Does wheat make us fat and sick?

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1. Introduction

Wheat is the most widely cultivated cereal grain worldwide, being grown in temperate climates from Scandinavia in the north to Argentina in the south, including upland regions in the tropics. It is third among the cereals, behind maize and rice, in total global production, which was 704 million tons in 2011. The demand for wheat for human consumption is also increasing globally, including in countries which are climatically unsuited for wheat production, due to the adoption of western-style diets. Wheat is relatively rich in micronutrients, including minerals and B vitamins, and supplies up to 20% of the energy intake of the global population (Cummins and Roberts-Thomson, 2009).

About 95% of the wheat that is grown and consumed globally is bread wheat (\textit{Triticum aestivum}). Bread wheat is a relatively new species, having arisen in southeast Turkey about 9000 years ago (Feldman and Millet, 2001). It is hexaploid with three related genomes (termed A, B and D) and probably arose by spontaneous hybridization between a cultivated form of tetraploid wheat (\textit{Triticum turgidum}) and a related wild grass species (goat grass, \textit{Aegilops tauschii}). Most of the remaining 5% of the wheat crop is tetraploid durum wheat (\textit{T. turgidum} var \textit{durum}) which is more adapted to the dry Mediterranean climate. However, small amounts of “primitive” wheats are also grown, mainly for specialist health foods: einkorn (diploid \textit{Triticum monococcum}), emmer (tetraploid \textit{T. turgidum} var \textit{dicoccum}) and spelt (hexaploid \textit{T. aestivum} var \textit{spelta}). The latter essentially differs from bread wheat in that the hull is not removed by threshing; resulting in a higher fibre content when consumed as whole grain.

Although wheat is a young species, it is immensely diverse, with forms adapted to a wide range of local environments and selected for different end uses. Feldman et al. (1995) estimated that at least 25,000 genetically distinct forms occur, but this is undoubtedly an underestimate with previously unreported diversity being described in recent years in countries such as China. Determination of the full genome sequence of bread wheat has been hindered by the massive genome size (17 gigabases, which is 40 times the size of...
the rice genome and 5 times the size of the human genome) and the hexaploid nature. However, a recent study identified 96,000 to 98,000 genes, many of which were assigned to the three genomes (Brenchley et al., 2012). The large genome size, with a high content of mobile elements, and the hexaploid nature have, however, also resulted in high genome plasticity, which has facilitated rapid adaptation and contributed greatly to the global success of the wheat crop (Dubcovsky and Dvorak, 2007).

The wheat grain contains many hundreds of individual proteins, which may have structural, metabolic, protective or storage functions (as reviewed by Shewry (2009)). They include the gluten proteins, which are the major storage components and may account for up to 80% of the total grain protein (Wrigley et al., 1988). The protein composition of the grain is determined by the genotype, but also strongly influenced by the environment (climate and agronomy). For example, the contents of protective proteins may be greater when the plant is subjected to heat or drought stress while the total content of gluten proteins and the proportions of different gluten protein components are influenced by the availability of mineral nutrients (nitrogen and sulphur) (Shewry, 2011).

Several popular nutritional plants, such as the Paleolithic diet (Cebb, 2012; Johnson et al., 2006, 2005; Rose, 2011) and more recently the proposal of the U.S. cardiologist W.R. Davis, in his recent bestseller book, Wheat Belly (2011), have suggested that (whole-)wheat consumption has adverse health effects, based on different and controversial hypotheses. With this, they follow a recent trend to pinpoint the cause of obesity to one specific type of food or food component, rather than to overconsumption and inactive lifestyle in general. Hence, following discussions on the roles of fat, fructose, high fructose corn syrup and added sugar in foods, it seems that it is now the turn of wheat to take the blame for obesity. These discussions fail to take into account that obesity has a multifactorial causation (Grundy, 1998; Keith et al., 2006).

For centuries, there have been populations who consume wheat-based breads and other wheat products as the main source of their energy intake, such as in Turkey, without indices of causing weight gain. Moreover, the consumption of whole grain products, which in the U.S. and Europe are mainly based on wheat, has been shown to be associated with reduced risks of type 2 diabetes, cardiovascular disease, some types of cancer as well as a more favourable weight management (Ye et al., 2012). It is also argued that the current worldwide wheat production consists of “genetically modified” varieties, which contain new components that cause adverse health effects. In reality, the presence of such new components is not supported either by comparative studies of old and recently bred types of wheat (Ward et al., 2008) or by analyses of genomic sequences (Brenchley et al., 2012). Moreover, hard data about adverse effects of wheat, consumed in baked, extruded, and other processed foods, are not available, and there are no grounds to advise the general public not to consume this common dietary staple. Only individuals with a genetic predisposition for celiac disease, or suffering from allergy or other forms of sensitivity to gluten and other wheat proteins, will benefit from excluding wheat and related cereals from their diet.

2. Materials and methods

To ensure the quality of the research, and to obtain transparent and reproducible results, we made use of certain guidelines. In our search strategy, we used several databases of controlled scientific articles. All articles are referred to in the text and are available in English. We discuss most the relevant articles and critically evaluate the data. We also consider the scientific evidence for possible mechanisms based on recent literature.

3. Discussion

In a recent interview (CBS, 2012), the cardiologist W.R. Davis discussed his recent bestselling book: Wheat Belly: Lose the Wheat, Lose the Weight, and Find Your Path Back to Health (Davis, 2011). The author stated that the wheat that we eat these days is “created by genetic research in the 60s and 70s” leading to the inclusion of an unnatural protein in our “modern wheat” called gliadin. When coming to a conclusion, Davis explained that everybody is ‘susceptible’ to this gliadin protein as “gliadin binds into the opiate receptors in your brain and in most people stimulates appetite, such that we consume 440 more calories per day, 365 days per year’.

In this light, it should be noted that gliadins are present in all wheat lines and in related wild species (Goryunova et al., 2012). In addition, seeds of certain ancient types of tetraploid wheat (e.g.; Graziella Ra, Khorasan wheat/Kamut) have even greater amounts of total gliadin than modern accessions (Colomba and Gregorini, 2012). Moreover, although the genetic engineering of wheat is technically possible, it has only been used in research programs and “GM wheat” has not been marketed or grown commercially in any country. However, it could be argued that wheat has been “genetically modified” by plant breeding in the same way that other crops and livestock species have been improved by selective breeding. Because bread wheat arose in cultivation, rather than from domestication of a wild species, it has probably been subjected to selection for the whole of its 9000 year history, initially subconsciously by early farmers and later (over the past century) by the application of scientific breeding. This has exploited variation controlled by endogenous wheat genes, resulting particularly from the high genome plasticity, with the limited use of related species to transfer useful traits. The main traits selected have been high yield, good resistance to pests and pathogens and good processing properties (for bread, cookies, noodles and, in durum wheat, pasta).

There is no evidence that selective breeding has resulted in detrimental effects on the nutritional properties or health benefits of the wheat grain, with the exception that the dilution of other components with starch occurs in modern high yielding lines (starch comprising about 80% of the grain dry weight) (Shewry et al., 2011). Selection for high protein content has been carried out for bread making, with modern bread making varieties generally containing about 1–2% more protein (on a grain dry weight basis) than varieties bred for livestock feed when grown under the same conditions (Monaghan et al., 2001; Snape et al., 1993). However, this genetically determined difference in protein content is less than can be achieved by application of nitrogen fertilizer (Godfrey et al., 2010).

We consider that statements made in the book of Davis, as well as in related interviews, cannot be substantiated based on published scientific studies. For the sake of brevity, we focus on four of these arguments which we consider are most relevant to the present discussion (other critical remarks are listed by Jones (2012)), while further expanding on sound nutritional and cereal science.

“The proliferation of wheat products parallels the increase in waist size”

This statement implies that a correlation between two variables can be interpreted as a true causal relationship. It is certainly true that the increase in wheat sales has a parallel with an increase in obesity. However, there are also parallel increases in the sales of cars, mobile phones, sports shoes and the average speed of winners of the Tour de France. Similarly, a correlation between the national consumption of chocolate and the number of Nobel Prize winners has been reported (Messerli, 2012).
However, it is not valid to consider these correlations as causal relationships, and in the examples listed above any such claim would be ridiculed. Moreover, the proliferation of wheat products has a much longer history than the much more recent drastic increases in occurrence of obesity, which has also occurred in populations that eat little wheat, such as several Asian countries (Yoon et al., 2006).

“...starch in wheat is different from that found in other carbohydrate-rich foods such as bananas, potatoes and vegetables. The amylopectin structure allows it to be very efficiently converted to raise blood sugar” (undesirably).

The starch present in all plant tissues (including grains and some vegetables and fruits) is a mixture of two polymers of glucose, amylopectin and amylose. Amylose has a linear chemical structure and is relatively slowly digested while amylopectin has a more branched structure and is more rapidly digested. With the exception of mutant lines, the ratio of the two polymers varies little, being about 20–25% amylose and 70–75% amylopectin (Hoover and Zhou, 2003). Mutant lines include waxy lines which comprise almost 100% amylopectin. Some waxy lines are grown commercially (notably waxy rice) but not waxy wheat. Furthermore, the ratio of amylose to amylopectin is generally not the decisive factor for an effect on the blood sugar level. It is also necessary to take into account other nutritional factors such as prior meals, the content of fat, protein and fibre in the meal as well as the matrix of the food product/meal. There are also large differences between carbohydrate-rich foods that easily fall apart in an aqueous environment, such as white bread, and therefore are readily accessible to digestive enzymes and foods that have a more solid and compact matrix, such as pasta, macaroni and spaghetti which are digested less rapidly (Juntunen et al., 2003). A study reported by Riccardi et al. (2003) tested different foods to show that composition, preparation and food matrix influence glycemic response significantly, as depicted in Fig. 1. However, the blood glucose response after bread consumption was lower than the response after eating the same amount of potatoes or white rice (reflected in the corresponding GI values (Foster-Powell et al., 2002)), which refute the suggestion that starch from wheat generally leads to a higher glycemcic response.

“Whole-wheat bread has a Glycemic Index (GI) of 72, which is higher than that of sugar (GI = 59)”

This statement may lead to the perception that, based on GI, consuming sugar is better for your health than eating wheat. For clarification, the GI is a measure of blood glucose response and is expressed as an index comparing the consumption of a particular food to the blood glucose response after intake of 50 g of glucose. Since sugar (sucrose) consists of 50% glucose (GI = 100) and 50% fructose (GI = 27), the GI of sugar, contrary to what many people think, is relatively low. The internationally accepted average GI of sucrose is not 59, as Davis indicates, but 67 (Foster-Powell et al., 2002). This value is very close to the GI of white wheat bread, which has a range of 69–73, with a mean of 70 (mean of 7 studies (Foster-Powell et al., 2002)). Furthermore, whole-wheat bread has a slightly lower GI of 65.9 (mean of 8 Canadian studies (Foster-Powell et al., 2002)). In fact, the amount of a particular carbohydrate eaten x the GI, expressed as the glycemic load, is much more meaningful than the GI value alone. The statement above therefore misinterprets the background to the GI methodology (Brouns et al., 2005) as well as the related digestive and metabolic mechanisms.

“Wheat opioids are so addictive that they cause people to be unable to control their eating, and removal of wheat from the diet causes withdrawal”.

There are no data available to substantiate this suggestion. The gluten storage proteins of wheat belong to a broader class of proteins with closely related forms being present in closely related species (rye and barley) and less closely related forms in other cereals (oats, millets, sorghum, corn and rice). Gluten proteins are also present in the “primitive” wheat species discussed above: einkorn, emmer and spelt. Gluten proteins are classically divided into two fractions, the gliadins which are present as monomers and the glutenins which are polymeric. Incomplete digestion of gliadin has been shown to release a peptide, called gliadorphin, that can induce opiate like effects, as demonstrated in laboratory tests in rats that were infused with the intact peptide (Sun and Cade, 2003). However, gliadorphin consists of seven amino acids (Tyr-Pro-Gln-Pro-Gln-Pro-Phe) and, as such, cannot be absorbed by the intestine. This is because the intestine peptide transporter PepT1 transports only di- and triptides (Gilbert et al., 2008) and transporters for larger peptides have not been identified. Gliadorphin is therefore not present in intact form in the human circulatory system and cannot reach and have an effect on the cells of the central nervous system. In this respect, Davis extrapolates effects observed on cells in a laboratory setting to the in vivo situation in humans. There are no studies in which gliadorphin has been shown to be absorbed in intact form by the intestine and no evidence that gliadin either stimulates appetite or induces addiction-like withdrawal effects. The author references a study to support his argument in this respect, but the study referred to did not include actual feeding of any food (Juntunen et al., 2003). By contrast, Giacco, et al. (2011) and Koh-Banerjee et al. (2004) concluded that regular consumption of whole grains was negatively correlated with weight gain. These authors described 14 cross sectional studies, most of which were performed in the USA, in which higher intake of whole grains was correlated with a lower body mass index (BMI). In addition, they presented three studies in which a significantly lower waist circumference was noted. The argument that refraining from consumption of wheat in the daily diet induces weight loss should also be interpreted in the light of the fact that a very limited number of foods available in the market do not contain wheat. This limited availability of wheat-free foods may itself cause consumption monotony, leading to reduced overall intake of food and energy. The latter will result in weight loss, which will improve (type 2) insulin sensitivity and diabetic state, a dieting-related phenomenon which occurs during virtually all popular diet interventions.
4. Gluten sensitivity

Very recently, Soares et al. (2013) fed mice an *ad libitum* high-fat diet to induce obesity. The mice were divided into a control group, containing no gluten, and a group receiving 4.5% wheat gluten, for 8 weeks. The high-fat diet was composed of 25%, 61% and 15% of the total energy from carbohydrate, fat and protein, respectively. As the diet composition (excessive fat and low carbohydrate) was not representative for the human diet, and there was no control group in which the added gluten was exchanged for another isolated protein type, to assure out that the effects observed were gluten specific effect rather than a general protein content effect, we feel that it is premature to follow the authors conclusion that gluten exclusion helps in reducing body weight and that it can be a new dietary approach to prevent the development of obesity and related sickness in the general human population. Such statements on the adverse effects of gluten-containing (whole-)wheat are diametrically opposite to the observations that the consumption of whole grain and whole grain fibre significantly improves blood glucose control, improves cholesterol levels, reduces blood pressure and lowers the serum concentration of high sensitivity C-reactive protein, a marker of low grade inflammation (Gaskins et al., 2010; Jenkins et al., 2007; Masters et al., 2010; Qi et al., 2006; Raninen et al., 2011). These observations all indicate improvement in overweight related metabolic dysregulation (syndrome X) and have been attributed largely to the fibre (β-glucan and arabinogalactan) and phytochemicals (phenolics, sterols, tocols and vitamins) that are concentrated in the aleurone layer of the bran (Brouns et al., 2011) as well as present in the wheat germ fraction. These compounds, as depicted in Fig. 2 (adapted from Barron et al., 2007), are thought to exert synergistic effects on specific health-related metabolic processes (Fardet, 2010).

Recently, Björck, et al. (2011) summarized the findings of the HEALTHGRAIN project supported by the European Commission which included 26 academic research centres. They concluded that in well-controlled studies a negative correlation was observed between the circulating levels of short-chain fatty acids (SCFA) resulting from grain fibre fermentation in the colon and improved insulin sensitivity and glucose homeostasis. As a consequence, insulin production at a certain carbohydrate load was favourably reduced. This points to important effects of components that are either not present, or only present in insignificant amounts in white wheat flour, but are present in whole wheat and whole grain flour. In this respect, it is also noteworthy that the digestion and metabolism of whole grain goods induces significantly different effects on insulin-, incretin- and satiety hormone responses compared to the consumption of refined (white flour based) wheat bread (Juntunen et al., 2003).

Hauner et al. (2012), summarized the evidence on carbohydrate intake and focused on the relation between wheat and nutrition-related diseases. The authors conclude that the evidence regarding the relevance of refined grain and whole-grain product intake for the risk of obesity is judged as insufficient. Moreover, they conclude that existing cohort studies show a possible relationship between whole-grain product intake and a reduced risk of obesity, a probable relationship with a lower risk of diabetes (see also: de Munter et al., 2007) and coronary heart disease, and a convincing relationship with a reduced level of LDL cholesterol. In addition, Aune, et al. (2011) concluded that the intake of dietary fibre from cereals and other whole grains is associated with a reduced risk of colorectal cancer.

Although the studies discussed above indicate that whole grain consumption has health benefits, it should also be noted that part of the population cannot tolerate wheat or other cereals containing related proteins, particularly those suffering from celiac disease. CD is a genetically predisposed condition (Catassi and Fasano, 2008; Fasano and Catassi, 2001) and results from an autoimmune response initiated by the binding of modified gluten peptides to T-cells of the immune system. The presented peptides are then recognized by specific CD4+ T cells which release inflammatory cytokines leading to damage of the gut villi. Individuals carrying HLA-DQ2 or HLA-DQ8 as major genetic predisposition are affected, representing ~1% of the population. Rubio-Tapia et al. (2009) concluded that the prevalence of CD in the United States was 0.71% (1 in 141), similar to that found in several European countries (Mustalahl et al., 2010).

Very recently, gluten sensitivity has been defined as a new etiologically heterogeneous syndrome in which environmental factors may play a role in addition to that of food (Biesiekierski et al., 2011; Carroccio et al., 2012a; Di Sabatino et al., 2012; Pietzak, 2012). Other data shows that gluten sensitivity occurs in approximately 30% of the people suffering from irritable bowel syndrome (IBS). Given the prevalence of IBS in most countries, 10–15% (in some countries >30%) (Carroccio et al., 2012b; Verdu et al., 2013).
flamylase inhibitors, serpin (serine proteinase inhibitor), acyl-}

addressing wheat gluten sensitivity (Biesiekierski et al., 2010), a re-

mains underlying gluten sensitivity. Patients who were not

about 0.3–3.0% in adults and children. Wheat grain proteins are

As measured by urinary lactulose/mannitol test). In the only

in vivo

The very recent studies of Schuppan et al. (2012) and Junker

patients with irritable bowel syndrome in whom celiac disease was excluded and who were

maining on allergy and intolerance to wheat is also warranted,

ATIs are accumulated to suf

The recent development of commercial high yielding varieties of oats

Preliminary studies showed that neither gliadin which had been

digested in vitro with trypsin and pepsin nor the celiac-active peptide

31–43 from α-gliadin elicited innate immune responses in

intestinal epithelial cells. The pepsin-trypsin digested gliadin

(but not p31–43) did strongly activate inflammatory responses

but this activity was due to the presence of contaminating ATIs.

These findings identify cereal ATIs as novel contributors to celiac
disease. Moreover, the authors suggest that ATIs may fuel inflam-
mation and immune reactions in other intestinal and even non-

intestinal immune disorders (Junker et al., 2012). This clearly

warrants further research to unravel oral tolerance and gut disease

related mechanisms. However, the existence of many anecdotal

patient reports should not be ignored due to lack of scientific data

evidence, but used as a basis for well-designed studies and

with more specific biomarkers.

In this respect, some medical doctors advise those who suffer

from physical complaints that cannot be explained on the basis of

routine medical testing (no physical cause can be established) to

request a gluten sensitivity test and/or to refrain for several weeks

from consuming gluten-containing foods to see whether their

symptoms (such as sensitive intestinal system, gastrointestinal

distress, bloating, rumbling, colic, chronic fatigue, poor concen-

tration, ADHD, frequent headache, migraine, repeating episodes of

loose stools of diarrhoea and arthritis) disappear.

5. Conclusion

Although the adverse effects of wheat on some individuals

should not be ignored, five major recent scientific reviews ad-

ressing the impact of cereal consumption on health and disease

concluded that the consumption of whole grains, of which globally

most widely consumed is wheat, generally exerts positive effects on

health, thus recommending increased intake of whole grain for the

general public, in exchange for refined foods (Björck et al., 2011;

Fardet, 2010; Hauner et al., 2012; Jonnalagadda et al., 2011).

Wheat-containing foods prepared in customary ways and eaten

in recommended amounts have been associated with numerous

health benefits. In particular, the regular consumption of whole-

grain products has been shown to be associated with significant

reductions in risks for type 2 diabetes and heart disease and more

favourable long term weight management. These findings are

supported by the outcome of a recent cohort, where it was

observed that individuals who consumed recommended amounts

of (whole)-wheat had the least amount of visceral fat accumulation

(Molenaar et al., 2009). Arguments that the currently consumed

wheat has been genetically modified resulting in adverse effects on

body weight and illnesses cannot be substantiated. In particular,

populations in some countries have obtained the major part of their

daily energy intake from wheat-based foods for many years, such as

Turkey, without reporting any detrimental effects on body weight

or chronic disease. In line with this is the evidence that grains and

grasses have already been consumed and processed throughout

Europe during the Mid–Upper Palaeolithic era (Revedin et al.,

2010). However, individuals who have a genetic predisposition for

developing celiac disease or who are sensitive to gluten and/or

allergic to wheat will benefit from avoiding wheat and other cereals

containing related proteins, including primitive wheats (einkorn,

emmer, spelt), rye and barley. It is important that the food industry

should be developing a much wider spectrum of foods for this

section of the population, based on crops that do not contain pro-

teins related to gluten, such as teff, amaranth, oat, quinoa, chia. The

recent development of commercial high yielding varieties of oats

(considered safe for those suffering from intolerance to gluten)
is an important step in this respect. Further research and
development on allergy and intolerance to wheat is also warranted,
with various strategies being proposed to reduce exposure to gluten (Gilissen et al., 2012; Shewry et al., 2012). These include the reduction of (celiac) immunogenic epitopes in existing foods/grains that contain gluten, the production of guaranteed safe, gluten-free foods for patients with celiac disease and gluten intolerance and increasing the production of foods based on crops that do not contain proteins related to gluten. Since about 1% of the current population of Europe and the U.S. the population suffers from celiac disease and probably 5–10% from gluten sensitivity (due to difficulties to diagnose this condition, the real number may even be higher), these strategies will have both global economic and public health impacts.

Conflict of interest

The authors declare to have no conflict of interest.

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