Advancing Therapeutic Strategies for Celiac Disease: From Gluten-Free Diets to Novel Biopharmaceutical Approaches

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Abstract

Gluten is a type of protein primarily present in wheat, barley and rye, which contributes towards the texture and elasticity of bread and other baking products. Gluten is considered safe in the majority of cases but leads to dangerous health conditions in cases of gluten intolerance or gluten-related diseases. In such situations, the immune response to gluten harms the small intestine, provoking inflammation, digestive problems, and chronic complications. The effects of this reaction include bloating, diarrhea, nausea, vomiting, stomach pain, and fatigue. This immune reaction may eventually cause the destruction of the fingerlike structures that make up the villi in the intestine where nutrients are absorbed. Consequently, individuals who have celiac disease usually become malnourished, lose weight, experience osteoporosis, and may even have neurological problems. Besides, gluten enhances intestinal permeability — commonly known as leaky gut — that permits harmful elements as well as undigested proteins to enter the blood, which may enact additional immune responses. Complete abstinence from gluten prevents the symptoms and permits the intestine to heal. Nonetheless, unintentional exposure to gluten remains a significant issue since gluten can be found in most processed foods. Researchers are also developing new interventions, which include enzyme-based therapy that will aid in the breakdown of gluten before it reaches the intestine, and probiotics which could help curb the inflammation process. These approaches are still under investigation but have brought hope in the management of gluten-related disorders. This paper emphasizes the significance of gluten awareness and the need for further research to develop better treatment strategies.

Keywords: Gluten structure, Intestinal permeability, Enzyme therapy, Dietary management

1 Introduction

Gluten is a form of protein commonly present in wheat, barley, and rye. It is highly necessary in baking since it makes the dough stretch, rise, and retain its shape, imparting softness and chewiness to bread and other baked products [1]. Gluten consists of two chief forms of proteins known as gliadins and glutenins. Although gluten is absolutely healthy in most individuals, it may lead to severe health complications in other people, particularly those with gluten intolerance or celiac disease [2].

Consumption of gluten by individuals with celiac disease causes an abnormal immune response. Their immune system perceives gluten not as an inert food substance but as something harmful, such as a virus or a bacterium, and begins to attack the lining of the small intestine [3]. This leads to extensive inflammation and damage to the intestinal wall. The small intestine contains finger-like structures known as villi, which aid in the absorption of food nutrients. The immune system invades and destroys such villi, rendering individuals with celiac disease unable to absorb the required nutrients, leading to malnutrition, weight loss, weak bones (osteoporosis), anemia, and neurological problems such as headaches, depression, and numbness in the hands and feet [4]. Celiac disease (CD) presents with symptoms that vary considerably among individuals. Some experience very severe symptoms such as intense stomach pain, vomiting, diarrhea, and extreme fatigue, while others may experience only trivial symptoms such as bloating or gas, making CD difficult to diagnose [5].

Non-Celiac Gluten/Wheat Sensitivity (NCGWS) remains a baffling problem to clinicians and researchers due to the lack of diagnostic biomarkers. Unlike celiac disease or wheat allergy, NCGWS does not have a definitive test and is primarily determined by excluding other conditions and measuring the symptomatic response to dietary modifications. Researchers have investigated a number of possible diagnostic tools such as zonulin levels, confocal laser endomicroscopy (CLE), fecal calprotectin (FCP), and anti-gliadin antibodies (AGA), each with limitations in accuracy, specificity, or clinical practicability [6]. Emerging data indicate that NCGWS may not be a single disease but rather a continuum involving various mechanisms, some immune-related and others not.

At present, the standard treatment for celiac disease is a strict gluten-free diet, avoiding foodstuffs composed of wheat, barley, rye, and even oats unless certified gluten-free [6]. This diet is difficult to follow as gluten is present in several foods including

soups, sauces, candies, and even some medicines. Even the slightest traces of gluten can harm the intestine and recur the symptoms [7]. Scientists are investigating other methods to assist people with celiac disease, including special enzymes capable of breaking down gluten in the stomach, probiotics which are healthy bacteria that may lower inflammation, and vaccines or medicines which may train the immune system not to react to gluten [8]. Genetic research is also being done to create new varieties of wheat with less harmful gluten content [9].

The protein structure of gluten is particularly high in proline and glutamine, rendering it highly resistant to digestion, which allows harmful peptides to survive and elicit an immune reaction. Researchers have been keen on developing enzyme-based therapies capable of breaking such tough gluten fragments prior to their causing damage. Potential candidates include natural and engineered proteolytic enzymes such as prolyl endopeptidases (PEPs), cysteine proteases such as EP-B2, and enzymes with specific gluten-degrading properties. These enzymes, either individually or in combination, have shown positive results in preclinical and clinical trials [10].

Celiac disease is the most frequent autoimmune disease in which the intake of gluten provokes an immune attack on the small intestine [2], resulting in villous atrophy, malnutrition, diarrhea, weight loss, fatigue, osteoporosis, and neurological complications [11, 12]. Non-celiac gluten sensitivity is another condition wherein individuals experience symptoms of celiac disease (bloating, stomach pains, and fatigue) without intestinal lesions [13]. Wheat allergy is a further gluten-related disease in which the immune system responds rapidly to wheat proteins, leading to hives, breathing difficulties, and potentially fatal allergic reactions [14]. A thorough gluten-free diet which avoids foods with wheat, barley, and rye remains the only known means of treatment [15]. This paper examines the structure of gluten, its place in the food industry, the diseases linked to gluten, its functions in the body, and current research on improved treatment strategies [15].

2 What is Gluten

Gluten is a complex combination of proteins consisting of two major classes: gliadins and glutenins (Fig. 1). Gliadins are monomeric, single-chain proteins that render the dough soft and stretchy. Glutenins are polymeric proteins — long chains connected to each other — that provide the dough with its strength and hardness [2]. Gliadins and glutenins are strongly bound to create a protein network when water is added to flour. The proteins absorb water and interact with one another through disulfide bonds, hydrogen bonds, and hydrophobic interactions. Disulfide bonds in particular aid in joining the various protein molecules into a strong and elastic network. This gluten network becomes more organized and stronger during kneading [2], which contributes to the alignment of protein chains and the formation of a tight network that entraps air bubbles. During fermentation and baking, these air bubbles are expanded by yeast or baking powder, causing the dough to rise and giving bread its spongy and soft characteristics [1].

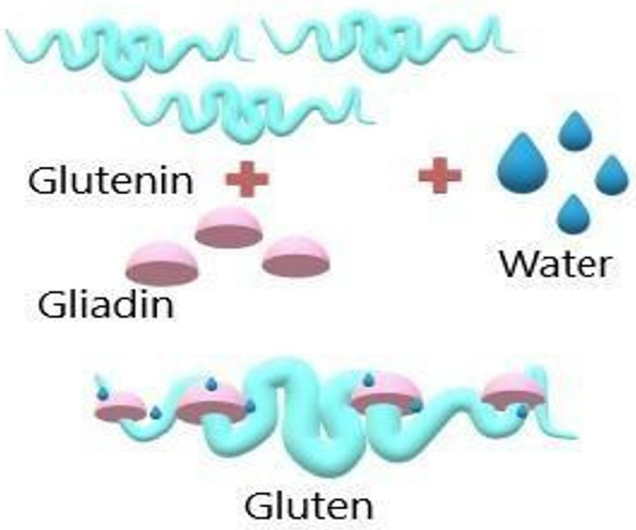

Fig. 1 The two predominant protein components in wheat are gliadin and glutenin. When mixed together with water, they form gluten — a protein network that gives elasticity and structure to the dough.

The gluten structure consists of various layers. Strong covalent bonds such as disulfide bonds bind the inner portions, while weaker bonds such as hydrogen bonds and hydrophobic interactions govern the outer portions [11]. This multi-layered network is capable of stretching and adapting to pressure during rising or baking. At the molecular scale, gliadins have been found to be disordered in their structure, i.e., they lack a rigid three-dimensional form, which makes their flow and stretchability possible. Glutenins, however, are larger, more structured complexes that provide strength and stability [11]. The high-molecular-weight (HMW) subunits of glutenins are particularly significant in providing dough elasticity, whereas the low-molecular-weight (LMW) subunits play a role in dough strength and extensibility.

The special structure of gluten also makes it difficult to completely digest because of the presence of amylase, protease, thionins and putative defense- related proteins with multiple interchain disulphide bonds that are tough to degrade even in heating process of food and in gastro-intestinal tract. The Human digestive enzymes cannot fully disintegrate all the bonds in gluten proteins, leaving large peptide fragments intact. In individuals with celiac disease, some peptide groups, particularly from gliadin, cause an immune response [16]. The 33-amino-acid α-gliadin peptide is among the most toxic, most resistant to digestion, and most potent activators of the immune system. The abundance of glutamine and proline in gluten proteins makes them particularly inaccessible to the human digestive enzymes, as these enzymes have difficulty cleaving proline-rich regions [11]. Gluten proteins have evolved over millions of years; those of ancient grains such as einkorn and emmer differ from modern wheat, which has been selectively bred for more robust gluten networks, enhancing the availability of immunogenic gluten peptides [17]. Knowledge of gluten's molecular structure is therefore of relevance not only to baking science but also to medical studies of celiac disease, non-celiac gluten intolerance, and related disorders [18].

3 Structure of Gluten

Gluten refers to a form of protein inherent in grains such as wheat, barley, and rye. It contributes significantly to the structure, elasticity, and chewiness of bread and other baked products [1]. There are two primary classes of protein present in gluten: gliadins and glutenins. Both are abundant in the amino acids glutamine and proline, which partly account for gluten's characteristic structure and functioning [11]. Gliadins and glutenins do not interact in the same way, yet they combine into a powerful network that provides dough with its strength and elasticity [2].

Gliadins are smaller, single chains of proteins that move more freely and are responsible for the softness and stretchability of dough, making them particularly suitable for the baking of cakes and pastries. They are also most probably the fraction of gluten responsible for the majority of immune responses in individuals with gluten-related disorders [14]. In celiac disease, certain gliadin-derived peptides are not digested in the small intestine due to their high proline content. Once they pass through the intestinal lining they can lead to inflammation and damage of the gut. Glutenins, in turn, are larger proteins that combine to form extensive networks providing dough with its elasticity and structure [19]. During kneading, glutenins associate via disulfide bonds — powerful chemical links between sulfur atoms in the proteins — forming a network that traps air bubbles and enables bread to rise and stabilize its form. Glutenins are further classified as high molecular weight (HMW) and low molecular weight (LMW) subunits (Fig. 2).

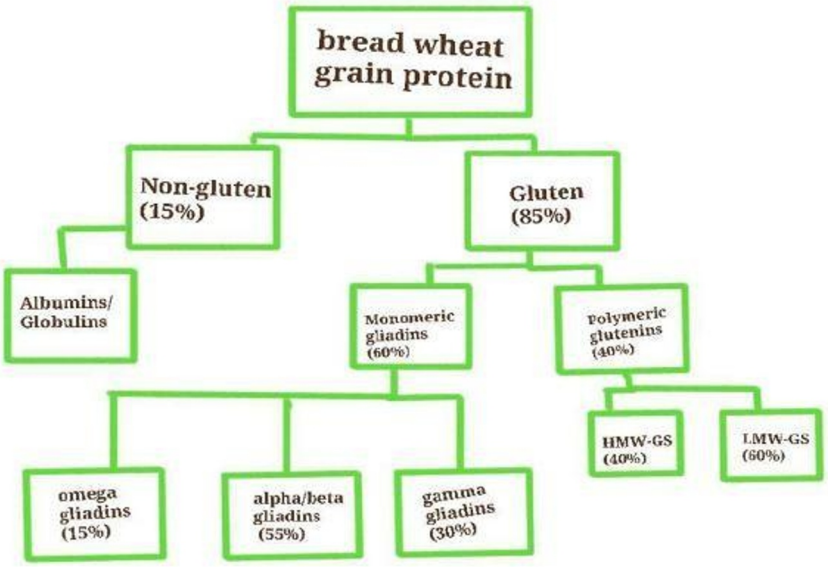

Fig. 2 The proteins of wheat are widely divided into gluten (polymeric glutenins and monomeric gliadins) and non-gluten (albumins/globulins) fractions. Gluten consists of low molecular weight glutenin subunits (LMW-GS, 60%), high molecular weight glutenin subunits (HMW-GS, 40%), and gliadin subtypes: ω-gliadin (15%), α/β-gliadin (55%), and γ-gliadin (30%). The HMW glutenins are particularly crucial in the bread-making process since their long chains make the dough strong [20].

Types of grain contain variations of gluten proteins. The prevalent proteins in wheat are α-, β-, γ-, and ω-gliadins, and HMW and LMW glutenins [21]. The analogous proteins in barley and rye are named hordeins and secalins, respectively, all of which can present issues for individuals with celiac disease or non-celiac gluten sensitivity. Unlike most other dietary proteins, which are broken down to form amino acids, gluten tends to leave long peptide fragments [22]. Some of these fragments, including gliadin-derived peptides, can penetrate the intestinal barrier and react with immune cells, provoking an autoimmune reaction that destroys the mucous membrane of the small intestine [11]. Researchers are studying ways to alter wheat varieties or develop enzymes to better digest gluten in the intestines, as well as developing new medicines to make the body accept gluten or prevent the immune response [11].

4 Distribution of Gluten

The food products most evidently containing gluten are those prepared using wheat flour, such as bread, pasta, pizza, cakes, pastries, and cookies [1]. White bread, whole wheat bread, rolls, buns, and bagels are all high in gluten. Pasta dishes such as spaghetti, macaroni, and lasagna noodles are also high in gluten unless specifically prepared gluten-free. Baked products such as cupcakes, muffins, croissants, and donuts rely on gluten for their soft, fluffy, and chewy characteristics. Barley and rye are the other two grains that naturally contain gluten. Many malt products are made using barley, including malted milk, malt vinegar, beer, and some cereals. Rye is incorporated primarily in rye bread and rye-based crackers. Even some oats can contain gluten, not intrinsically, but due to cross-contamination during growing, harvesting, or processing, meaning that individuals who exclude gluten should consume only certified gluten-free oats [23].

Many packaged and processed foods contain gluten in disguise. Soups, gravies, sauces, salad dressings, and marinades often use wheat flour or modified food starch as a thickener [24]. Some brands of soy sauce contain wheat and consequently gluten. Snack foods such as flavored chips, pretzels, and crackers often contain gluten unless specifically labeled gluten-free. Breakfast cereals may be sweetened or flavored using barley malt [25]. Hidden gluten can also be contained in candy and sweets, while processed meat products such as hot dogs, sausages, and deli meats occasionally contain gluten-based fillers or seasonings [26].

Beverages constitute another unexpected source of gluten. Beer is generally made from barley and contains gluten unless specifically brewed gluten-free. Some wine coolers and malt-based alcoholic beverages also contain gluten. Flavored coffees, milkshakes, and certain herbal teas may contain hidden gluten depending on preparation [27]. Imitation meat products and plant-based proteins are frequently made with wheat gluten, commonly in the form of seitan, which is nearly pure gluten [28]. Frozen or pre-prepared meals are also often risky, as gluten may be used to correct texture, shelf life, or flavor. Gluten can even

be found in non-food items such as vitamins, supplements, medications, lipsticks, and toothpastes, where minimal traces may nonetheless affect highly sensitive individuals [29].

Gluten-intolerant individuals must therefore read labels thoroughly and verify gluten-free status. In most countries, regulations prescribe inclusion of wheat as an allergic ingredient, yet barley and rye are not always emphasized [30]. The availability of gluten-free products has increased rapidly in recent years, with supermarkets and restaurants offering gluten-free alternatives. Nonetheless, cross-contamination continues as a serious issue, particularly in kitchens and bakeries where wheat products are common [31]. Even a few crumbs of bread may trigger a reaction in the most severely gluten-sensitive individuals, meaning that those who need to avoid gluten must not simply eat gluten-free foods but also ensure that food was handled safely, without contact with gluten-containing substances [26].

5 Diagnostic Tools for Non-Celiac Gluten/Wheat Sensitivity (NCGWS)

Non-Celiac Gluten/Wheat Sensitivity (NCGWS) is frequently misperceived due to the absence of a definitive diagnostic biomarker. Unlike celiac disease (CD), which can be diagnosed using serological tests and intestinal biopsy, or wheat allergy confirmed by IgE testing, NCGWS is based on symptomatic assessment and elimination of other gastrointestinal disorders [32]. The double-blind placebo-controlled crossover challenge (DPBC-C) remains the most scientifically accepted approach but is labor intensive, expensive, and not suitable for routine clinical practice. Scholars have therefore sought to identify surrogate endpoints and diagnostic methods to reduce clinical burden [6].

Zonulin, a protein regulating the permeability of tight junctions in the intestinal lining, is one of the most investigated potential biomarkers. High serum zonulin concentrations are linked to high intestinal permeability, commonly known as leaky gut, which is one of the initiating events in both celiac disease and NCGWS [33]. Studies have shown that zonulin levels are significantly higher in CD and NCGWS groups and reduce considerably following a gluten-free diet after six months in HLA-DQ2/8positive groups. A diagnostic plan combining zonulin levels with gender and symptom patterns may increase diagnostic accuracy to 89%. However, zonulin levels may also be elevated in asymptomatic individuals with genetic predisposition, raising concerns about its specificity [34].

Confocal laser endomicroscopy (CLE) is another innovative diagnostic method enabling real-time observation of mucosal responses in the small intestine following exposure to suspected antigens [35]. Positive CLE findings — characterized by fluorescein leakage (major criterion) and increased intraepithelial lymphocytes or villous changes (minor criteria) — have been related to increased probability of wheat sensitivity. Patients with a positive CLE outcome on a gluten-free diet showed more symptomatic improvement [36]. However, CLE is rather invasive and has relatively low sensitivity/specificity (under 80%), limiting its routine clinical use.

Fecal calprotectin (FCP) has been suggested as a possible non-invasive method to differentiate NCGWS from IBS and functional dyspepsia (FD) [32]. Approximately 31% of confirmed NCGWS patients showed high FCP while all IBS/FD controls showed normal levels. Six months following a strict gluten-free diet, 65% of FCP-positive patients normalized their values, suggesting a correlation between intestinal inflammation and symptomology in this subgroup. These results confirm that NCGWS might not be a homogenous disorder but could have immunologically active and non-immune-mediated subtypes [35].

Anti-gliadin antibodies (AGA), including IgA and IgG, have sometimes been linked to NCGWS and may have some diagnostic value. In a study of 492 IBS patients, subjects testing positive for AGA who adhered to a gluten-free diet showed more than 50% improvement in symptoms [33]. Although AGA may be present in other diseases or even healthy individuals, it may prove useful as a parameter within a multi-parametric diagnostic tool [6]. In general, a combined diagnostic pattern containing multiple markers — the presence of HLA-DQ2/8, clinical symptoms, and dietary intervention responses — may prove more effective than any single standalone marker [37]. This integrative model is consistent with the current understanding of NCGWS as a heterogeneous condition with diverse pathophysiological mechanisms.

6 Gluten's Interaction with Immunity and Inflammation

Gluten is known to bring about inflammation when it causes an abnormal immune reaction, especially in individuals diagnosed with celiac disease or non-celiac gluten sensitivity [38]. In celiac disease, following gluten ingestion, the immune system mistakenly perceives elements of gluten — particularly gliadin — as a foreign aggressor. The high proline content of gluten means that its fragments are not easily digested by normal digestive enzymes, leaving large gliadin peptides intact in the gut. The so-called 33-mer peptide of gluten is particularly harmful since it is extremely recalcitrant to digestion and highly capable

of activating the immune system [20]. These undigested peptides are capable of traveling across the intestinal lining, especially when the gut barrier is compromised.

Even isolated gluten can reduce intestinal permeability resistance by modulating a protein named zonulin that regulates the tightness of the junctions between cells of the gastrointestinal lining [39]. Zonulin release in response to gluten increases tight junction permeability, resulting in a leaky gut that allows entry of gliadin peptides and other harmful substances into the bloodstream, causing a strong immune response [40]. When the gliadin peptides penetrate through the gut barrier, they encounter immune cells in the tissue below the intestinal lining. The enzyme tissue transglutaminase (tTG) modifies the gliadin peptides through deamidation, introducing additional negative charges that make the peptides more visible to the immune system (Fig. 3) [41]. These altered gluten peptides are gathered by antigen-presenting cells (APCs) which present them to T cells [42].

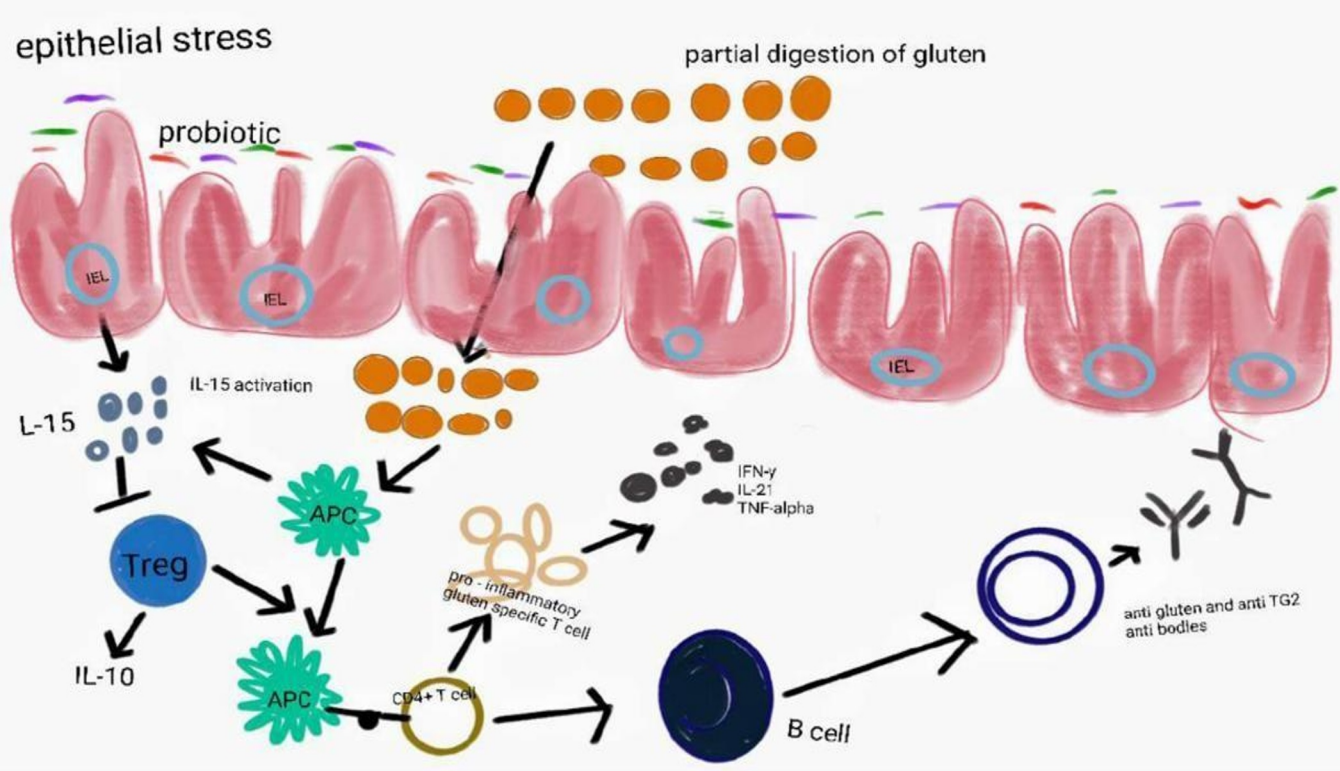

Fig. 3 Immune response activation mechanism in celiac disease. Human proteases partially digest gluten-containing food, releasing immunogenic gluten peptides. Such peptides penetrate the intestinal lining under conditions of epithelial stress, triggering intraepithelial lymphocytes (IELs) and antigen-presenting cells (APCs). The APCs stimulate CD4+ T cells to produce a pro-inflammatory cytokine response (IFN-γ, IL-21, TNF-α), and B cells generate anti-gluten and anti-tTG2 antibodies. Regulatory T cells (Tregs) can modify this response with IL-10 and TGF-β; however, the balance shifts towards inflammation in celiac disease patients.

In individuals who possess genetic risk factors, particularly the HLA-DQ2 or HLA-DQ8 genes, T cells perceive the gluten peptides as toxic and become stimulated to generate inflammatory cytokines such as interferon-gamma and interleukin-15 [43]. This inflammatory environment causes the destruction of villi, reducing nutrient absorption and resulting in malnutrition, weight loss, anemia, and related complications. In some individuals, the immune response extends beyond the gut, causing skin diseases such as dermatitis herpetiformis, joint aches, headaches, and neurological issues [14]. This occurs because the immune system produces antibodies not only to gluten but also to tissue transglutaminase (tTG), which is a body enzyme [44]. These antibodies can travel in blood and destroy other tissues, making celiac disease an autoimmune disorder analogous to type 1 diabetes and rheumatoid arthritis.

In individuals with non-celiac gluten sensitivity, the mechanism differs slightly; it is not likely to involve the full autoimmune reaction and may not indicate villous destruction as observed in celiac disease [45]. Nevertheless, they still experience

inflammation and symptoms upon gluten intake. It is thought that in gluten sensitivity, the innate immune system could be more activated against gluten, causing low-grade inflammation without complete destruction of the intestine [46]. Additionally, gluten may impact the gut microbiota; research has revealed that gluten can alter the natural balance of intestinal bacteria, decreasing beneficial microbes and enabling harmful microbes to proliferate [47]. This dysbiosis may enhance inflammation and gut permeability, creating a vicious cycle in which the gut barrier weakens and the immune system remains on high alert.

Exposure to gluten causes epithelial cells lining the gut to release molecules that attract immune cells such as intraepithelial lymphocytes (IELs). When over-stimulated, these immune cells directly attack the gut lining (Fig.4), contributing to inflammation and tissue damage. Gluten exposure highly upregulates the production of interleukin-15, which in turn stimulates IELs and the resultant death of epithelial cells [48]. The primary intervention for gluten-related diseases therefore remains the complete elimination of gluten from the diet. A strict gluten-free diet gives the gut barrier an opportunity to repair and inflammation an opportunity to resolve [15]. Nevertheless, emerging therapies targeting enzyme-mediated gluten peptide degradation, inhibition of tissue transglutaminase activity, or immune desensitization through vaccination are also under investigation [48].

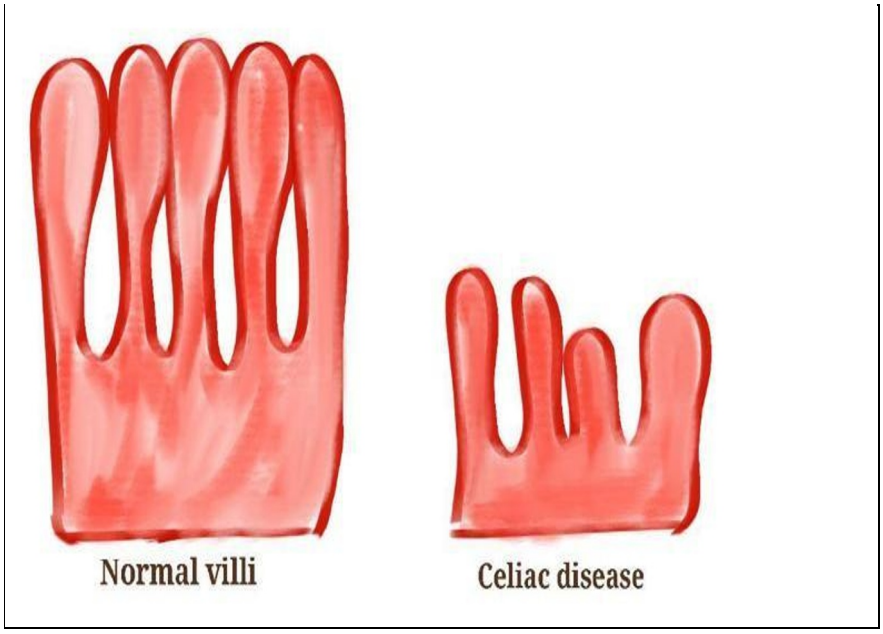

Fig. 4 Comparison of small intestine morphology of a healthy person and a patient with celiac disease (CD). In the normal small intestine, villi are intact and crucial for nutrient absorption. In a CD patient, immune-mediated destruction results in villous atrophy, a flattened mucosal surface, and severely impaired nutrient absorption.

7 Advances in Gluten-Degrading Enzymes

Gluten protein poses an enormous challenge to people with celiac disease (CeD) and non-celiac gluten sensitivity (NCGS). The high levels of proline and glutamine in gluten peptides make them resistant to complete digestion by human gastrointestinal enzymes [49]. This results in the persistence of immunogenic peptides, including the notorious 33-mer of α-gliadin, capable of eliciting adverse immune responses in susceptible individuals. To overcome this, studies have focused on producing exogenous enzymes capable of degrading these resistant peptides and reducing their immunogenicity in vivo [50].

Prolyl endopeptidases (PEPs) have emerged as promising candidates for this task. These enzymes take specific cleavages by cutting peptide bonds at the back side of proline amino acids, effectively degrading proline-containing gluten peptides. Different microbial PEPs from *Flavobacterium meningosepticum*, *Sphingomonas capsulata*, and *Myxococcus xanthus* have been shown to be effective in vitro degradation of immunogenic gluten sequences. A randomized controlled study utilizing PEP from *F. meningosepticum* found that pretreatment with PEP decreased carbohydrate and fat malabsorption after two weeks in an asymptomatic cohort of 20 celiac patients [51].

Interactions between PEPs and other proteases have been studied to provide better gluten degradation. Conjugation of PEP from *S. capsulata* with EP-B2, a glutamine-selective cysteine endoprotease of barley, has been developed as ALV003, which has demonstrated the prospect of destroying antigenic gluten pieces in the intestines [52]. EP-B2 binds to glutamine residues that complement the proline residue-specific activity of PEPs, resulting in more complete gluten degradation [53]. Plant-derived enzymes have also been explored; the carnivorous pitcher plant enzymes nepenthesin and neprosin demonstrate strong glutendegradation activity at acidic gastric pH, efficiently breaking down gliadin peptides to make them less immunogenic. Neprosin represents a new category of prolyl endoprotease that expands the range of available enzymes for gluten degradation.

Protein engineering has resulted in improved synthetic enzymes with enhanced gluten-degrading capabilities. KumaMax, a variant of kumamolisin-As from *Alicyclobacillus sendaiensis*, demonstrates high specificity and efficacy against immunogenic gliadin peptides. Further constructions led to Kuma030, which showed better activity in breaking the 33-mer peptide than earlier models [53]. These genetically modified enzymes are an important advancement in the creation of effective oral treatments for gluten-related disorders.

Exopeptidases such as dipeptidyl peptidase IV (DPP-IV) from *Aspergillus* species have also been investigated as adjuncts, splitting dipeptides at the N-terminus of peptides including those with proline residues [52]. Although DPP-IV alone may be insufficient to completely breakdown immunogenic gluten peptides, its combination with endopeptidases such as PEPs can augment overall gluten degradation. The human microbiome is also a potential source of gluten-degrading enzymes; oral and intestinal bacteria including *Rothia mucilaginosa* and *Bacillus* species express subtilisin proteins that can cleave immunogenic oral gliadin peptides [49]. TAK-062, a synthetic orally administered enzyme, has successfully completed Phase 1 clinical trials and has shown safety and efficacy in degrading gluten in the stomach [50]. These advances emphasize the promise of enzyme therapy as an adjunct or substitute to a strict gluten-free diet [52].

8 Conclusion

Gluten is not harmful to the majority of the population; however, it is a severe health-threatening factor for patients with celiac disease, wheat allergy, or non-celiac gluten sensitivity (NCGS). Its high content of proline and glutamine makes it indigestible, allowing immunogenic peptides, especially from gliadin, to penetrate the gut barrier and cause immune reactions in genetically predisposed individuals (HLA-DQ2/DQ8 carriers). This causes chronic inflammation, villous atrophy, and systemic symptoms in CD. Gluten also promotes intestinal permeability, causing leaky gut and extraintestinal manifestations. Modern wheat varieties may exacerbate this due to increased immunogenic gluten content. The existing treatment based on a strict gluten-free diet is difficult to adhere to and does not ensure total recovery for all patients. Genetically modified cereals, engineered enzymes (e.g., PEPs, EP-B2, KumaMax), probiotics, and gluten-degrading enzymes hold considerable promise. Further studies are needed to develop safer food substances and effective treatments for individuals with gluten-related disorders.

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Author Contributions

Aindree wrote the main manuscript. R.P.S. designed and supervised the study.

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Competing Interests

The authors declare no competing interests.

Declaration of Generative AI and AI-Assisted Technologies in the Writing Process

The authors used AI tools to correct grammar, improve the quality of writing and paraphrasing, and enhance the quality of images.

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