paste. Tonic contraction in the antrum and body of the stomach results in movement of solid food particles to the distal section of the stomach for further mixing with gastric juice, while liquid components are released into the duodenum through the pyloric sphincter ~~(Hellstrom, (Hellström, Grybäck, & Jacobsson, 2006 Grybaek, & Jacobsson, 2006)-).~~ The solid components are slowly broken down into smaller particles by mechanical, chemical and enzymatic action until they are homogenous enough to pass through the pylorus and into the duodenum.

During gastric emptying, there is an increase in peristaltic contraction frequency in parallel with increasing occurrences of pyloric sphincter relaxation that allows passage of homogenous liquid into the duodenum while at the same time tending to return larger particles of solid material to the proximal stomach (Azpiroz, Feinle-Bisset, Grundy, & Tack, 2014). The control of gastric emptying is governed by neurohumoral mediators released by the gut, as well systemically-produced hormones like leptin and oxytocin (Blevins & Ho, 2013; Hellström et al., 2006). The rate of gastric emptying is controlled through the action of enteroendocrine cells in response to the chemical content of the duodenal, and gastric luminal milieu (Akiba & Kaunitz, 2014; Saqui-Salces, Dowdle, Reiter, & Merchant, 2012). While it is generally accepted that an increased energy content of a meal will reduce gastric emptying, some evidence exists to suggest that specific dietary components could act to affect gastric emptying rate. Intragastric infusion of a free fatty acid-based meal instead of a triglyceride-based meal significantly reduced gastric emptying rates and increased retention of contents in the proximal stomach in healthy human participants (Little et al., 2007), suggesting that pre-intestinal lipolysis may play an important role in the control of gastric motility. The aromatic and neutral amino acids tryptophan and phenylalanine are known to be strong stimulators of the release of a range of duodenally secreted hormones (secretin, motilin, gastric inhibitory peptide and cholecystokinin) which are believed to delay gastric emptying (Buchan, 1999).

While increased viscosity of the gastric contents appears to be an important stimulus to drive gastric mixing, the chemical composition of digesta could be more important in relation to the drive for gastric emptying. Previous studies on gastric emptying rates after meals of different viscosities (by adjusting locust bean gum content) with and without the presence of caloric nutrients (fats and carbohydrate) suggested that the presence of nutrients within the meal had a larger impact on reducing gastric emptying rates than viscosity alone (Marciani et al., 2001). Nonetheless, there was a reduced gastric emptying rate in the high viscosity (nutrient-free) control versus the low viscosity one. More recent work by the same group has highlighted that wholemeal bread has reduced gastric emptying in comparison to an isocaloric meal of white rice pudding (Marciani et al., 2013). It was suggested that the wholemeal bread formed a homogenous mass within the

stomach and may have acted to reduce gastric emptying time by slowing the separation of solid and liquid components of the meal into the proximal and distal ~~stomach~~~~stomach~~, respectively. These studies again highlights that the form and physicochemical action of dietary fibres drive their physiological actions. It is also important to note that the external measurement of the rheological or textural properties of fibre-based food items may be less relevant to actions on gastric mixing and emptying than how these foods act within the gastric lumen and in the presence of other nutrients. While a number of model gut systems exist (Houghton et al., 2014; Ramasamy, Venema, Gruppen, & Schols, 2014; Wickham, Faulks, Mann, & Mandalari, 2012) and can be utilised to mimic digestion, it must be noted that gastric (as well as intestinal motility) are extremely difficult to recreate effectively. Therefore, human studies, particularly those involving minimally invasive methods like MRI, are invaluable in the design of fibre-based formulations with targeted physiological actions.

5 Gastric involvement in satiation and satiety

While intragastric volume may be an important factor driving feelings of satiation (the absence of drive to continue eating at the end of a meal), gastric emptying rates are believed to be key determinants of postprandial feelings of satiety (not eating again following a meal), that could be linked to meal rheology. There is a complex neurohumoral cascade that is also involved in the modulation of feelings of hunger and fullness as well as gastric motility that is described elsewhere (Chambers, Sandoval, & Seeley, 2013; Clark & Slavin, 2013; Fiszman & Varela, 2013) and will be further discussed in subsequent reviews within this series. A recent study assessing the impact of addition of β -glucans of different molecular weight to soups did not reduce ~~ad libitum~~ad libitum consumption of a soup meal and energy intake after the soup meal or increase subjective feelings of satiety and fullness post-consumption compared to a β -glucan-free (low viscosity, available carbohydrate-based) control soup in 23 healthy participants (Clark & Slavin, 2013). This work highlights that factors other than intragastric viscosity (e.g. nutrient content of the meal and rate of consumption) could also play an important role in satiety.

While assessment of biomarkers (particularly gut and incretin hormones) have previously been used as adjunct measures of satiation and satiety (De Graaf, Blom, Smeets, Stafleu, & Hendriks, 2004), it is important to consider that the measures themselves are related to an individual's subjective desire to consume or not consume food at the time. As such, it is important to consider how test participants may have difficulty understanding terminology in relation to satiation and satiety. Previous work considering this has noted that participants particularly related the term "satiating" to feelings of fullness as opposed to a lack of need to intake further food (Fiszman, Varela, Diaz, Linares, & Garrido, 2014). Feelings of fullness were linked to both positive and negative connotations within these participants of Fiszman et al. (2014), where the particular focus on satiating foods was linked to sources of protein. Similarly divergent opinions on feelings of fullness have also been previously reported in relation to intake of whole grain foods over a longer period of time (Kuznesof et al., 2012), where it was noted that some participants were happy about feeling full for longer, while others noted that this was negative as they felt lethargic and affected their hedonic eating habits. These previous studies highlight caution in interpreting findings on feelings of fullness in relation to the development of new food products focused on prolonging satiety or inducing satiation.

It is important to remember that measurements of satiation and satiety tend to relate to acute assessment of the impact of a single meal intake within previous studies. Fewer studies have assessed the impact of repeated exposure on measures of satiety and satiation. Touyarou, Sulmont-Rossé, Gagnaire, Issanchou, and Brondel (2012) assessed the impact of 15-days of intake of breads enriched with fibre (isolated oat and rye fibres) at breakfast time on satiety over the course of the morning compared to a comparator breads without added fibre and a self-selected breakfast (including a small amount of the fibre isolate to ensure sensory habituation is controlled for). The fibre-enriched bread reduced hunger throughout the morning compared to non-fibre enriched breads. Satiety ratings also seemed to stay relatively constant over the 15 days but did highlight a large amount of intra-individual variation (Touyarou ~~et al.~~et al., 2012). Covert manipulation of the energy and viscous dietary fibre (tara gum) content of pre-load drinks consumed over a seven-day period suggested that differences in perceived satiety were mainly related to the initial consumption of the beverage, as opposed to changes in viscosity and energy content following initial trial (Yeomans, McCrickerd, Brunstrom, & Chambers, 2014). In comparison to a gelatin/starch-based control, a pectin-containing gel-based food initially resulted in a lower elective intake of energy following this meal on the first day of dietary exposure, although this effect was seemingly lost after repeated exposures over 15 days (Wanders, Mars, Borgonjen-Van Den Berg, De Graaf, & Feskens, 2014). These previous findings highlight that effects of fibre inclusion on post-meal energy intake are not necessarily retained over a relatively short time period. These results highlight that initial changes to measures of satiety and satiation of novel food products should be extrapolated to longer-term changes on eating habits and efficacy as weight management adjuncts with caution.

6 Gastric exocrine and endocrine secretion

The stomach produces a number of exocrine secretions from a selection of different epithelial cell types. These secretions are either involved in the chemical and enzymatic digestion of ingested foods, or form an important defence barrier against exogenous and endogenous damage. As with gastric motility, one of the major drives for gastric exocrine secretion comes from the physicochemical constitution of the digesta contained within the gastric lumen.

Hydrogen ions are concentrated by approximately a million-fold across the gastric epithelium as a result of the action of two ATP-driven membrane-bound ~~transporters—the~~~~transporters—the~~ basolateral Na/K antiporter and the luminal H/K antiporter (Isackson & Ashley, 2014). The release of these hydrogen ions (along with chloride ions) into the gastric lumen results in a highly acidic gastric juice. The gastric acid is secreted from the parietal cells that occur at the base of the gastric pits. The high acidity in the gastric juice is important for activation of gastric enzymes (Pearson, Parikh, Robertson, Stovold, & Brownlee, 2012), as an innate defence against swallowed microbes (Howell et al., 2010; Lombardo, Foti, Ruggia, & Chiecchio, 2010) and to denature dietary proteins to aid in both homogenisation of gastric contents and allow improved access of proteolytic enzymes sites of cleavage (Herman, Gao, & Storer, 2006).

Acid secretion occurs as a result of cholinergic stimulation of parietal cells by vagal afferents during both the cephalic and gastric phases of digestion but is also stimulated as a result of release of both histamine and gastrin by enteroendocrine cells within the gastric mucosa (Schubert & Peura, 2008). In brief, prior to food entering the stomach, a basal amount of acid will occur in the stomach due to the thought, smell and sight of food. As food enters the stomach, there will be a further stimulation for acid production (Brownlee, 2011). Negative feedback tends to come to the system as a result of low pH within the gastric lumen, resulting in the release of somatostatin from D cells (another specific type of enteroendocrine cell) which inhibits further stimulation of parietal secretion (Isackson & Ashley, 2014).

A number of previous studies have suggested stimulatory and inhibitory roles for various luminal factors of dietary origin. In a study on G cell rich gastric epithelial cell isolated primary culture, a variety of luminal nutritional used resulted in stimulation of gastrin release, including glucose, caffeine and capsaicin (Kidd, Hauso, Drozdov, Gustafsson, & Modlin, 2009). These studies also found that isolated, gastrin-producing G cells were also stimulated to produce gastrin as a result of mechanical stress, but this stimulation was considerably higher when cells were still within sections of gastric mucosal tissue, presumably driven by the presence of mechanoreceptors within the myenteric plexus. In contrast, isolated human antral cells collected before and after chilli (and the putative active component capsaicin) ingestion resulted in reduced gastrin secretion, possibly through an increase in somatostatin release (Ericson, Nur, Petersson, & Kechagias, 2009). This action may not have been seen in the isolated G cell model used by Kidd et al. (2009) due to the much lower numbers of somatostatin-secreting cells present in this method. Further dietary factors are believed to be important in driving gastric secretion include luminal calcium, high concentration of digested proteins (particularly free amino acids) and mixed dietary fat (Brownlee, 2011; Saqui-Salces ~~et al.~~, 2012; Torii, Uneyama, & Nakamura, 2013; Zolotarev, 2014).

From the above, evidence for a drive for acid secretion as a result of mechanical and chemical stimulation exists. However, there is a paucity of studies that have been carried out to consider the impact of dietary fibre consumption on acid secretion within the stomach. Previous rodent studies highlighted that dietary pectin increased both total gastric juice volume and H⁺ output (Figler, Szabó, & Mózsik, 1999). This could be due to pectin's ability to bind to hydrogen ions, thereby impacting on the free hydrogen ion concentration within gastric juice and inhibiting the feedback mechanisms. It is possible that that other hydrogen ion-binding fibres (e.g. high guluronate alginates) or other foods with a water-binding capacity could act to sequester secreted stomach acid and stop it being sensed by the enteroendocrine cells in the gastric epithelium. Previous ~~in vitro~~ in vitro digestion studies simulating the human stomach noted that the presence of rice bran on cooked brown rice greatly reduced the absorption of hydrogen ions into the endosperm component compared to white rice (Kong, Oztop, Singh, & McCarthy, 2011). Such an effect is unlikely to be seen in the consumption of fibre-rich foods that have a high water content and relatively high acidity (e.g. many fruits and vegetables).

Human pepsin is a series of aspartate proteases secreted in their inactive form (pepsinogen) by the chief cells situated towards the base of the gastric pits (Hayat et al., 2014). Pepsinogen is autocatalytic under acidic conditions; at a pH of 5 and below, a conformational change occurs that results in the peptide chain covering the active site swivelling into the catalytic cleft and being cleaved off (Pearson ~~et al.~~ et al., 2012). Active pepsin cleaves polypeptide chains into shorter chain, with a preference for action between hydrophobic residues, often with aromatic residues close to the site of cleavage (Pearson & Brownlee, 2005; Roberts, 2006). Pepsinogen secretion is stimulated by cholinergic activity from vagal afferents and a range of other neurohumoral mediators, as a result of intake of food (Fiorucci et al., 2003; Pearson & Brownlee, 2005).

Although the impact of fibre consumption is likely to impact on pepsin secretion by similar actions on the luminal milieu as highlighted for gastric acid secretion, there is a distinct lack of evidence in this area of the literature. One previous study has suggested that this classic protease may also have non-specific catalytic activity on galactomannan, acting to branched areas of the molecule (Shobha, Gowda, & Tharanathan, 2014). While these results would need to be reproduced, it can be noted that the catalytic triad of the aspartate proteases is somewhat similar to some enzymes with glycolytic activity, so additional, non-specific catalytic activity of pepsin is possible but may not be physiologically relevant.

Mucin is secreted by gastric mucus cells (situated towards the top of the gastric gland) and rapidly swells in the aqueous environment to form mucus gels (Harada et al., 2013; Nakahari et al., 2002). Gastric mucus is believed to exist in a functional bilayer, with the outermost layer (i.e. that closest to the lumen) being loosely adherent and easily removed by shear stress, while the inner layer is firmer and more resistant to removal (Phillipson et al., 2008; Taylor, Allen, Dettmar, & Pearson, 2004). Mucus secretion is governed by cholinergic stimulation as well as gastrin and secretin but is quickly increased within gastric tissues when the presence of potentially noxious agents (e.g. alcohol) is sensed (Allen & Flemström, 2005).

Previous animal studies have suggested an impact of dietary fibre inclusion on gastric mucin secretion. However, it must be noted that these effects are only seen at intakes of dietary fibre much higher than would be expected to be seen in humans. Ispaghula husk included at 20% dry weight within the rat diet over a 4-week period resulted in an increased output of gastric mucin and total mucin (i.e. secreted and still remaining within the gastric tissue) compared to a fibre-free control, whereas diets with 20% rice bran or 20% cellulose did not increase mucin production (Satchithanandam, Klurfeld, Calvert, & Cassidy, 1996). Ispaghula husk is a hygroscopic, gel-forming dietary fibre (Majmudar, Mourya, Devdhe, & Chandak, 2013) whose ingestion could lead to repeated mechanosensation within the stomach resulting in increased secretion and production of gastric mucus (i.e. a long-term upregulation in mucus production). Similar results were seen with a relatively low daily dosage (250 mg) of methylcellulose given to male mice over ~~2, 3 and 4 week~~ ~~2-4 week~~ time periods resulted in an increased number of mucus cells within the gastric mucosa (Takabayashi & Sekiguchi, 2013). A single oral dosage of guar gum or a mixture of orange pulp and guar gum at 160 mg/kg in male Wistar rats resulted in a significant increase in estimated mucosa-adherent gastric mucus compared to a saline control after a 4.5 ~~hour~~ h time period (Magri et al., 2007). These results suggest that mucus production can also be affected by a short-term intake of a single dosage of a fibre-rich meal (approximately 40 mg within 10 ml of fluid). The dosage appears to still be high enough to cause an increased viscosity of stomach contents within an average male rat and therefore suggests that mechanical stimulation of the stomach also leads to an immediate effect on mucus secretion.

The stomach also produces a series of peptide neurohumoral factors that act on other areas of the gut and target tissues around the body. As discussed above, the major endocrine secretions of the stomach (gastrin, somatostatin and histamine) are all targeted at paracrine control of gastric exocrine secretions, particularly stomach acid. Recent work has also highlighted that some cells within the gastric mucosa can also produce leptin, suggesting a role of the stomach on whole body metabolism (Cammisotto et al., 2005). A variety of other peptide-based gastrointestinal endocrine secretions are believed to feedback through the somatostatin pathways to inhibit gastric acid secretion. In particular, cholecystokinin and gastric inhibitory peptide (released by the duodenal I and K cells, respectively) are believed to be of major importance in this mechanism (Schubert & Peura, 2008).

7 Dietary fibre and diseases of the oropharynx, oesophagus and stomach

While the above sections have mainly focused on acute effects of dietary fibre consumption, the final section will focus on the association between fibre intake and long-term health outcomes in relation to the upper gastrointestinal tract (particularly cancer). The vast majority of evidence linking fibre to such long-term outcomes is from observational studies in large populations. As previously stated, it is important to consider that the vast majority of fibre consumed by participants of such studies will be in the form of plant foods (particularly fruits, vegetables and grains). Separation of health benefits of dietary fibres from other dietary components in these foods is therefore not possible from even the most careful data interrogation. Further from this, while supplementation of fibres such as oat and barley beta-glucan can be demonstrated to improve markers of cardiovascular health in randomised, controlled trials (Shimizu et al., 2008; Wolever et al., 2010), this does not necessarily mean that supplementation with non-targeted fibre isolates will result in reduced risk to other longer-term health problems (Bonithon-Kopp, Kronborg, Giacosa, R ath, & Faivre, 2000; Schatzkin et al., 2000). The evidence below considers human rather than animal studies and, wherever possible, includes summary tables to pool together larger bodies of evidence. The range of diseases covered is not exhaustive but covers all major mucosal diseases of the upper gastrointestinal tract.

8 Oropharyngeal conditions

The loss of normal dentition not only has a major influence of subsequent dietary intake (Savoca et al., 2010), including a reduction of fruit and vegetable intake (Bradbury et al., 2008; Sheiham & Steele, 2001), possibly due to perceived difficulty in chewing but has also been highlighted as a major predictor of morbidity and mortality in older populations (Hung, Colditz, & Joshipura, 2005). As such, a reduction in the risk of major oral diseases has important public health implications. Periodontal disease refers to any condition, either inherited or acquired, that affects the tissues surrounding and supporting the teeth (Pihlstrom, Michalowicz, & Johnson, 2005). Table 1 below highlights previous evidence linking periodontal disease risk to dietary fibre intake. A recent high-fibre, low-fat dietary pilot intervention for 8 weeks carried out in Japan resulted in significant improvements to a number of biomarkers of periodontal disease after the intervention period. Biomarker values returned to baseline 24 weeks after the intervention had finished (Kondo et al., 2014).

Table 1 Dietary fibre and observational risk of oral conditions and head and neck cancers.

Disease/condition	Study design	Comparative statistics (95% CI)	Notes	Reference
<i>Periodontal disease</i>	Prospective follow-up periodontal disease progression in 625 community-dwelling older men	HR 0.76 (0.60–0.95) per serving of high fibre foods/d for alveolar bone loss and HR 0.72 (0.53–0.97) for tooth loss	Significantly lower HR in individuals over 65 years of age only	Schwartz, Kaye, Nunn, Spiro Iii and Garcia (2012)
	Prospective follow-up of 34,160 males for periodontal disease	RR 0.77 (0.66, 0.89) for highest vs 1 (lowest) intake of whole grain intake quintile	No significant association for vegetable and fruit fibre intake with disease risk	Merchant, Pitiphat, Franz, and Joshipura (2006)
<i>Oropharyngeal cancer</i>	Case-control study with 804 cases of oral cancer	OR 0.47 (0.34–0.65) for highest vs 1 (lowest) quintile of fit for dietary pattern “Vitamins and fiber”	Animal products (positively) and unsaturated fats (negatively) patterns also associated with risk	Edefonti et al. (2010)
	Case-control study with 598 cases of oral and pharyngeal cancer	RR 0.40 (0.26–0.62) for >6 characteristics of the Mediterranean diet vs <3 (RR=1)	A total of 8 characteristics of the Mediterranean diet template were considered	Bosetti et al. (2003)
	Case-control study with 524 cases of oral and pharyngeal cancer	OR 0.3 (0.1, 0.4) for intake of whole grains >3 d/wk versus no or rare consumption of whole grains (OR=1)		La Vecchia, Chatenoud, Negri, and Franceschi (2003)
	Case-control study with 232 cases of pharyngeal cancer	OR 1.6 (1.3–10.1) for no intake of “Dietary fiber-containing food” vs 1 for some intake. OR 3.80 (1.58–9.12) for very low intake of “Uncooked vegetables” vs 1 for higher intake	“Dietary fiber-containing foods” defined as legumes and cereals except for wheat bread. Very low intake defined as 1 to 3 times per month	Escribano Uzcudun et al. (2002)
	Case-control study with 485 cases of	OR 0.96 (0.94, 0.99) for highest quartile of total dietary fibre intake vs 1		Hebert et al. (2002)

	precancerous oral lesions in “reverse-smoking” females	(lowest quartile)		
<i>-Disease/conditionStudy designComparative statistics (95% CI)NotesReferenceOropharyngeal cancer (cont.)</i>	Case-control study with 598 cases of oropharyngeal cancer	Continuous OR of 0.51 (0.40–0.66) for highest quintiles of total fibre intake versus lowest (OR=1)		Soler et al. (2001)
<i>Head and neck cancers</i>	Pooled analysis of 61,647 adults following different habitual diets	RR 0.94 (0.62, 1.43) vegetarians and vegans versus 1 for meat eaters for “upper GI cancer”	Upper GI cancer defined as malignant neoplasms of lip, oral cavity, pharynx and oesophagus	Key, Appleby, Crowe, Bradbury, Schmidt, and Travis (2014)
	Case-control study with 2452 case of head and neck cancer	OR 0.56 (0.45–0.69) for highest vs 1 (lowest) quintile of fit for dietary pattern “Antioxidant vitamins and fiber”	Included oral, pharyngeal and laryngeal cancer cases. Negative association between fit to “Fats” pattern and OR	Edefonti et al. (2012)
	Prospective, 11-y follow-up in 494,991 participants	HR 0.61 (0.42–0.89) highest total fibre intake vs 1 (lowest intake) in women	No significant trend for association of total fibre and HR in men. Risk of head and neck (oral, pharyngeal and laryngeal) cancers assessed	Lam et al. (2011)

HR = Hazard Ratio, OR = Odds ratio, RR = relative risk. Data searches were carried out using www.scopus.com and focused on publications from 2000 and onwards. Mixed-site head and neck cancers (many of which are oropharyngeal) were also included within this literature research strategy.

While inspection of the oropharyngeal cavity for lesions is simpler and less invasive than at other sites of the gut, many cancers are still not detected until they are at an advanced stage of progression (Ford & Farah, 2013). Treatment (normally aggressive surgery, chemotherapy or radiotherapy) often results in a loss of normal oral processing function and greatly reduced quality of life (Bessell et al., 2011; Furness et al., 2011; Glenny et al., 2010; Pavitt et al., 2007).

9 Diseases of the oesophagus and stomach

Oesophageal cancer incidence and mortality is rapidly increasing in some European populations, particularly amongst men (Rutegård, Nordenstedt, Lu, Lagergren, & Lagergren, 2010). This is believed to be linked to an increased incidence of non-standard gastric reflux (the retrograde movement of gastric contents back up the oesophagus and potentially further beyond), which may drive mucosal damage (resulting in oesophagitis long-term) and/or preneoplastic changes in the oesophagus. Reflux is particularly strongly associated with the occurrence of oesophagitis and Barrett’s oesophagus, a metaplastic condition where the normal stratified, squamous epithelium of the oesophagus becomes replaced with a columnar epithelium that is more predisposed to subsequent carcinogenesis (Singh, Garg, Singh, Iyer, & El-Serag, 2014; Spechler, 2013). One previous intervention study tested the effect of a controlled, parallel trial assessing the impact of a low-fat, high fruit and vegetable diet on biomarkers of neoplastic change to the oesophageal tissue of 87 participants with Barrett’s oesophagus. This study found no impact up to 3 years intervention with the diet on any of the biomarkers tested, although it must be noted that biomarkers did not deviate from baseline values to a high degree in either the intervention or control group (Kristal et al., 2005). A recent meta-analysis noted a total of eight studies demonstrated a consistent inverse association with increasing fibre intake and oesophageal adenocarcinoma risk, with an overall adjusted odds ratio of 0.66; (95% CI of 0.44–0.98), although five studies overall suggested no significant impact of dietary fibre inclusion of squamous cell carcinoma. Two further studies also suggested a significant inverse with increasing fibre intake and Barrett’s oesophagus risk (Coleman et al., 2013).

Gastric refluxate may contain a variety of potentially damaging factors of dietary (e.g. partially digested food), bacterial or endogenous (e.g. stomach acid, pepsin) origin (Griffin et al., 2013). The occurrence of gastric reflux is, itself complex and may be associated with dietary intake. Previous observational evidence highlights that excess body weight and increasing consumption of (saturated) fat, coffee and alcohol could all be linked to increased reflux frequency and/or gastro-oesophageal reflux disease (El-Serag, Satia, & Rabeneck, 2005; Festi et al., 2009). Previous work has also suggested that intake of highly fermentable carbohydrates can lead to increased incidence of transient relaxations of the lower oesophageal sphincter (Piche et al., 2000) which tends to increase the risk of gastric reflux occurring (Iwakiri et al., 2005). Recent data linking oesophageal disease (i.e. Barrett’s oesophagus and oesophageal cancer) to fibre intake are highlighted in Table 2.

Table 2 Summary of associative studies linking dietary fibre intake and observational risk of oesophageal and gastric conditions.

Disease/condition	Study design	Comparative statistics (95% CI)	Notes	Reference
<i>Oesophagitis</i>	Case-control study with 219 cases of reflux oesophagus	Adjusted OR 0.71 (0.32–1.60) for >19.1 g Englyst fibre/d vs 1 for <14.3 g/d		Mulholland et al. (2009)

<i>Barrett's oesophagus</i>	Case-control study with 304 cases of Barrett's oesophagus	Adjusted OR 0.50 (0.28–0.90) for total dietary fibre >8.9 g/d vs 1 for <6.8 g/d	Increasing legume and green leafy vegetable intake was associated with reduced risk whereas total vegetable and fruit intakes were not	Jiao et al. (2013)
	Case-control study with 220 cases of long-segment Barrett's oesophagus	Adjusted OR 0.40 (0.22–0.73) for >17.7 g Englyst fibre/d vs 1 for <13.7 g/d		Mulholland et al. (2009)
	Case-control study with 296 cases of Barrett's oesophagus	OR 0.34 (0.15–0.76) for highest quartile of total fibre intake vs 1 for lowest quartile of intake	Cases were matched to "controls" with gastro-oesophageal reflux disease. Fibre from fruits and vegetables was significantly associated with reduced risk while fibre from grains and beans was not	Kubo, Block, Quesenberry, Buffler and Corley (2009)
<i>Oesophageal cancer</i>	Case-control study with 47 cases of oesophageal squamous cell carcinoma	Adjusted OR 0.30 (0.15–0.78) for highest tertile of fibre intake vs 1 for lowest	Lower glycaemic index and glycaemic load were also associated with lower OR	Eslamian, Jessri, Hajizadeh, Ibiebele, and Rashidkhani (2013)
	Case-control study with 359 cases of oesophageal cancer	Adjusted OR 0.47 (0.32, 0.69) for >27 g/d total dietary fibre versus 1 for <16 g/d		Tang, Xu, Zhang, Lei, Binns, and Lee (2013)
	Case-control study with 224 cases of oesophageal adenocarcinoma	Adjusted OR 0.79 (0.43–1.44) for >17.7 g Englyst fibre/d vs 1 for <13.7 g/d		Mulholland et al. (2009)
<i>Oesophageal cancer (cont)</i>	Case-control study with 206 cases of oesophageal adenocarcinoma	Adjusted OR 0.44 (0.3–0.8) for highest quartile of fibre intake vs 1 for lowest		Wu, Tseng, Hankin, and Bernstein (2007)
	Case-control study with 304 cases of oesophageal cancer	RR 0.23 (95% CI, 0.13–0.40) for >6 characteristics of the Mediterranean diet vs <3 (RR=1)	A total of 8 characteristics of the Mediterranean diet template were considered	Bosetti et al. (2003)
	Case-control study with 124 cases of oesophageal adenocarcinoma	Adjusted OR 0.5 (0.3–0.9) for highest quartile of total fibre intake vs 1 for lowest		Chen et al. (2002)
	Case-control study with 304 cases of oesophageal cancer	Continuous OR of 0.70 (0.51–0.96) for highest quintiles of total fibre intake versus lowest (OR=1)		Soler et al. (2001)
	Case-control study with 189 cases of oesophageal	Adenocarcinoma: Adjusted OR 0.8 (0.5–1.3) for highest quartile of total fibre intake vs 1 for lowest		Terry, Lagergren, Ye, Wolk, and Nyrén (2001)
	adenocarcinoma and 167 cases of oesophageal squamous cell carcinoma	Squamous carcinoma: Adjusted OR 1.1 (0.6–1.9) for highest quartile of total fibre intake vs 1 for lowest		
	Case-control study with 282 cases of adenocarcinoma and 206 cases of squamous cell carcinoma	Adenocarcinoma: Adjusted OR 0.28 (0.19–0.40) for highest quartile of total fibre intake vs 1 for lowest	Similarly significant effects of inclusion of soluble and insoluble fibre noted, as well as fibre intake/kJ	Mayne et al. (2001)
		Squamous carcinoma: Adjusted OR 0.24 (0.14–0.38) for highest quartile of total fibre intake vs 1 for lowest		

Disease/condition Study design Comparative statistics (95% CI) Notes Reference

Disease/condition Gastric cancer	Pooled analysis of 61,647 adults following different habitual diets	RR 0.37 (0.19, 0.69) for vegetarians and vegans versus 1 for meat eaters for stomach cancer		Key et al. et al. (2014)
	Case-control study with 256 cases of gastric	Cardia: Adjusted OR 0.58 (0.4–0.9) for highest		Wu et al. et al. (2007)

	cardia and 366 distal cases of gastric adenocarcinoma	quartile of fibre intake vs 1 for lowest		
		Distal: Adjusted OR 0.69 (0.5–1.0) for highest quartile of fibre intake vs 1 for lowest		
	Case-control study with 300 cases of distal gastric adenocarcinoma	Men: Adjusted OR 0.4 (0.3–0.7) for highest tertile of total non-starch polysaccharide intake vs 1 for lowest		Nomura, Hankin, Kolonel, Wilkens, Goodman, and Stemmermann (2003)
		Women: Adjusted 0.5 (0.3–1.0) for highest tertile of total total non-starch polysaccharide intake vs 1 for lowest		
	Case-control study with 124 cases of distal gastric cancer	Adjusted 0.4 (0.2–0.8) for highest quartile of total fibre intake vs 1 for lowest		Chen et al. (2002)
	Case-control study with 262 cases of gastric cardia adenocarcinoma	Adjusted OR 0.4 (0.3–0.8) for highest quartile of total fibre intake vs 1 for lowest	Increased cereal and vegetable (but not fruit) fibre intakes were associated with reduced OR	Terry et al. et al. (2001)
	Case-control study with 255 cases of gastric cardia adenocarcinoma and 352 cases of non-cardia cancer	Cardia: Adjusted OR 0.43 (0.30–0.61) for highest quartile of total fibre intake vs 1 for lowest	Similarly significant effects of inclusion of soluble and insoluble fibre noted, as well as fibre intake/kJ	Mayne et al. (2001)
		Non-cardia: Adjusted OR 0.38 (0.28–0.53) for highest quartile of total fibre intake vs 1 for lowest		
	Follow-up cohort study on gastric carcinoma for 6.3 years in 120,852 participants aged 55–69	Adjusted RR 0.8 (0.6–1.2) for highest quintile of total fibre intake vs 1 for lowest	Total, soluble and insoluble non-starch polysaccharides also did not significantly correlate with subsequent gastric carcinoma occurrence	Botterweck, Van Den Brandt, and Goldbohm (2000)

HR = Hazard Ratio, OR = Odds Ratio, RR = relative risk. Data searches were carried out using www.scopus.com and focused on publications from 2000 and onwards.

Much of the recent research effort into mucosal lesions in the stomach have centred around the association of *Helicobacter pylori* with gastric ulcer and/or gastric cancer occurrence. To the author's knowledge, no recent observational studies linking dietary intake to gastric ulceration (or infection with *H. pylori*) have been carried out. The prevalence of gastric cancer appears to be higher in those of Japanese and Chinese ethnicity than in other populations (Goh & Parasakthi, 2001; Naylor et al., 2006). A meta-analysis looking at dietary fibre intake and gastric cancer noted a consistent inverse association of increasing dietary fibre intake with gastric cancer risk. It was suggested that an increment of 10-g/day of dietary fibre could be expected to reduce gastric cancer risk by over 40% (Zhang, Xu, Ma, Yang, & Liu, 2013). Previous studies assessing associations between fibre intake and gastric cancer are outlined in Table 2.

The role that fibre may play in the disease processes highlighted in Tables 1 and 2 is not fully elucidated. Considerably more research has been carried out to consider the potential mechanisms for the actions of dietary fibre intake on the large bowel than has been reported for the upper gastrointestinal tract. As the potential for fermentation in the upper gastrointestinal tract is limited (due to comparatively short transit times and low numbers of microbes in this part of the gut compared to the bowel). However, it is still possible that higher intake of plant-based foods relates to a reduction of number in potentially harmful bacteria in the upper gut. For example, lower occurrence of cariogenic bacteria in the mouth have previously been associated with higher dietary fibre intake (Coogan, MacKeown, Galpin & Fatti, 2008). It can be hypothesised that consumption of plant-based foods may directly help to remove bacterial plaques by increasing shear stress at the surface of teeth, or indirectly reduce bacterial numbers by increasing salivary flow (resulting in an increased output of bacteriocidal factors).

Fibre from plant-based foods has also previously been suggested to bind to potentially toxic compounds that occur within the gut lumen. The reduction of the concentration of these products that come into contact with the mucosa would be expected to reduce potential damage to the underlying tissue. While in the large bowel, dietary fibre tends to act to reduce transit time, previous studies suggest fibre intake tends to increase the length of time ingested foods may stay in the stomach, as a result of delayed gastric emptying (e.g. Marciani et al., 2013). This might mean that while the gastric mucosa is exposed to a reduced concentration of damaging luminal agents, this could be over a longer period of time. Therefore, the overall effect on mucosal exposure to such factors remains unclear. Effects of habitual dietary fibre intake on mucosal development and maintenance of mucosal integrity are also possible but not, to the author's knowledge, well studied in the upper GI tract.

10 Summary

The above evidence relating to dietary fibre intake and diseases of the upper gastrointestinal tract is not aimed at being a systematic review. Nonetheless, the recent evidence covered in Tables 1 and 2 tends to show a consistent association of increasing dietary fibre with reduced disease risk. While this is perhaps unsurprising, due to fibre-rich foods being a key component of healthy dietary templates used around the world, it must be noted that results from such studies are not consistent across all studies. A more complete consideration of this evidence would include a much more careful analysis of the target populations involved and the adjustment factors used within these studies. Most of the current evidence in this area comes from case-controlled studies, suggesting the need a range of prospective cohort studies in the future.

It appears as though most of the actions of dietary fibre on upper GI physiology are possible through actions on luminal bulking, increasing luminal viscosity and potential binding to other nutrients. It is difficult to predict whether effects of dietary fibre or fibre-rich food consumption at a single meal can appropriately model factors that may lead to disease progression. It is therefore recommended that such acute physiological data are rationally considered and discussed critically within the scientific literature. Further longer-term studies modelling the impact of fibre (and other dietary factor) intake are necessary before attempting to relate these findings to health outcomes. The above review has highlighted occasional intervention studies assessing the impact of dietary change relating to dietary fibre on upper gastrointestinal health outcomes (Kondo et al., 2014; Kristal et al., 2005). Whole diet interventions are challenging to carry out over long periods of time due to difficulties with compliance and standardisation (Larsen et al., 2010). Running interventions for shorter periods of time has the potential that lifelong disease trajectory in a series of months may not adequately model changes relating to lifelong disease trajectory (Brownlee et al., 2010). Validated biomarkers of current health or future disease risk are also required which may limit the applicability of such studies to, for examples, cancers of the upper gastrointestinal tract. Metabolomic approaches to disease progression monitoring currently demonstrating potential to develop such disease biomarkers (Bonne & Wong, 2012; Song et al., 2012; Zhang et al., 2012). The previous observational evidence would rationalise testing high fibre diets in biomarker studies for upper gastrointestinal health. Such studies would allow a step closer to consideration of causal relationships between intake of fibre-rich foods and gut health but would still not effectively separate the casual factor (if it is believed that only one component of such foods is responsible for the effect). Isolated fibre types should not be used in such disease-related intervention studies until their effects have been appropriately modelled in laboratory studies and acute physiological experiments with human participants.

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Graphical abstract

	Acute effects	Long-term effects		
Mouth	Organoleptic quality	Food choice development	Regulation of mucosal action	Health maintenance
	Saliva production			
	Bolus formation			
Oesophagus	Swallowing			
	Motility			
Stomach	Mixing			
	Secretion			
	Emptying			

Highlights

- Dietary fibre's presence can affect foods' organoleptic quality, the process of swallowing and gastric secretion mixing and emptying.
- Dietary fibre can alter the rheological properties on gastrointestinal contents and access of chemosensors to other dietary factors.
- Consumption of higher amounts of fibre-rich plant foods is generally associated with reduced risk of upper gastrointestinal mucosal disease.
- "Added fibres" and inherent dietary fibre may not have comparable effects.

Queries and Answers

Query:

Please confirm that given name and surname have been identified correctly.

Answer: I can confirm this

Query:

The references given here and elsewhere are cited in the text but are missing from the reference list – please make the list complete or remove these references from the text: "Chen (2011)", "Furness (2000)" and "Little et al. (2007)".

Answer: "Chen (2011)" should be "Chen (2009)".

"Furness (2000)" relates to the following article:

Furness J.B. Types of neurons in the enteric nervous system, *Journal of the Autonomic Nervous System* **81** (1-3), 2000, 87-96.

"Little et al., (2007)" relates to the following article:

Little T.J., Russo A., Meyer J.H., Horowitz M., Smyth D.R., Bellon M., Wishart J.M., Jones K.L. & Feinle-Bisset C. {A figure is presented}Free Fatty Acids Have More Potent Effects on Gastric Emptying, Gut Hormones, and Appetite Than Triacylglycerides *Gastroenterology* **133** (4), 2007, 1124-1131.

Query:

The spelling of the author name(s) in the text has been changed to "Hellström, Grybäck, and Jacobsson (2006)" to match the reference list. Please check the spelling, and correct if necessary.

Answer: The spelling suggested by the Editors is correct and should be used both in-text and within the reference list.