4.3 Food-related strategies towards reduction of gluten intolerance and gluten sensitivity

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Around 1 % of the Western population suffers from coeliac disease (CD), a food-related inflammatory disorder of the small intestine caused by the ingestion of gluten in genetically predisposed individuals. This prevalence is still increasing [1,2]. Recently, a new and less well defined gluten (or wheat) related syndrome has emerged that seems to be unrelated to coeliac disease, named gluten sensitivity (GS). The so-called 'gluten-free diet' appears to improve significantly the health condition of these GS patients. In some studies, a direct correlation was found with gluten consumption [3], whereas other authors pinpoint on protein compounds that are co-extracted with gluten, such as amylase trypsin inhibitors (ATIs) [4]. The prevalence of GS is estimated at 5 - 10 % of the western population [5], but a clear definition is lacking, and no biomarkers and epidemiological data are available as well to confirm this percentage anyhow. However, the fact that the gluten-free market goes mainstream and is growing to several billion Euro sales annually reflects a steady trend that goes beyond coeliac disease [6].

The major difference between CD and GS is in the small intestine where cases of GS do not show the CD-specific villous atrophy. Other symptoms of CD and GS are similar and are highly diverse in both, including chronic abdominal pain, diarrhoea, and growth retardation in children, and chronic fatigue and headache, bowel complaints, reduced fertility, dermatitis herpetiformis, osteoporosis, nerve and brain (behaviour) disorders, increased risk of intestinal cancer in adults, to mention the most common ones. This wide variety of symptoms largely hampers good diagnosis. As a result, only 10 - 20 % of the CD population has been properly diagnosed, as will also be an unknown but possibly minor fraction of the GS population. This implies that the vast majority of the individuals with CD and GS are unaware of their disease. They continue their daily consumption of large amounts of gluten and worsen their health status and health perspectives, which is a major concern.

The high food industrial qualities of wheat gluten have led, in recent decades, to a steady increase in its food-industrial applications. A survey in Australia of more than 10,000 supermarket items detected wheat in almost 30 % of labelled products [7]. In some of these products, the connection to wheat was visible and even proactively

marketed; in other products, it was invisible. The latter group consisted not only of processed foods, but also foods that are not commonly associated with wheat, such as canned vegetables, milk, meat and even seafood and medicines; obviously, a big problem for individuals with CD and GS. Therefore, because of the apparent increase in the prevalence of wheat- and gluten-related symptoms, new applications of wheat gluten (in natural or modified forms), particularly in non-cereal-based food products should be considered deliberately, and the current use of wheat and gluten in saleable foods should be re-evaluated. Labelling of packed food products (according to Directive 2003/89/EC) [8] is helpful, but only for diagnosed individuals. As mentioned, these form only a minority of the patients.

This creates a challenge. The question now arises how the food industrial quality of wheat and its gluten can be maintained while reducing or, even better, eliminating negative health effects.

Two strategies can be put forward:

1. Reduction of (coeliac) immunogenic proteins in regular wheat- and gluten-containing foods. As the induction of CD appears to be related to, amongst others, the dose of exposure to gluten-derived epitopes, we assume that every reduction in the consumption of harmful (CD-immunogenic) gluten will contribute to a general reduction of the prevalence of the disease(s) and of symptom severity in the population. This will, therefore, in time, benefit the general population, including the non- and wrong-diagnosed groups of CD and GS individuals.
2. Production of guaranteed safe and healthy foods for individuals that are already diagnosed with CD and have to follow a life-long gluten-free diet. Such food products will also be of benefit for people with GS.

Strategy 1 can be performed in two ways:

a) The systematic application of well-characterised low CD-immunogenic wheat varieties, which are currently under development [9,10] (Fig. 1). To achieve this goal, low CD-immunogenicity with regard to coeliac disease epitopes should become an additional wheat breeders' aim. The currently developed immunological and molecular (e.g. deep 454-sequencing of expressed gluten genes, Fig. 2) tools for quantification of toxicity and for molecular marker-assisted breeding (Salentijn et al., in preparation) will be very helpful in the development of low CD-immunogenic wheat varieties. Until being mainstream, such varieties will need to be processed in separate and strictly controlled production lines. This is a long-term approach.

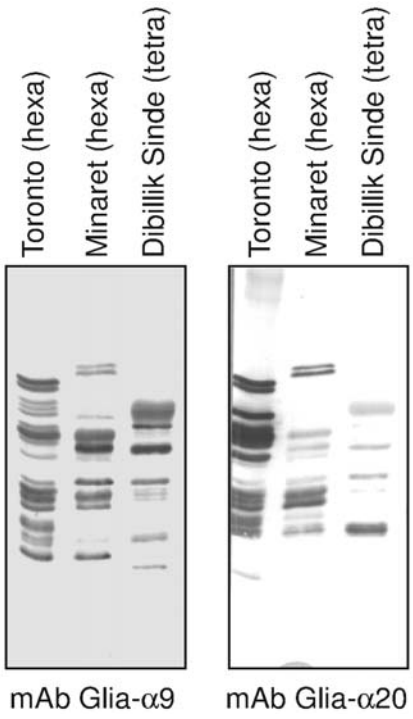

Fig. 1. *Low toxic wheat (tetraploid accession Dibillik Sinde and hexaploid variety Minaret compared to variety Toronto)*

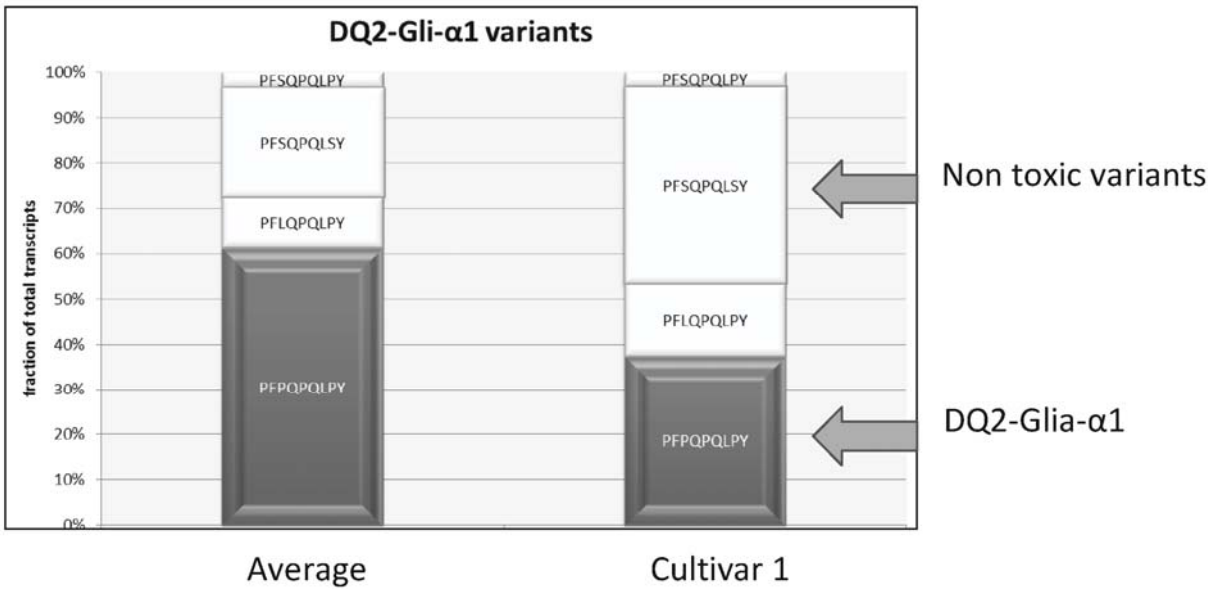

Fig. 2. *Deep sequencing*

b) The general reduction of gluten in food products, comparable to the current goals of reduction of salt, fat and carbohydrates. This may include the development of technologically more efficient but less toxic gluten. With regard to industrial and technological quality characteristics, the glutenin component of gluten is much more relevant than the gliadin component. As the gliadins contain most of the coeliac disease epitopes, separation of specifically the glutenin fraction from the gluten may

result in an economically and technologically profitable product with significantly reduced CD immunogenicity (van den Broeck et al. in preparation) (Fig. 3). This approach requires a change in the current industrial gluten production.

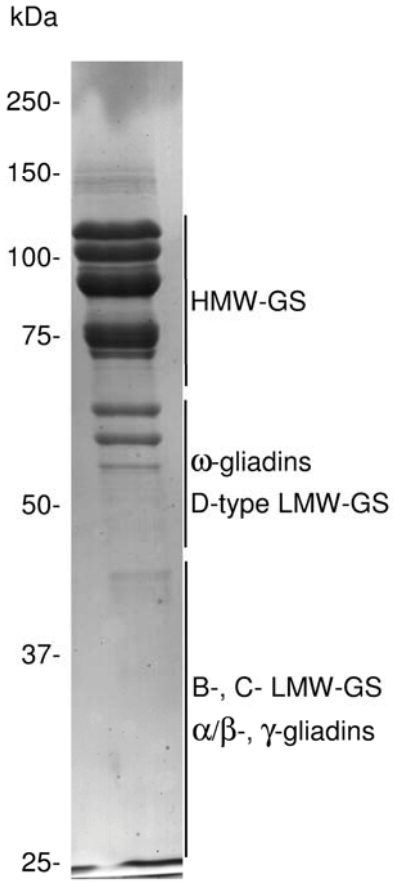

Fig. 3. *Electrophoresis of 10 µg HMW-GS isolated from gluten of bread wheat variety Bussard*

Strategy 2 may include:

a) The application of alternative processing techniques that eliminate (break down) the CD epitopes, such as sourdough fermentation [11,12].

b) The production of completely safe gluten proteins, either recombinant or by processing, based on currently gained knowledge on the elimination of the toxic fragments (Fig. 4) [13,14].

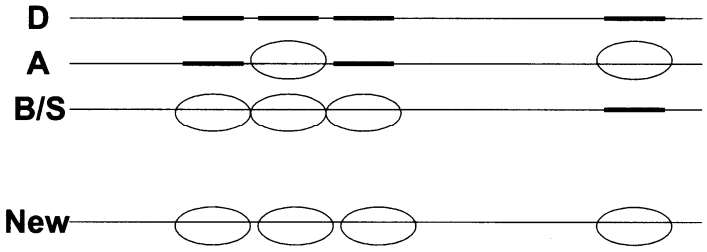

Fig. 4. *Schematic diagram of a new non-immunogenic gluten gene [14]*

c) Alternative cereals which are safe and also may provide sufficient technological properties. Among these cereals, oats are currently the best possible replacement for wheat, rye and barley. According to EC Regulation 41/2009 [15], oat products containing less than 20 ppm gluten are now allowed to be sold as gluten-free. In addition, oats contain many healthy components (especially beta-glucans) and thus can serve as an important supplement to the patient's daily diet. Although a very low minority of CD patients may be sensitive to oats, several CD-patient societies in Europe promote the opportunistic approach: just try, and introduce oats in your diet gradually. One of the most beloved oat products may become the gluten-free oat bread. This requires new baking technologies and recipes (Londono et al., in preparation) (Fig. 5). Currently, the first generation of pure oat bread is on the market in The Netherlands (www.broodpakket.nl)

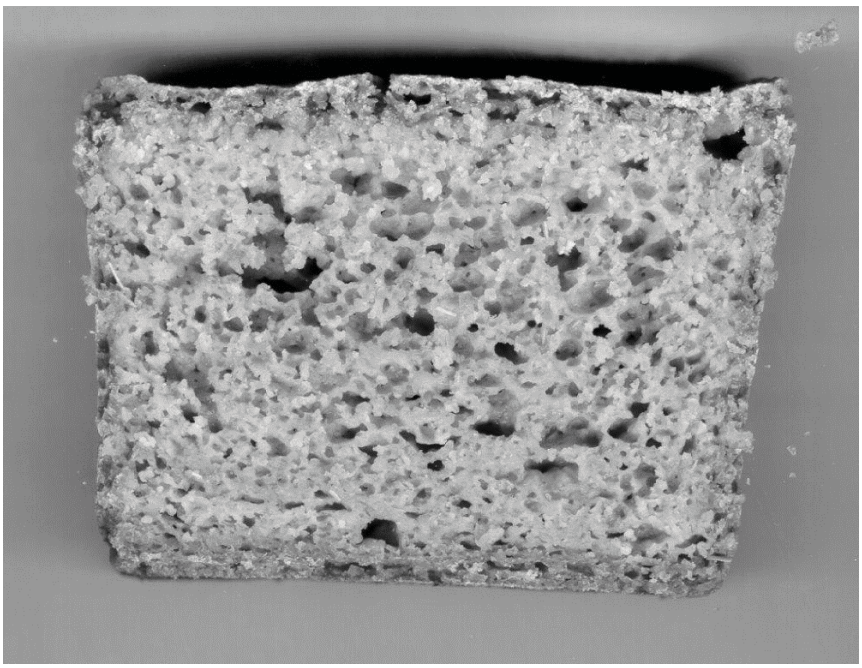

Fig. 5. *Oat bread*

In conclusion, a variety of alternative strategies are under development to lower the level (the burden) to the consumers of gluten in foods in general, as well as to eliminate CD-immunogenic epitopes in particular, aiming at significantly fewer and less severe cases of CD and GS.

Acknowledgements

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