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REVIEW ARTICLE

What is gluten?

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Abstract

Gluten is the main storage protein of wheat grains. Gluten is a complex mixture of hundreds of related but distinct proteins, mainly gliadin and glutenin. Similar storage proteins exist as secalin in rye, hordein in barley, and avenins in oats and are collectively referred to as "gluten." The objective was to discuss the biochemical and functional properties of the gluten proteins, including structure, sources, and dietary intakes. Literature was reviewed from food science and nutrition journals. The gluten protein networks vary because of different components and sizes, and variability caused by genotype, growing conditions, and technological processes. The structures and interactions of this matrix contribute to the unique properties of gluten. The resulting functions are essential to determining the dough quality of bread and other baked products. Gluten is heat stable and has the capacity to act as a binding and extending agent and is commonly used as an additive in processed foods for improved texture, moisture retention, and flavor. Gliadin contains peptide sequences that are highly resistant to gastric, pancreatic, and intestinal proteolytic digestion in the gastrointestinal tract. The average daily gluten intake in a Western diet is thought to be 5–20 g/day and has been implicated in several disorders. Gluten containing grains (wheat, rye, barley, and oats) are important staple foods. Gluten is among the most complex protein networks and plays a key role in determining the rheological dough properties.

Introduction

Wheat is one of world's major food crops, cultivated, consumed, and traded worldwide. The common wheat species (*Triticum aestivum* L.) is often used to describe many other cultivated wheat species and genotypes.

The wheat kernel contains 8%–15% of protein, from which 10%–15% is albumin/globulin and 85%–90% is gluten (Fig. 1).[1] Gluten is a complex mixture of hundreds of related but distinct proteins, mainly gliadin and glutenin. Different wheat varieties vary in protein content and in the composition and distribution of gluten proteins.[1] Collectively, the gliadin and glutenin proteins are referred to as prolamins, which represent seed proteins insoluble in water, but extractable in aqueous ethanol and are characterized by high levels of glutamine (38%) and proline residues (20%).[1]

The gluten proteins can be classified into subgroups dependent on key differences including sulfur content and molecular weight and then further classified according to their different primary structures into alpha, beta, gamma, and omega (α, β, γ, and ω) gliadins.[2] Individual gluten proteins are bound by strong covalent and non-covalent forces, which, together with the structure and interaction of these proteins, contribute to the unique properties of gluten.[2]

Gluten properties and sources

The gluten matrix and its resulting functions are essential to determining the dough quality of bread and other baked products such as pasta, cakes, pastries, and biscuits. Gluten is heat stable and has the capacity to act as a binding and extending agent and is commonly used as an additive in processed foods for improved texture, flavor, and moisture retention. Therefore, less obvious sources of gluten include processed meat, reconstituted seafood, and vegetarian meat substitutes; and as thickeners, emulsifiers, or gelling agents in candies, ice cream, butter, seasonings, stuffings, marinades and dressings; and as fillers and coatings used in medications or confectionary. In addition, gluten is increasingly separated from wheat (known as "vital wheat gluten") or modified for specific uses (known as "isolated wheat proteins") to improve the structural integrity of industrial bakery products and to fortify low-protein flours.[3]

The unusual rheological and functional properties of gluten are dependent upon the ratio of glutenins to gliadins, and the interactions of these structures. Each component has slightly different functions crucial in determining the viscoelastic properties (entrapment of carbon dioxide released during bread leavening) and quality of the end product. For example, purified hydrated gliadins contribute more to the viscosity and extensibility of the dough, whereas hydrated glutenins are cohesive and contribute to dough strength and elasticity.[1] Much work has focused on improving dough strength, for example, increasing the high molecular weight subunit gene copy number to improve glutenin elasticity.[4]

Similar proteins to the gliadin found in wheat exist as secalin in rye, hordein in barley, and avenins in oats and are collectively referred to as "gluten." Derivatives of these grains such as triticale

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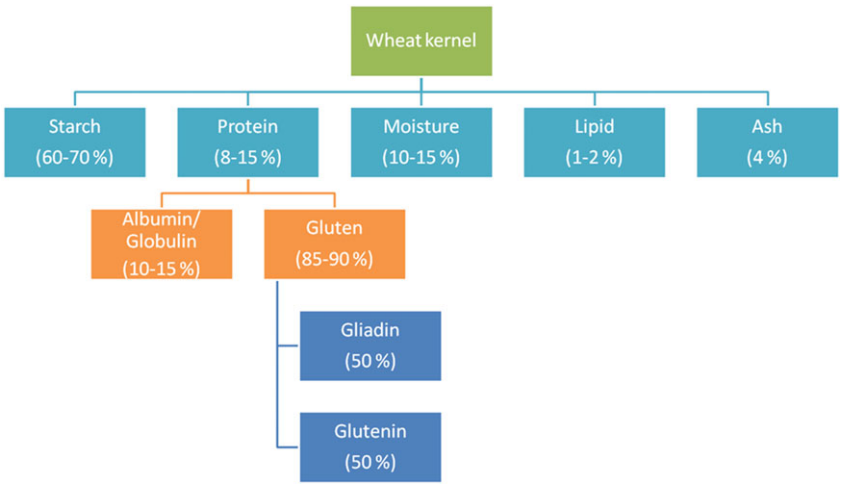

Figure 1 Approximate breakdown of wheat components.

and malt and other ancient wheat varieties such as spelt and kamut also contain gluten. The gluten found in all of these grains has been identified as the component capable of triggering the immune-mediated disorder, coeliac disease.

Structure

Gluten is a very complex compound, characterized by high allelic polymorphism encoding its specific proteins, glutenin, and gliadin. Furthermore, each wheat genotype produces unique types and quantities of these compounds, which can also differ by varied growing conditions and technological processes. The protein (and also carbohydrate) expression of one genotype can change depending on the environment where it was grown, for example, the ω-5 gliadin content increases with fertilization and temperature during maturity.[3] Some of the α gliadins located in the subaleurone of the wheat kernel can be partially removed by roller milling.

Potential toxic components

Gliadin contains peptide sequences (known as epitopes) that are highly resistant to gastric, pancreatic, and intestinal proteolytic digestion in the gastrointestinal tract, escaping degradation in the human gut. This difficult digestion is due to gliadin's high content of the amino acids, proline, and glutamine, which many proteases are unable to cleave.[5] These proline-rich residues create tight and compact structures that can mediate the adverse immune reactions in coeliac disease.

A variety of sequences from α, γ, and ω gliadins, as well as from the glutenins, have been identified to activate coeliac disease. However, several hundred gluten peptides are predicted to be immunogenic and trigger the T-cell mediated response.[6] The most immunodominant T-cell epitope is from α gliadin, although T-cell cross-reactivity against gluten-derived, secalin-derived, and hordein-derived peptides have been confirmed. Additionally, within each grain, there exists a distinct hierarchy of immunostimulatory gluten peptides.[6] Of all the peptides known to stimulate the T-cell response in coeliac disease, a given patient may react to only a few.

Amylase-trypsin inhibitors. Amylase-trypsin inhibitors (ATIs) account for approximately 2%–4% of the total protein in modern wheat (where gluten accounts for 80%–90%). ATIs are albumin proteins, acting as plant defense proteins and have recently been implicated in wheat sensitivity. Some of the ATI fractions have been reported to activate a toll-like receptor-4 dependent pathway leading to the release of pro-inflammatory cytokines from monocytes, macrophages, and dendritic cells derived from both coeliac and non-coeliac patients.[7]

Wheat germ agglutinin. Wheat germ agglutinin is a carbohydrate binding protein (a lectin), found mostly in the wheat kernel. In vitro, wheat germ agglutinin has been shown to have epithelial-damaging and immune effects and, therefore, might also contribute to both intestinal and extraintestinal manifestations associated with gluten intake.[8]

Dietary gluten intakes

Wheat is an important staple food because of its high nutritional characteristics, technological properties, and long shelf life. Wheat is a good source of several nutrients and is a fermentable substrate for the human colonic microflora, which conveys substantial benefits to the host. Wheat can form the basis of all daily meals and is eaten in large amounts worldwide. Information regarding gluten intake in the general population is scarce, because there is a lack of detailed information on the gluten content of food products. Calculations of dietary gluten intakes are approximate as they are normally estimated by calculating the amount of cereal protein within gluten-containing cereals and from recipe information. The average daily gluten intake in a Western diet is thought to range from 5 to 20 g/day, with the most recent data coming from a national Danish survey showing a mean total gluten intake of 10.4 g/day for adults aged 20–75 years.[9]

While wheat-containing bread is one of our major sources of gluten (each slice of bread contains approximately 4 g of gluten), there is some evidence that exposure to gluten may be increasing with changes in cereal technology. Modern baking practices have

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shortened bread leavening, increased the use of chemical/yeast leavening agents, and increased inputs of nitrogen fertilizer and agrochemicals for higher yields of protein content required for bread making.[10]

Gluten-free diet

There is a lack of a consensus definition of the term, "gluten free." Food Standards Australia New Zealand defines gluten free as having no detectable gluten (less than 5 ppm) using the most sensitive and specific testing method and must not contain oats or malt. The Food and Drug Administration in the United States and the International standard, the Codex Alimentarius Commission, define gluten free as the allowable level of gluten detectable to 20 ppm. The Australian Food and Grocery Council has made an application to Food Standards Australia New Zealand to alter the definition to the 20 ppm to be in line with the Codex.

Historically, there has been controversy about the inclusion of oats in the gluten-free diet, because although there is a low rate of avenin-specific T-cell response after oat challenges in certain patients with coeliac disease and reports of oats being tolerated by most,[11] there have also been reports of patients with coeliac disease who are oat sensitive and develop histological damage.[12] Likewise, the safe threshold of gluten consumption for individuals with coeliac disease can vary significantly (10–100 mg/day).

Gluten analysis

The original ELISA is adopted as the official method of detection by the Association of Official Analytical Chemists. The ELISA is able to quantify native and heated gluten but lacks sensitivity to barley prolamins. It can overestimate or underestimate gluten content and cannot accurately quantify hydrolysed gluten. The sandwich R5 ELISA assay endorsed by the Codex Alimentarius can quantify gliadins and hordeins in unprocessed and heat-processed wheat-based and barley-based products and can also estimate the gluten content of hydrolysed foods. As testing methods become increasingly sensitive, manufacturers have raised concerns that many products will no longer meet "gluten-free" labeling criteria.

Gluten (wheat)-related disorders

Evaluation of exclusion diets has historically and consistently shown wheat to be one of the most common factors inducing gastrointestinal symptoms.[13] Specific diagnosis of wheat-related conditions (including wheat allergy, coeliac disease, and the suggested entity of non-coeliac gluten sensitivity) can follow the algorithm shown in Figure 2.

Coeliac disease. Dietary gluten unequivocally causes coeliac disease, an immune-mediated disease that affects about 1% of Western populations. Coeliac disease is the best studied of the spectrum of disorders related to gluten ingestion, whereby the immune response triggered is specific to toxic peptides within the gliadin fraction of the gluten protein and initiates an immune response causing mucosal inflammation, small intestinal villous atrophy, and increased gut permeability. The damage in the small intestine can cause common gastrointestinal symptoms (distension and altered bowel habits) that may or may not relate to malabsorption. There is a genetic disposition where the disease is triggered in susceptible individuals carrying the human leukocyte antigen (HLA)-DQ2 or DQ8.[14] The only known treatment is a lifelong, strict gluten-free diet.

Wheat allergy. Wheat allergy is an IgE-mediated reaction to the insoluble gliadins of wheat. The symptoms usually develop within minutes to hours after ingestion and include itching and swelling, skin rash, and life-threatening anaphylaxis. Symptoms can encompass baker's asthma and rhinitis (from inhaled flour), atopic dermatitis (from skin exposure), urticaria (forming hives after contact with wheat), or wheat-dependent exercise-induced anaphylaxis (when wheat is consumed before vigorous physical activity). An estimated 0.4% of the world's population are allergic to wheat, where the majority of cases are children, and most will outgrow their wheat allergy by age 6.[3]

Non-coeliac gluten sensitivity. While coeliac disease is a well-established entity, much debate remains around whether the gluten proteins can trigger symptoms in patients with no features of coeliac disease, so-called non-coeliac gluten sensitive. Considerable research is needed for confirmation of diagnosis,

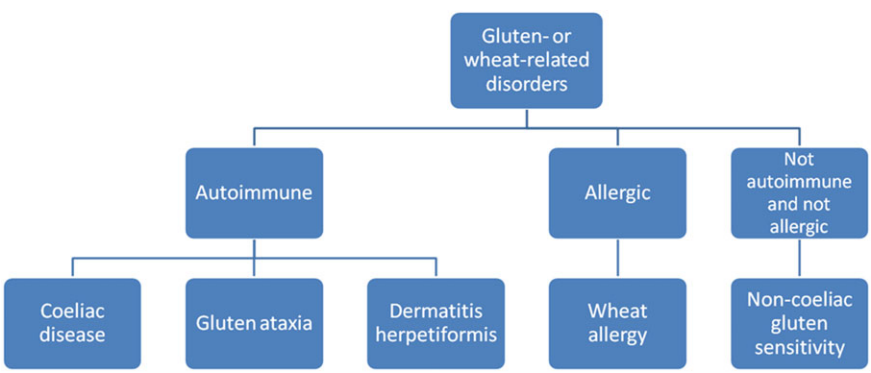

Figure 2 Classification of gluten-related disorders.

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mechanism, prevalence, and management. However, it is likely that this syndrome encompasses a heterogeneous group of patients, reporting a range of gastrointestinal and extraintestinal symptoms, clinical histories and characteristics, and may only exist in a small number of people.[15]

Conclusions

Gluten-containing grains (wheat, rye, barley, and oats) are widely consumed. Gluten is a complex protein network and plays a key role in determining the rheological dough properties and baking qualities. The protein structure can vary dependent on several factors, making analysis and definitions difficult. Coeliac disease and wheat allergy are well-defined disorders associated with gluten (or wheat intake), but further work is needed to completely understand non-coeliac gluten sensitive. Interpreting data from gluten-related and wheat-related studies must be performed with caution and with consideration of all components of wheat, including non-gluten proteins and carbohydrates.

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