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A comprehensive review of biochemical, functional, and dietary implications of Gluten

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Abstract

In wheat grains, gluten serves as a major storage protein comprising a mixture of many related proteins, *i.e.*, gliadin and glutenin. This class of proteins includes storage class proteins such as secalin (rye), hordein (barley), and avenins (oats). The present discussion will therefore address the biochemical and functional features of gluten duly examining their structures, rich sources, and evidence-based dietary implications. This study is based on literature from food science and nutrition journals. The network composition of gluten protein varies depending on genotype, growing conditions, or processing methods resulting in different components and sizes. The complicated structure and interactions contribute to the exclusive characteristics of gluten, thus determining the quality of dough for bread making among other baked products. Due to its heat stability, gluten serves as a binder and is often included as an additive in processed sort of foods to enhance texture, moisture holding, and flavour adding. Gliadin is a constituent of gluten that has peptide strings that are not easily digested in the digestive system comprising of the stomach, pancreas, and intestines. It is estimated that the average daily intake of gluten by individuals living on Western diets ranges between 5 to 20 g, and its consumption has been linked to several conditions. However, grains containing gluten like wheat, rye, barley, and oats will continue to be important food sources. To sum up, gluten is one of the most intricate protein networks that have critical implications for dough's rheological attributes.

1. Introduction

The food business is moving forward, but people's dietary choices and sedentary lifestyles are challenging their health and wellness worldwide. Staple foods like cereals, including wheat, rice, and corn, meet the huge demand from consumers globally. Wheat, in particular, is a primarily cultivated and consumed grain because it is affordable, has viscoelastic properties, and is widely available. However, eating wheat has become problematic, with nutritional issues coming from common disorders (Anania *et al*., 2017). Celiac disease affects about 0.35% to 1% of the population, while other gluten-related disorders impact 1-3% (Aramburo-Gálvez *et al*., 2020). This rising prevalence may be because modern wheat varieties have more gluten and highly processed foods often contain vital wheat gluten or refined forms (Giannou and Tzia, 2016). Wheat gluten, particularly its components gliadin and glutenin, is implicated in various digestive disorders, including celiac disease, wheat allergy, and non-celiac gluten sensitivity. Ingestion of gluten complicates digestion in the stomach and pancreas, leading to these conditions (Biesiekierski *et al*., 2017; Henggeler *et al*., 2017). Diagnosing them is challenging and requires integrating clinical, antibody, and biopsy data (Shiha *et al*., 2023). From 2000 to 2018, worldwide wheat consumption per person steadily declined by 9%, with more people choosing gluten-free (GF) alternatives instead, like pseudocereals, grains, starches, legumes, tubers, and roots. Market reports show substantial growth in the GF products market, with a projected 9.2% compound annual growth rate from 2020 to 2027, reflecting rising gluten-related diseases (Reilly *et al*., 2016).

Moreover, compared to gluten-containing foods, GF foods tend to have more fat, sugar, and sodium but less protein and minerals. The popularity of GF diets and the desire for taste diversity have motivated researchers to develop new GF formulations with functional and nutraceutical properties (Taetzsch *et al*., 2018). Innovative technologies, including modified wheat, detoxifying gluten, inhibiting gliadin, breaking down gluten peptides, and binding gliadin, among others, address these challenges (Juhasz *et al*., 2020). This literature review on gluten-related disorders promotes approaches for GF diets and their therapeutic measures, risk associations, and novel technologies to mitigate potential risks.

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2. History of gluten

Around 10,000 years ago, human civilization began to emerge, creating a need for more food. Evidence shows early farming started in the Fertile Crescent in Southwest Asia around 4000 BC (Harlan and Zohary, 1966). Wild Einkorn wheat was a common grain then, although, it required extra processing due to its coating (Freeman *et al*., 2013). Through hybridization, new wheat varieties with more gluten were developed that were easier to grind. These spread from Turkey worldwide since they grew in diverse climates and seasons (Heun *et al*., 1997). This transitioned humanity from hunter-gatherers to agricultural societies focused on wheat farming. Continuous efforts to alter wheat enabled efficient farming by breeding wheat adapted to extreme weather, with better bread-making and disease resistance. This changed the genetic diversity and potentially immunogenic features of wheat over time, leading to celiac disease antibodies like antitissue transglutaminase and antiendomysial (Van den broeck *et al*., 2010; Ludvigsson *et al*., 2014).

Now, about 95% of wheat grown globally is hexaploid bread wheat (*Triticum aestivum*), from ancient tetraploid and diploid hybridization. Its superior seed size and number made it preferable (Kasarda *et al*., 2013). Recently, extracting gluten from seeds has become common in food processing to improve texture and supplement protein (Dubcovsky and Dvorak, 2007). Cereal consumption, especially wheat, rose steadily over time, partly due to increased production during the World Wars (Copping *et al*., 1978). Currently, more than 700 million tons are produced annually. However, this rapid gluten exposure raises questions about whether our immune systems have adapted optimally, though this theory requires further study. The increasing incidence of gluten disorders suggests reverting to older, less modified grains or reducing gluten intake may be advisable. This article explores the diverse clinical manifestations of gluten disorders and identifies areas for future research (Catassi *et al*., 2005).

3. Epidemiology and economy of gluten-free diets

Consumption of gluten-free foods has increased significantly over the past three decades, with retail spending exceeding $15.5 billion in 2016, more than double the amount in 2011(Statista, 2013). This increase can be attributed to a variety of factors, including extensive news coverage in the media, aggressive marketing by manufacturers, and reports highlighting the health benefits of gluten-free diets (GFDs). While GFD is essential for treating conditions such as celiac disease, gluten ataxia, and wheat allergies, many people without these conditions adopt the diet due to perceived health benefits or concerns about the effects of gluten (Rubio-tapia *et al*., 2013). Research suggests there may be a link between diet and irritable bowel syndrome (IBS) symptoms, with various diets including low-fat, low-carb, gluten-free, and low-fermentable oligosaccharides, monosaccharides and polyols diets showing promise in relieving symptoms (Staudacher *et al*., 2012; De roest *et al*., 2013). Non-celiac gluten sensitivity (NCGS) has become a diagnosis for people who develop irritable bowel-like symptoms after eating gluten-containing foods, even if they do not have celiac disease or a wheat allergy (Unalp arida *et al*., 2017). In addition, healthy people seeking direct health benefits or disease prevention also choose to avoid gluten, which helps increase acceptance of gluten-free diets (Aziz *et al*., 2014). Data shows a significant increase in the number of people avoiding gluten, with a large proportion doing so without a confirmed medical diagnosis. Although, only a small proportion of the population suffers from gluten-related diseases, the prevalence of gluten avoidance has increased dramatically (Lis *et al*., 2015). However, significantly reducing or eliminating gluten-containing foods from your diet may have negative health and financial consequences. Despite widespread interest in gluten-free diets, research in the medical literature on this topic remains limited (Aziz *et al*., 2016; Lionetti *et al*., 2017).

4. The chemical structure of gluten and proteins

Gluten, a continuous and viscoelastic network that emerges throughout the mixing process, plays a crucial role in determining the quality of dough and bread. It is composed of two primary categories of proteins: Alcohol-soluble gliadins and alcohol-insoluble glutenins (Figure 1). These proteins are distinguished by their elevated levels of glutamine, glycine, and proline, alongside minimal quantities of charged amino acids. In essence, gluten can be likened to a ‘two-component adhesive,’ where gliadins serve as plasticizers for glutenins (Sivam *et al*., 2010). Gliadins predominantly enhance dough viscosity and extensibility, while glutenins offer toughness and flexibility (Wieser *et al*., 2007). Gliadins, as monomeric proteins are classified into three sets (α-,β-, γ-, and ω-gliadins) depending on their mobility in gel electrophoresis under acidic conditions (Barak *et al*., 2015). They differ in their molecular weight and the creation of disulfide bonds. For example, ω-gliadins do not contain cysteine and do not establish disulfide bonds, comprising repetitive sequences abundant in glutamine and proline (Tatham *et al*., 1985). Conversely, glutenins are polymeric proteins with molecular weights spanning from 500 kDa to 10 MDa. They encompass low molecular weight (LMW) and high molecular weight (HMW) subunits (Delcour *et al*., 2012; Shewery *et al*., 1992). LMW-GS exhibits similarities to gliadins in structure but also plays a role in forming interchain disulphide bonds, which are pivotal for constructing a branched glutenin framework. HMW-GS, with their distinct three-domain structure, contribute to a stiff rod-like configuration (Don *et al*., 2003).

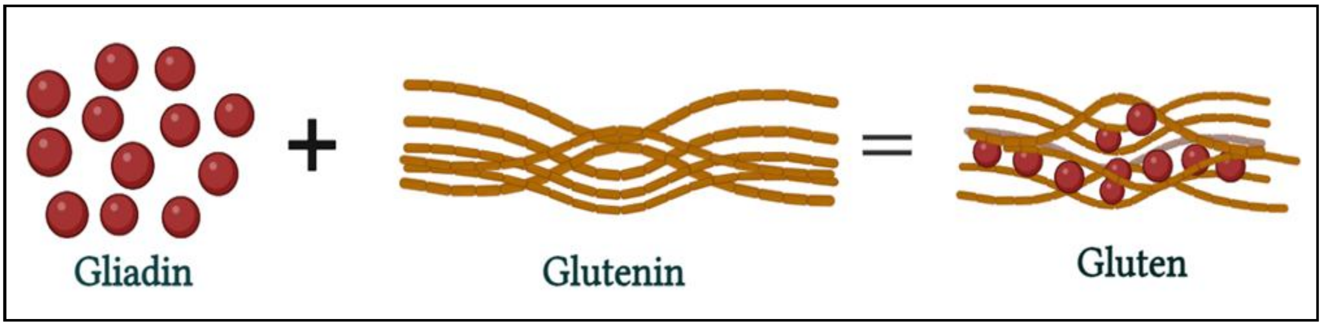

Figure 1: Structure of gluten.

Gliadins and glutenins engage in various types of bonds, encompassing covalent (*e.g*., disulfide bridges) and non-covalent (*e.g*., hydrogen bonds, ionic bonds, hydrophobic bonds, and van der waals forces) interactions (Shewry *et al*., 2000; Tilley *et al.,* 2001). Disulphide bridges are critical for establishing the gluten network, with gliadins forming bonds within chains and glutenins forming bonds within and between chains (Hanft and Koehler, 2005; Piber and Koehler, 2005). Furthermore, tyrosine-tyrosine crosslinks and tyrosine-dehydro ferulic acid bonds also play a role in the network, albeit less frequently. These interactions collectively contribute to the establishment of the gluten network, which is indispensable for the structure of dough and the quality of bread (Piber *et al*., 2005).

5. Bioactive compounds present in gluten

Gluten, predominantly composed of gliadins and glutenins, encompasses a variety of potentially bioactive constituents. Remarkably, glutamine, found abundantly in gluten, plays pivotal roles in cellular metabolism, immune function, and gastrointestinal well-being, particularly in times of stress or sickness. Proline, another predominant amino acid present in gluten, contributes to the distinctive structure and stability of gluten proteins by participating in the process of protein folding. Moreover, despite gluten not being of plant origin, it is sourced from cereals such as wheat, barley, and rye, which harbour phytochemicals like polyphenols known for their antioxidant attributes (Piironen *et al*., 2009).

Additionally, whole grains containing gluten act as significant reservoirs of dietary fibre, vital minerals (iron, magnesium, zinc), and B vitamins (niacin, thiamine, riboflavin), crucial for numerous physiological functions. Furthermore, gluten-containing grains contain lignans, which are phytoestrogens with plausible health advantages, encompassing antioxidant and anti-inflammatory effects, along with potential roles in regulating hormones (Adom *et al*., 2003).

Cereals contain significant amounts of terpenoids, such as sterols and tocols. Wheat and other plants have three types of sterols: Des methyl sterols, 4α-monomethyl sterols, and 4,4-dimethyl sterols. Sterols have cholesterol-lowering abilities in humans, which is a widely recognized health advantage in Europe (Salo *et al*., 2012).

Tocols are composed of a chromanol ring with a C16 phytol side chain and originate in two forms: Saturated tocopherols (T) and tocotrienols (T-3), which have three double bonds at carbons 3, 7, and 11. Although, all tocopherols are referred to as vitamin E, their biological activity differs, with α-tocopherol being the most effective (Shewry *et al*., 2015). Vitamin E is an important lipid-soluble antioxidant in the human body, combining with other antioxidants such as vitamin C to form an effective protective network against oxidative stress. Although, highly reactive α-tocopherol degrades first, potentially lowering its antioxidant efficiency in food systems gradually (Hoevenaars *et al*., 2020). As a result, a mixture of tocols is frequently used to provide comprehensive antioxidant protection. According to certain research, tocotrienols may have comparable or even higher antioxidant capacity than tocopherols. It is crucial to emphasize that individuals with celiac disease or non-celiac gluten sensitivity may encounter detrimental responses to gluten, highlighting the importance of tailored dietary selections. Additionally, the bioactive nature of these substances may vary depending on factors such as processing, culinary techniques, and individual metabolic processes (Hoevenaars *et al*., 2020).

6. Nutritional value of gluten

Gluten does not have special health benefits or certain nutritional value of its own. The grains that comprise gluten, like wheat, barley, and rye, have various nutrients and health benefits. Gluten is a type of protein that is incorporated into the structure and texture of many meals. The following is a summary of the nutritional value and health benefits of gluten-containing grains (Sramkova *et al*., 2009).

Grains with gluten are significant carb sources. Carbs are the body's primary source of energy (Wirfalt *et al*., 2002). Although, gluten is not a "complete" protein due to its lack of some amino acids when it is consumed with other sources of protein, it may create a dietary allowance for protein. Wheat, barley, and rye are packed with dietary fiber, which supports gut health, and regular bowel movements, and reduces the risk of chronic conditions like heart disease and diabetes. These grains are rich in several vitamins, including B vitamins, such as thiamine, riboflavin, niacin, and folate, which support energy metabolism, nerve function, and cell health. Gluten grains also provide a variety of essential minerals, such as iron, zinc, magnesium, and selenium, which are required for carrying oxygen, immune function, and bone health (Sramkova *et al*., 2009).

Whole-grain grains are more likely to be associated with a high risk of CVD. Moreover, they contain fibre, antioxidants, and various phytochemical compounds that lower cholesterol and inflammation and modulate heart function (Mellen *et al*., 2008). The fibre present in gluten-containing whole grains is important for promoting digestive health. This is achieved through easing bowel movements, from constipation and stool softening to maintaining a healthy gut microbiota. Whole grains have a moderate to low GI compared to refined grains, helping to avoid rapid increases in blood sugar. The effect is to stabilize blood sugar and reduce the risk of type 2 diabetes (De munter *et al*., 2007). The fibre present in gluten-containing whole grains helps satiety, which enables appetite control and may aid in measures to maintain weight. Several gluten-containing grains nutrients contribute to maintaining the brain and cognitive function, including folate and vitamin E (Hu *et al*., 2020). Including grains that contain gluten as part of a diet can contribute to your overall health and well-being even though gluten itself may not offer specific health benefits. It is important to remember that people, with disease gluten sensitivity or wheat allergy, should steer clear of gluten-containing foods to avoid health consequences.

7. Gluten-related diseases

There are three kinds of gluten-related diseases namely autoimmune, allergic, and non-autoimmune/non-allergic (Table 1). Celiac disease is the most common autoimmune gluten-related disorder (CD), which is characterized by small intestine damage due to gluten and gluten-related proteins. It is a combination of factors such as genetic predisposition and environmental influence that cause this type of celiac disease. The wheat allergy (WA) has both IgE and non-IgE-mediated immune responses resulting in allergies when wheat touches or is ingested by certain individuals (Cabanillas, 2020). Even though the allergic reactions mainly occur with wheat intake there may be some cross-reactivity with other cereals like barley or rye due to IgE-mediated responses in few individuals. Non-celiac wheat/gluten sensitivity refers to symptoms similar to those observed in celiac disease but CD tests negative for it. However, they are adversely affected by eating anything containing gluten.

7.1 Auto-immune related disorders

7.1.1 Celiac disease

Celiac disease is also known as celiac sprue or gluten-sensitive enteropathy and is a chronic autoimmune disease caused by an abnormal immune response towards gluten, which is a protein found in wheat, barley, and rye. After ingested by a person with celiac disease, gluten triggers one's body's abnormal immune response that leads to the destruction of the lining of the small intestine. The latter is lined with villi, which are numerous tiny finger-like structures responsible for absorbing needed nutrients (Cabanillas *et al*., 2020). Manifestations of celiac disease can vary significantly between individuals; symptoms are primarily manifested with numerous gastrointestinal problems, including diarrhoea, abdominal pain, bloating, and constipation. Alternatively, celiac disease may present as various non-gastrointestinal symptoms such as fatigue, anaemia, weight loss, skin rash called dermatitis herpetiformis, joint pain, or neurological problems (Tye-Din *et al*., 2018). Diagnosing celiac disease is based on several tests, which consist of analysing medical history, physical examination, serological tests to find antibodies to celiac disease, and small bowel biopsy for confirmation (Kaswala *et al*., 2015). The patient must maintain the usual consumption of gluten-containing foods before performing the small bowel biopsy to avoid faux test results. The prevailing treatment for celiac disease is a very rigid lifetime gluten-free diet. This essentially involves eliminating all sources of gluten from the diet, including wheat, barley, and rye, as well as products derived from such grains. By eliminating gluten from one's diet, people with celiac disease can help alleviate symptoms, boost healing of the small intestine, and minimize the risks of long-term complications linked to untreated celiac disease. These complications can include nutrient malabsorption, osteoporosis, infertility, and certain types of cancers (Sharma *et al*., 2015).

7.1.2 Gluten ataxia

Gluten ataxia (GA) is a cerebellar ataxia that mainly involves the purkinje cells. It results from the immune reaction triggered by the presence of specific antibodies against gluten that mistakenly targets the brain regions of genetically predisposed and sensitive individuals (Hadjivassiliou *et al*., 2015). GA clinical manifestations are similar to other types of ataxia including gait ataxia, lower limb ataxia, gaze-evoked nystagmus, upper limb ataxia, dysarthria, or movement abnormalities with chorea, myoclonus, opsoclonus-myoclonus, or palatal tremor (Hadjivassiliou *et al*., 2003). The diagnosis of GA can be made by identifying specific antibodies, including anti-tissue transglutaminase (anti-t TG), anti-gliadin, and anti-transglutaminase 6 (anti-TG6) in the serum. On the other hand, the best diagnostic method for GA that should be used in any suspected patient has yet to be established, although, it appears that IgG antigliadin antibodies may offer higher sensitivity than other markers (Hadjivassiliou *et al*., 2006). In patients with GA, anti-t TG antibodies were found to be present in the brain based on imaging studies. Having positive serology for celiac disease (CD) might direct further investigation *via* intestinal biopsy to confirm the existence of CD. Magnetic resonance imaging (MRI) can also help identify GA, as 60% of GA patients show moderate cerebellar atrophy on MR scans. GA is mainly managed by following a strictly gluten-free diet. In other respects, various reports have demonstrated that immunotherapy through steroids and intravenous immunoglobulin can bring relief from GA symptoms (Hadjivassiliou *et al*., 2015).

7.1.3 Dermatitis herpetiformis

Dermatitis herpetiformis (DH), often associated with celiac disease (CD), is an autoimmune disorder that causes chronic and recurring skin and intestinal symptoms in genetically sensitive people (Clarindo *et al*., 2014). Gluten exposure can cause the formation of anti-tissue transglutaminase (t TG) antibodies, which also target epidermal transglutaminase (ETG), the major antigen in DH since it is structurally identical to t TG. The deposition of IgA antibodies in the dermal papillae causes itchy, vesicular, and localized lesions on the extensor surfaces of joints such as the knees, buttocks, elbows, and scapula (Antiga *et al*., 2019). Patients with suspected DH have direct immunofluorescence (DIF) tests performed on skin samples around the lesions to determine the diagnosis (Mendes *et al*., 2013). In cases with negative results, additional samples may be collected, noting the patient's gluten consumption, which could influence the test. Further investigations, which include anti-t TG antibody assays, may be utilized to confirm DH in patients who exhibit symptoms but have a negative DIF. Treatment for DH includes adhering to a gluten-free diet, similar to that recommended for CD patients because people with DH share the same HLA haplotypes (DQ2 and DQ8). Symptoms may also be treated with drugs such as dapsone or sulfonamides (Mendes *et al*., 2013).

7.2 Allergic-related gluten disorders

Allergens are compounds that can cause allergic reactions, and wheat is among the top five food allergens in children. Wheat, after milk and eggs, is the most common allergy in nations such as Japan, Germany, and Finland (Longo *et al*., 2013). Wheat allergy (WA) affects approximately 1% of children and adults, with variations depending on age and geographic area (Nwaru *et al*., 2014). Wheat allergy, unlike celiac disease (CD), is characterized by wheat-specific components, including water-insoluble proteins (such as gliadin and glutenin) and water/saline-soluble proteins (such as albumin and globulin), which play a role in its development (Longo *et al*., 2013).

7.2.1 IgE-mediated wheat allergy

It is possible to develop an IgE-mediated wheat allergy (WA) by consuming, breathing in, or coming into contact with wheat. When wheat antigens are presented to $CD4^+$ T cells by dendritic cells, Th2 cells are produced and cytokines such as IL-4, IL-5, and IL-13 are released (Ortiz *et al*., 2017). This causes B cells to develop IgE antibodies, which attach to mast cells or basophils and release histamine and other mediators when exposed to wheat allergens again, resulting in allergic reactions like WA. The onset of symptoms might happen minutes to hours after exposure and impact different systems. Wheat-dependent exercise-induced anaphylaxis (WDEIA) is a severe allergic reaction that manifests as angioedema, dysphagia, diarrhoea, and syncope (Christensen *et al*., 2019). It is caused by consuming wheat and then engaging in vigorous activity. Another type of IgE-mediated WA, known as baker's asthma, is brought on by occupational exposure to wheat allergens. Raw wheat flour intake triggers the onset of symptoms. Wheat has several allergens that can cause severe allergy reactions, including heat-resistant proteins like α-amylase/trypsin inhibitors and plant defence proteins like Tri A 37 allergen (Christensen *et al*., 2019). Clinical history, physical examination, and specialized tests like skin prick tests and IgE antibody levels are all part of the diagnosis process. Avoiding allergens and removing wheat from the diet is part of the treatment. Research is being done on immunotherapy as a possible treatment for wheat allergy (Rongfei *et al*., 2014).

7.2.2 Non-IgE-mediated wheat allergy

Usually appearing two hours after consuming wheat, non-IgE-mediated wheat allergy can be related to eosinophilic gastritis (EG) or eosinophilic esophagitis (EoE), which are both defined by eosinophil infiltration in the gastrointestinal system. Indigestion, diarrhoea, vomiting, arthralgia, and headaches are some of the symptoms that may appear hours or days after consuming an allergen (Cianferoni, 2016). An oesophageal biopsy is necessary for the diagnosis of EoE *via* an esophagogastroduodenoscopy (EGD), and confirmation of the diagnosis requires the presence of at least 15 eosinophils per high-power field (eos/hpf). It can be difficult to identify the exact meal that causes EoE; frequently, the need for an elimination diet followed by another EGD after eight weeks to determine the effect of food allergies on the pathophysiology of EoE. The diagnosis of eosinophilic gastritis is based on clinical symptoms, and biopsies demonstrating eosinophilic inflammation (≥ 50 eos/hpf in the duodenum and ≥ 30 eos/hpf in the stomach) are used to confirm the diagnosis (Prussin *et al*., 2014). Avoiding allergens and using corticosteroids are common treatments for EoE. It is usual practice to treat IgE-mediated food allergies with steroids. Elemental diets, particular antigen avoidance based on dietary history or allergy testing, and empirical food exclusion aimed at common food antigens are examples of nutritional methods. Both very restrictive therapies, such as the consumption of amino acid-based formula with a restricted diet, and empirical dietary elimination therapy, which eliminates major food triggers identified for EoE, have demonstrated success in both pediatric and adult patients. But because the symptoms are so severe, diet alone is frequently insufficient, and systemic steroids (0.5-1 mg/kg/day for 5-14 days) are required, along with a progressive 2-4 weeks for symptom management (Cianferoni, 2016).

7.2.3 Non-celiac wheat allergy sensitivity

Symptoms of non-celiac wheat/gluten sensitivity (NCWGS) are similar to those of celiac disease (CD) and wheat allergy (WA), although IgA anti-TG2 autoantibodies and specific IgE against wheat proteins are absent. Abdominal pain, diarrhoea, and gas are common symptoms that appear hours or days after consuming wheat or gluten. Extraintestinal symptoms include headaches, exhaustion, and skin problems (Leonard *et al*., 2017). Recent studies have linked the development of NCWGS to wheat components other than gluten, including fructans, α-amylase/trypsin inhibitors, and wheat-germ agglutinin (Skodje *et al*., 2018). Although, initial research to involvement of innate immune activation rather than adaptive immunity, as seen in CD, the pathophysiology of NCWGS is still poorly known. Innate immunological activation in NCWGS is indicated by increased expression of toll-like receptors (TLRs) in the small intestine, specifically TLR2, TLR1, and TLR4 (Sapone *et al*., 2011). Studies on intestinal permeability in NCWGS produce conflicting results, requiring additional research to determine the role of gut barrier dysfunction in the condition. Diagnosing NCWGS currently relies on clinical symptom evaluation and exclusion of CD and WA. To validate the diagnosis, the Salerno Experts' criteria recommend a double-blind, placebo-controlled gluten challenge after a wheat/gluten exclusion diet. Although, gliadin antibody (AGA) may be present in certain NCWGS patients, its presence is not specific (Catassi *et al*., 2015). Potential diagnostic biomarkers, such as zonulin levels, have been suggested by recent research; however, additional confirmation is required. Although, there are currently no clear treatment guidelines for NCWGS, dietary modifications, such as low-fermentable oligosaccharides, disaccharides, monosaccharides, polyols, and gluten-free diets, are frequently advised. For the management of NCWGS, research on substitute wheat varieties with reduced immunoreactivity, such as *Triticum monococcum* ssp. *monococcum* and *tritordeum* are promising. Furthermore, genetic engineering developments such as CRISPR/Cas9 technology provide opportunities to create wheat types with lower immunogenicity; nevertheless, the environmental triggers of NCWGS are still unknown and need more research (Sanchez Leon *et al*., 2018).

Table 1: The primary features of the three distinct conditions associated with gluten: Celiac disease (CD), non-celiac gluten sensitivity (NCGS), and wheat allergy (WA) (Cenni *et al*., 2023)

Contents	Celiac disease (CD)	Non-celiac gluten sensitivity (NCGS)	Wheat allergy (WA)
Prevalence	Approximately 1% of the overall population	Unknown	0.5-9% of population
HLA-DQ2/8 haplotypes	Positive	Positive in 50% of the patients	Negative
Pathogenesis	Autoimmune	Activation of the innate and adaptive immune response	IgE-mediated
Serological markers Duodenal biopsy	Positive IgA-TG2, IgA-EMA, and IgA/IgG-DGP antibodies necessary *	IgA/IgG anti-gliadin positive in 50% of the patients necessary to rule out CD	Wheat-specific IgE antibodies or prick tests are not necessary
Therapy	Strict gluten-free diet	Gluten-free diet	Avoid all contact with wheat

*According to the most recent European Society for Pediatric Gastroenterology Hepatology and Nutrition (ESPGHAN) guidelines, pediatric patients with elevated anti-TG2 antibodies (>10 times) and positive anti-EMA antibodies in a subsequent sample may not require duodenal biopsy (Husby *et al*., 2020).

8. Clinical studies on gluten-related disorders

Clinical studies have identified a spectrum of gluten-related disorders (GRDs), which include conditions such as celiac disease (CD), dermatitis herpetiformis (DH), gluten ataxia (GA), wheat allergy (WA), and non-celiac gluten sensitivity (NCGS). These disorders present with a wide range of clinical manifestations and are usually diagnosed using a combination of clinical features, serological tests, and histopathological findings. Treatment typically involves dietary modification (Taraghikhah *et al.,* 2020). CD is an autoimmune condition triggered by gluten ingestion in genetically predisposed individuals. It has a prevalence of approximately 1% in the general population. The only treatment for CD is a life-long, strict gluten-free diet, which can improve quality of life and prevent complications. Advances in serological tests have increased the diagnosis of GRDs. The identification of tissue transglutaminase as the autoantigen confirmed the autoimmune nature of CD. Serological tests, such as tissue transglutaminase, endomysial, and deamidated gliadin peptide antibodies, have become important in the diagnostic work-up of CD. The global prevalence of GRDs is estimated at approximately 5%. Historically, GRDs were thought to be almost exclusively found in European populations, but they are now recognized as a significant global health issue. The cultivation of ancient grasses, which started approximately 10,000 years ago in the Fertile Crescent, coincided with the growth of the earliest civilizations and the appearance of symptoms consistent with GRDs. Modern agricultural practices, such as the use of pesticides, nitrogen-based fertilizers, and genetic modification, have led to the production of new types of wheat with high gluten content. For more detailed information on clinical trials and studies related to celiac disease and non-celiac gluten sensitivity, resources such as beyondceliac.org provide information on ongoing research. The article titled "An updated overview of the spectrum of gluten-related disorders: Clinical and diagnostic aspects" provides a comprehensive review of gluten-related disorders (GRDs), which include conditions like celiac disease (CD), dermatitis herpetiformis (DH), gluten ataxia (GA), wheat allergy (WA), and non-celiac gluten sensitivity (NCGS). These disorders are characterized by a variety of clinical manifestations and are known to be caused by the ingestion of gluten proteins found in wheat, barley, and rye. GRDs are heterogeneous, reflecting their autoimmune, allergic, and non-autoimmune-allergic etiology. CD, DH, and GA are considered autoimmune, while WA and NCGS are allergic and non-autoimmune-allergic diseases. The cultivation of ancient grasses, such as the progenitors of modern wheat and barley, began approximately 10,000 years ago in the Fertile Crescent. The mechanization of agriculture and the industrial use of pesticides, nitrogen-based fertilizers, and genetic modification have led to the production of new types of wheat with high gluten content, which are used in the global food industry. This emphasizes the importance of recognizing the diverse clinical presentations of GRDs and the need for accurate diagnostic and therapeutic approaches to manage these conditions.

8.1 Clinical trials for celiac disease patients

Clinical trials are essential for advancing treatment options for celiac disease. Here are some key points from recent trials and resources: A tool designed to help patients with celiac disease and non-celiac gluten/wheat sensitivity, as well as healthy controls, participates in clinical trials. This is crucial as up to 50% of patients continue to experience symptoms and/or intestinal damage while on a gluten-free diet. Innovate biopharmaceuticals has dosed the first patient in a Phase 3 clinical trial testing larazotide acetate (INN-202) as an adjunct treatment for patients with celiac disease still experiencing symptoms on a gluten-free diet. Larazotide acetate is a tight junction regulator that may help reduce the inflammatory process triggered by gluten. Offers a comprehensive listing of clinical trials related to celiac disease, both government and industry-sponsored, conducted across the U.S. These resources provide valuable information for those interested in participating in clinical trials and contribute to the development of new treatments for celiac disease. For more detailed information on specific trials, you can visit the provided references.

8.2 Gluten and patient response in celiac disease

Patients with celiac disease (CD) must adhere to a strict gluten-free diet (GFD), which is the primary treatment to manage the condition and improve outcomes. However, maintaining a GFD can be challenging due to the need for access to quality healthcare resources that facilitate optimal adherence (Simó *et al*., 2023). The proteins gliadins, which are rich in proline and glutamine residues and resistant to human protease digestion, are known triggers for CD in genetically predisposed individuals, contributing to increased intestinal permeability. A multinational survey presented at United European Gastroenterology Week highlighted the experiences of patients with CD on a GFD, emphasizing the importance of understanding patient responses to dietary management.

Furthermore, the global prevalence of gluten-related disorders (GRDs), including CD, dermatitis herpetiformis, gluten ataxia, wheat allergy, and non-celiac gluten sensitivity, is estimated at approximately 5% of the population. The diagnosis of GRDs can be complex due to the overlap of typical and atypical clinical manifestations. For patients with CD, it is also crucial to be aware of gluten content in pharmaceutical products, as inadvertent consumption can trigger symptoms and impede disease management (Lizano-Díez *et al*., 2021). These insights into gluten and patient response are critical for healthcare providers and patients alike to ensure the effective management of celiac disease.

8.3 Celiac disease diagnosis and evolving approaches

Celiac disease (CD) is an immune-mediated gastrointestinal disorder triggered by the consumption of gluten in genetically predisposed individuals. Over time, the presentation of CD has evolved, with non-GI symptoms such as anemia and osteoporosis becoming more common (Cichewicz *et al*., 2019). Traditionally, endoscopy with small bowel biopsy has been the gold standard for CD diagnosis. However, in selected cases, diagnosis based on positive serology (such as anti-tissue transglutaminase antibodies) and clinical symptoms may be sufficient. Unfortunately, diagnosis is often delayed, with an average delay of up to 12 years after symptom onset. Barriers include atypical presentation, lack of physician awareness, misdiagnosis, and limited access to specialists. Currently, strict adherence to a GFD remains the only recommended treatment for CD. However, it is not successful in all patients. Clinicians should create individualized goals for each patient, with the endpoint of GFD therapy being intestinal healing. Surprisingly, only one-third of patients are regularly monitored following diagnosis.

The American College of Gastroenterology updated its guidelines for CD diagnosis and management in 2023. Key recommendations include: Using upper gastrointestinal endoscopy with multiple duodenal biopsies for confirmation. Avoiding gluten detection devices, considering gluten-free oats as part of the diet, administering the pneumococcal vaccine to prevent infection, focusing on case finding rather than mass screening in clinical practice, and using immunoglobulin IgA anti-tissue transglutaminase as the preferred single test for CD detection in children aged 2 years and younger are required. Research should explore the impact of education about gluten-free eating and the availability of gluten-free foods in supporting adherence and improving outcomes for CD patients. In summary, early and accurate diagnosis, personalized treatment goals, and ongoing monitoring are crucial for effective CD management. Advances in diagnostic approaches continue to shape our understanding of this complex condition.

8.4 Non-celiac gluten sensitivity (NCGS)

Non-celiac gluten sensitivity (NCGS) is a clinical entity characterized by the absence of celiac disease and wheat allergy in patients who experience reproducible symptomatic responses to gluten-containing foods. Unlike celiac disease, which has well-defined serologic and histologic biomarkers, NCGS remains a heterogeneous and poorly understood condition with challenging diagnostic criteria (Cárdenas-Torres *et al*., 2021). Currently, there are no sensitive and reproducible biomarkers for NCGS diagnosis. Therefore, placebo-controlled gluten challenges are essential for confirming NCGS. These challenges can be either double-blind (for research purposes) or single-blind (for clinical practice). They involve assessing symptomatic responses to gluten consumption. Self-report-based epidemiological studies have been conducted to estimate the prevalence of NCGS in different populations, but gluten challenge-based prevalence remains to be determined. While gluten is often implicated, other grain components may play a role in symptom development. These include fermentable oligo-, di-, monosaccharides, polyols (FODMAP), and amylase and trypsin inhibitors. Research is needed to understand the molecular interactions between these components and the immune system in NCGS. The primary treatment for NCGS involves avoiding suspected triggers. However, controversy exists regarding the effectiveness of different dietary interventions, such as the gluten-free diet and low-FODMAP diet. Some NCGS patients may be susceptible to one or more triggers. Our understanding of NCGS is rapidly evolving due to new scientific information. Researchers continue to explore its pathogenesis, triggers, and optimal management strategies. In summary, NCGS remains a complex and multifaceted condition. As more studies delve into its mechanisms and treatment, clinicians can better diagnose and manage patients experiencing gluten-related symptoms.

8.5 Emerging therapeutic strategies for celiac disease

Celiac disease (CD) is a chronic intestinal disorder triggered by the ingestion of gluten from wheat, rye, and barley. Currently, the mainstay of treatment is a strict, lifelong gluten-free diet (GFD). However, adherence to the GFD can be challenging due to inadvertent gluten exposure and its social and economic burdens. Additionally, some patients experience persistent symptoms despite following the diet (Kivelä *et al*., 2021). Researchers are actively exploring novel therapeutic approaches to improve CD management.

8.5.1 Glutenase enzymes

These enzymes aim to break down gluten in the digestive tract, reducing the immunotoxic sequences responsible for inflammation. Clinical trials are investigating their safety and efficacy.

8.5.2 Monoclonal antibodies

Targeting inflammatory cytokines and T cells involved in the immune response to gluten. These have the potential to restore oral tolerance and reduce symptoms. Ongoing research to assess their effectiveness is required.

8.5.3 Zonulin modulation

Zonulin is a protein that regulates intestinal permeability. Therapies targeting zonulin may help prevent gluten-induced damage. They are still in the early stages of investigation.

8.5.4 Immunomodulatory drugs

Aim to modulate the immune response triggered by gluten. Various compounds are being explored, but more evidence is needed.

8.5.5 Vaccines

Vaccines are designed to induce immune tolerance to gluten. Promising results in preclinical studies, but clinical trials are ongoing.

8.5.6 Tight junction modulators

Targeting the intestinal barrier function to prevent gluten entry is necessary. Research is underway to identify safe and effective compounds. While the GFD remains essential, these emerging therapeutic strategies offer hope for better CD management. Continued research and clinical trials will determine their role in improving the lives of CD patients.

8.6 Non-celiac gluten sensitivity and emerging therapeutic strategies

Non-celiac gluten sensitivity (NCGS) is a condition where individuals experience symptoms similar to those of celiac disease (CD) when consuming gluten but without the characteristic autoimmune response seen in CD. While a lifelong gluten-free diet (GFD) remains the primary treatment for CD and NCGS, there are emerging therapeutic strategies aimed at improving treatment efficacy and patients' quality of life. Strict adherence to the GFD can be challenging due to social isolation, risk of gluten contamination, high cost, and poor quality of gluten-free products. Long-term adherence to the GFD may lead to nutrient deficiencies. Researchers have developed gluten-free wheat flour to create products that closely resemble gluten-containing counterparts. Various methods, including clinical assessment, questionnaires, serology for celiac disease, duodenal biopsies, and the detection of gluten immunogenic peptides (GIPs), are used to monitor adherence. However, none are entirely satisfactory. Alternative therapies beyond the GFD should be explored to enhance treatment efficacy and patient well-being. Other therapeutic approaches such as probiotics may help modulate gut health in CD and NCGS patients. Phyto and synthetic cannabinoids are being investigated for their potential impact on the host microbiome. Ongoing clinical trials explore novel approaches such as the digestion of peptides, tight junction modulation, and immune targets (Varma *et al*., 2022). As our understanding of NCGS grows, researchers are actively exploring new therapeutic avenues to complement the GFD. Technology advancements, follow-up strategies, and insights into a rapidly changing future will shape the management of NCGS (Mazzola *et al*., 2024).

9. Gluten-free diet

As previously stated, following a gluten-free diet (GFD) is essential for treating celiac disease (CD) and is crucial for controlling symptoms in non-celiac gluten/wheat sensitivity (NCGWS). A strict GFD involves removing gluten, the main protein in wheat, rye, and barley (Theethira *et al*., 2015). Even though, oats usually do not cause immune responses in CD, they are frequently mixed with gluten from other grains, so CD patients need to eat pure gluten-free oats. Unlike CD, there is no specific limit for gluten or wheat in NCGWS. A perfect gluten-free diet (GFD) mainly includes fresh, unprocessed foods that do not contain gluten naturally (Jivraj *et al*., 2022). However, certain processed items such as sauces, soups, ice cream, sausages, candies, desserts, and fruit nectars may still have gluten due to cross-contamination despite being made from gluten-free ingredients initially (Christoph *et al*., 2018). For a product to be considered gluten-free, it must contain gluten levels lower than a specific threshold, which is typically set at less than 20 parts per million (ppm) or 20 mg of gluten per kg of food in many countries. This standard is globally accepted in the Codex Alimentarius standard for foods for special dietary use for individuals with gluten intolerance. Consumers can identify gluten-free products by looking for clear gluten-free labelling, gluten-free logos, or reading labels that confirm the absence of gluten. Despite efforts by individuals to avoid gluten and manufacturers to create gluten-free foods, sticking to a gluten-free diet can still be a difficult task (Pinto-Sanchez *et al*., 2017).

9.1 The effect of gluten-free diet on gut microbiota in gluten-related diseases

The significance of gut microbiota in celiac disease (CD), non-celiac gluten sensitivity (NCGS), and wheat allergy (WA) is recognized, although its precise role in the development of these conditions remains uncertain.

Before diagnosis, individuals with CD often exhibit alterations in their intestinal microflora characterized by an increase in total bacteria and a higher proportion of potentially harmful species. It is not fully understood whether these changes are a consequence of the disease itself or contribute to its development by affecting intestinal permeability, gluten processing, or immune regulation (Kaliciak *et al*., 2022). Nevertheless, these alterations are associated with gastrointestinal symptoms' severity and disrupted bowel function. The gut microbiota plays a crucial role in modulating the immune system through various mechanisms, such as the production of short-chain fatty acids (SCFAs) that affect regulatory T cells (Heintzz-Buschart *et al*., 2018). Studies have demonstrated that adherence to a gluten-free diet (GFD) can lead to microbiota changes in CD, making the microbial composition more similar to that of healthy individuals. In contrast, CD patients not adhering to a GFD often have gut dysbiosis characterized by an abundance of pro-inflammatory bacteria and a depletion of beneficial probiotic species (Canova *et al*., 2014). Research in germ-free mice colonized with bacteria from CD patients and healthy individuals has shed light on the role of specific bacterial species in CD pathogenesis (Serena *et al*., 2019). For instance, *Pseudomonas* spp. abundant in CD patients have been shown to compromise intestinal barrier function and activate T-cells, while *Lactobacillus* spp. prevalent in healthy individuals aid in gluten peptide digestion, reducing their immunogenicity (Dargenio *et al*., 2016). Fewer studies have explored the relationship between gut microbiota and NCGS. However, preliminary findings suggest alterations in microbial composition in NCGS patients compared to healthy controls, with some evidence pointing to a protective role of certain bacterial genera. While GFD is the mainstay therapy for CD and NCGS and is associated with symptom improvement, its impact on gut dysbiosis is debated. While it may partially restore normal gut microbiota, it also reduces bacterial diversity. Overall, more research is needed to fully understand the relationship between GFD and gut microbiota in CD, NCGS, and WA, as well as their respective pathogenesis and management (Nobel *et al*., 2021).

10. Low gluten varieties

There are several wheat varieties which are low in gluten content. These are the choices for consuming wheat with lesser quantities of gluten. Devi *et al*. (2022) reviewed grain quality parameters in bread wheat varieties.

10.1 Emmer wheat

Emmer wheat, also known as "Khapli," is a lesser-known variety of wheat. It is considered a healthier substitute for regular wheat because it contains less gluten. Emmer wheat has versatile culinary utility and is a good source of nutrition. It has more protein than regular wheat, along with essential iron, magnesium, and fibre. Due to its low gluten content, it is more easily digestible and has a low glycemic index, making it suitable for diabetics. Emmer wheat is traditionally cultivated in parts of Karnataka, Maharashtra, Gujarat, Andhra Pradesh, and Tamil Nadu. It is available in speciality stores and online markets in India due to its high nutritional value and low gluten content.

10.2 Bansi wheat

Bansi wheat is another wheat variety. It is a good choice for those looking to avoid gluten.

10.3 Spelt wheat

Spelt is another wheat variety that is diabetes-friendly. It is popularly used for making bread.

10.4 Durum wheat

Durum wheat, also known as bread wheat, is commonly used for making pasta and semolina. While it contains gluten, it is still considered a better option than regular wheat for some individuals.

10.5 Red wheat

Red wheat is another variety that can be suitable for diabetes patients. It's essential to check individual tolerance and consult with a healthcare professional.

11. Gluten-free grains

In India, there are several gluten free grains that can be incorporated into the diet. These grains are not only nutritious but also suitable for those who need to avoid gluten. Rice is a staple in Asia and is widely consumed. Varieties like brown rice, red rice, black rice, and wild rice are available. Sorghum, known as "Jowar" in India, is easily available. It can be milled into flour for making rotis and is often blended with other gluten-free flour for baking. Millets come in various types: Pearl millet (Bajra) which can be used to make Bajra rotis. Finger millet (Ragi) which is rich in nutrients and is also versatile. Ragi flour can be used for rotis, patties, and breads. Proso millet is also known as Barri, it is another excellent grain for gluten-free cooking. Amaranth seeds are called "Ramdana" in India. They can be substituted for starch in gluten-free cooking. Try using powdered amaranth as a replacement for cornstarch in recipes. Buckwheat is another gluten-free option. It is commonly used during fasting periods and can be used to make pancakes, crepes, and more. Although not native to India, quinoa is gaining popularity. It is a complete protein and can be used as a rice substitute or in salads. In India, there are several gluten-free grains that can be incorporated into the diet.

12. Applications of gluten proteins in non-bakery industries

Gluten proteins, traditionally associated with bakery products, have unique viscoelastic properties that are utilized in various non-bakery industries are reviewed by Egea *et al*. (2023).

12.1 Meat industry

As binders and fillers in meat products, gluten proteins enhance texture and water retention. They serve as a meat substitute in vegetarian and vegan products due to their chewy texture (Egea *et al*., 2023).

12.2 Dairy alternatives

Gluten proteins help achieve the desired consistency and reliability in the production of dairy-free cheeses.

12.3 Brewing industry

They contribute to the stability and foam quality of beers. However, gluten-free options are also available for those with sensitivities.

12.4 Confectionery

In confectionery products, gluten proteins provide elasticity and structure to items like licorice and chewy candies.

12.5 Cosmetics and personal care

Due to their film-forming abilities, gluten proteins are incorporated into cosmetic products such as hair conditioners and skincare items.

12.6 Pharmaceuticals

Gluten proteins are used as excipients in pharmaceuticals to improve the texture and stability of tablets and other dosage forms.

12.7 Pet food

In pet food, gluten proteins are added to improve the nutritional content and to act as a binder in kibble.

12.8 Industrial applications

They are used in biodegradable films and packaging materials, contributing to sustainability efforts.

12.9 Agriculture

Gluten proteins are used as a natural herbicide, providing an eco-friendly alternative to chemical weed control

These applications demonstrate the versatility of gluten proteins in industries beyond bakery, highlighting their role in the development of specialised and functional ingredients.

13. Recent advancements in gluten-free product formulations

The development of gluten-free products has seen significant advancements to address the needs of individuals with celiac disease and gluten intolerance. Here are some of the recent innovations as reviewed by Gallagher *et al*. (2004). While gluten-free bakery products have received significant attention, there's a growing interest in expanding gluten-free options beyond traditional baked goods. Here are some innovative applications and ingredients (Egea *et al*., 2023).

13.1 Use of alternative flours

Researchers are exploring the use of flours from pseudocereals like quinoa and amaranth, which offer nutritional benefits and desirable baking properties.

13.2 Hydrocolloids and gums

The incorporation of hydrocolloids such as xanthan gum and guar gum improves the texture and shelf-life of gluten-free products.

13.3 Sourdough fermentation

Sourdough fermentation with selected *lactobacilli* can improve the flavor and texture of gluten-free breads (Papageorgiou *et al*., 2023).

13.4 High-pressure processing

This technique has been shown to improve the quality of gluten-free dough by altering its microstructure.

13.5 Microwave and extrusion technologies

These processing methods are being applied to enhance the nutritional profile and sensory attributes of gluten-free products.

13.6 Nutritional enhancement

Fortification with vitamins, minerals, and fibre is a focus to improve the nutritional value of gluten-free products (Gallagher *et al*., 2004).

13.7 Soy, corn, and bean by-products

Grain by-products from soy, corn, and beans are rich in dietary fibre and bioactive compounds. These have been studied as potential raw materials for gluten-free products.

13.8 Technological considerations

However, their use can impact technological properties (color, texture, volume, *etc*.) and sensory characteristics. Understanding these effects is crucial for establishing suitable processes.

Additives and ingredients

13.9 Hydrocolloids

These substances help maintain texture and stability in gluten-free products. Examples include xanthan gum, guar gum, and psyllium husk.

13.10 Pseudo-cereals

Pseudo-cereals like amaranth and teff offer unique properties for gluten-free products.

Challenges and opportunities

13.11 Shelf-life extension

Extending the shelf-life of gluten-free bread and bakery products is essential for wider distribution.

13.12 Cost-effectiveness

Gluten-free products are often more expensive. Using cost-effective ingredients and optimizing processes can help address this issue.

13.13 Sensory quality

Balancing nutritional improvements with sensory appeal is crucial to meet consumer expectations.

13.14 Environmental impact

Utilizing by-products contributes to sustainability and reduces waste.

13.15 Beyond bakeries

Gluten-free pasta made from alternative flour (*e.g.*, rice, corn, chickpea) is gaining popularity. Innovations in gluten-free snacks, such as crackers, chips, and extruded products, provide variety. Gluten-free ready-to-eat meals cater to convenience and dietary needs. Gluten-free beer, spirits, and other beverages are emerging.

The gluten-free landscape is evolving, and researchers and food technologists continue to explore novel ingredients and processing methods to create diverse, nutritious, and appealing gluten-free products for consumers with specific dietary requirements. These advancements aim to improve the quality, taste, and nutritional profile of gluten-free products, making them more comparable to their gluten-containing counterparts.

14. Marketing of gluten-free product formulations

The marketing of gluten-free products is a critical aspect of their success in the health and wellness market. Here are some key points regarding the marketing strategies for gluten-free foods and beverages (Joe Bogue and Douglas Sorenson, 2008). Involving consumers in the development and strategic marketing of gluten-free products is crucial. Understanding consumer preferences, needs, and acceptance helps create products that resonate with the target audience. The gluten-free market should be viewed as a long-term strategy for future growth rather than a short-term pursuit of high profitability. Given the niche nature of the gluten-free market, sustained efforts are essential. As consumer lifestyles evolve, so must the development and marketing of gluten-free cereal products. Adaptation to changing preferences ensures that these products remain relevant and appealing. Identifying key extrinsic (marketing-related) and intrinsic (sensory) attributes that influence consumer acceptance is vital. These attributes should guide the development of new gluten-free foods. Conducting market research provides a systematic means of managing consumer knowledge during new food product development. A market-oriented approach helps understand consumer choice motives and value systems. A market-oriented approach benefits research and development (R&D) personnel by making them more consumer-led in product design. Marketers can identify emerging market segments, and strategic decisions become more accurate when bringing gluten-free foods and beverages to market. Successful marketing of gluten-free products involves understanding consumer preferences, adapting to changing lifestyles, and strategically incorporating attributes that resonate with the target audience. By doing so, gluten-free foods can meet consumer needs while contributing to overall health and wellness.

15. Conclusion

Wheat is highly valued for its nutritional benefits, particularly its abundant dietary fibre, which is essential for balanced diets globally. Wheat has been a staple crop for millennia. Due to its adaptability in different forms, which is made possible by the gluten protein complex, it has become a staple food for an important portion of the world's population.

Although, it has nutritional advantages, there are serious problems due to the increase in wheat/gluten-related diseases such as non-celiac wheat/gluten sensitivity (NCWGS) and celiac disease (CD). While wheat allergy (WA) sufferers must completely avoid wheat, CD patients must strictly follow a gluten-free diet, and NCWGS patients may benefit from excluding wheat and/or gluten in addition to other dietary changes. It is important to realize that these problems impact a very small percentage of the population. Choosing a gluten-free diet including gluten-free grains and low-gluten wheat varieties in the absence of a medical necessity can be hazardous because wheat contains important elements that are necessary for good health. False beliefs about wheat have caused it to be unnecessarily eliminated from diets, depriving people of vital nutrients. Clearing up these myths and offering objective information on wheat-related illnesses and nutritional advantages is crucial for making well-informed food decisions and maintaining general health.

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Conflict of interest

The authors declare no conflicts of interest relevant to this article.

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