

## Gluten-Free Diet: A Review Focusing on Wise Food Choices

Lee Yeonjae<sup>1</sup>, Park Junghyun<sup>2</sup> and Lee Jeong-Sang<sup>3\*</sup>

<sup>1</sup>Hankuk Academy of Foreign Studies, South Korea

<sup>2</sup>Department of Korean Medicine, Gachon University, South Korea

<sup>3</sup>Department of Biotechnology and Functional Food, Jeonju University, South Korea

All the authors have contributed equally for this article.

**\*Corresponding Author:** Lee Jeong-Sang, Assistant Professor, Molecular Mechanisms of Functional Foods Laboratory, Department of Biotechnology and Functional Food, College of Medical Science, Jeonju University, South Korea.

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### Abstract

A Gluten-free diet has gained immense popularity not only among celiac disease patients but also in the normal people since they believe that the diet is a healthier alternative compared to regular diet. However, a vague belief toward a Gluten-free diet without precise information has resulted in an irrational choice of the diet. Originally, a Gluten-free diet is a medically advised diet for the celiac disease patients who are suffering from auto-immune disorder due to the gluten ingestion. However, misunderstanding and unverified belief regarding the diet have made consumers purchase expensive gluten-free products as well as not considering their own health conditions for the last 3 decades. The food industries, the media, and celebrities have encouraged these consumers to choose gluten-free foods over gluten-containing foods without precise information. The diet was revealed to be a top-searched keyword between 2005 and 2015 in the “Google search”. While a Gluten-free diet plays a vital role in celiac disease patients and achieved the popularity, consumers in particular without celiac disease should be judicious to follow the diet. This study aimed to provide plausible information and suggests a future direction in terms of the Gluten-free diet and its popularity based on the previous literature.

**Keywords:** *Gluten-Free Diet; Celiac Disease; Glutens; Consumers; Review*

### Abbreviations

GRDs: Gluten-Related Disorders; GFD: Gluten-Free Diet; CD: Celiac Disease; TTG: Tissue Transglutaminase; APC: Antigen-Presenting Cells; IELs: Intraepithelial Lymphocytes

### Introduction

Google ranked “Gluten-free diet” as the top-searched diet keywords between 2005 and 2015, which indicated that “gluten-free diet” is popular not only in patients suffering with gluten-related disorders’ (GRDs) but also in general population [1]. In fact, a gluten-free diet (GFD) has gained considerable popularity among people without gluten-related medical conditions [2]. The diet reflected as gluten-restricted diet is demonstrated to be an effective treatment for GRDs such as celiac disease, non-celiac gluten sensitivity, and wheat allergy [3-5]. A wide spectrum of GRDs triggered by the oral ingestion of gluten has been reported all around the world. Worldwide, wheat, a gluten-rich grain is considered to be the most consumed cereal grain which provides up to 50% of the total caloric intake in developed and developing countries [3]. Wheat contains structural/metabolic and storage proteins and gluten is a composite of storage proteins in wheat [3,6]. The gluten is a byproduct of wheat starch production and is insoluble in water. It is an important factor in determining the quality of flour in food processing, such as baking, noodles, and confectionery, and has the ability to make the dough chewy and soften the bread [7,8]. Globally, with the increase in the consumption of wheat products, the number of GRDs has also increased, which speaks about the importance of gluten in wheat products. This review aims to provide recent comprehensive information in terms of a GFD, and also deals with the popularity of multidimensional perspectives and future direction.

### Gluten-related disorders (GRDs): celiac disease

Gluten, named from the Latin gluten meaning glue, is a complex mixture of storage proteins from grains such as wheat, rye and barley and is composed mainly of gliadin and glutenin. Gliadin in gluten is soluble in alcohol, but glutenin is insoluble and plays an important role in baking. Gluten is mainly found in the Western diet and the gluten intake is increasing due to the growing replacement of rice by wheat in many countries according to the progressive Westernization. GRDs are simultaneously increasing in incidence [3]. Approximately 1% of the world's population suffers from celiac disease and 10~15% of them have potential [9]. A previous study reported that about 3 out of 10 people in the U.S. have the gluten sensitive constitution, and even people with latent risk include more than 80% of the total population suffering from the allergic diseases caused by gluten [10].

GRDs can be classified into three broad categories: autoimmune, non-autoimmune/non-allergic, and allergic disorders. Celiac disease (CD), also spelled coeliac disease is a multisystem autoimmune based disorder that is induced by dietary gluten in genetically susceptible individuals [11]. To be specific, a CD is known to occur in people who carry the DQ2 or DQ8 human leukocyte antigen haplotype [4]. Although various clinical symptoms of CD have been detected depending on the age of the patients and duration of out of intestinal manifestations [9], classical symptoms of CD are chronic diarrhea, abdominal distention, malabsorption, and loss of appetite. Patients with CD are usually diagnosed based on a combination of typical symptoms and an intestinal biopsy detecting gluten-sensitivity enteropathy [12,13].

In respect to the pathophysiology of CD, previous research related to adaptive immunity is more plentiful than the data regarding the innate immune response of CD. Since gluten proteins are rich in proline and glutamine that are difficult for humans to digest, when they fail to be broken completely, up to 33 amino acids long peptides are left. Subsequently, they pass through the epithelial barrier of the intestine and the peptides go into the lamina propria via a transcellular or paracellular route [4,14]. An adaptive immune reaction occurs within the lamina propria, a thin layer of connective tissue, that is a part of the mucosa. Tissue transglutaminase (TTG) deamidizes the gliadin, which increases immunogenicity by changing the charge on the gliadin particles that facilitates binding to the HLA-DQ2 or DQ8 molecule on the antigen-presenting cells (APC) [4]. Gliadin reactive CD4+T-cells identify gliadin peptides presented by APC and subsequently produce inflammatory cytokines, in particular, interferon- $\gamma$  [4,14]. In this process, the release of metalloproteinases causes tissue injury, nevertheless TTG antibodies are formed through ambiguous metabolism during the process, though the role of these antibodies is also obscure [15,16]. On the other hand, the innate immune response to gluten appears due to the expansion of intraepithelial lymphocytes (IELs) since cytotoxicity of epithelial layer is mediated by MICA/NKG2D induced IELs. However, the mechanism in the epithelium and lamina propria remains unclear [4,5].

Celiac disease should be well managed as it is associated with other comorbidities such as liver disease, pancreatic disease, and cardiovascular disease [4]. CD is also linked to nutritional deficiencies, osteoporosis, growth inhibition, infertility, skin diseases, small bowel cancer, as well as symptoms of limited absorption of nutrients due to inflammation of small intestinal villi [4,5].

### Gluten-free diet

A GFD is a gluten excluded diet and has been regarded as the main remedy for GRD, especially CD. Wheat including spelt, kamut, semolina, and triticale, rye, and barley including malt are the grains that CD patients should avoid in order to alleviate gastrointestinal manifestation [11]. On the contrary, it has been reported that safe grains for GFD are rice, amaranth, buckwheat, corn, millet, quinoa, sorghum, teff (an Ethiopian cereal grain), and oats [11]. Although there are substitute grains of wheat, rye, barley, and hybrids including kamut and triticale, they are not often fortified with vitamins, and vitamin deficiency has been detected in patients who maintained the diet for a long time, so the diet should be implemented under the supervision of skillful dietitian [9,11]. Besides, lifelong strict adherence to the diet for CD individuals is a considerable challenge [4,5,11]. In general, since substitutes of gluten-containing foods are expensive, a GFD can be a financial burden for CD population. In addition, a recent study indicated that better adherence for a GFD was associated with greater self-regulation, habit, self-efficacy, priority, facilitation, and support [17]. Another aspect of the GFD to consider is quality of life for CD patients. Hidden gluten is found in numerous industrialized foods and the strict adherence of the GFD has an unavoidable impact on CD patients' social life, so they can be socially isolated. Thus, in order to maintain the diet, experts pointed out that the behavioral intervention and psychological support are required within the multi-disciplinary treatment team [17].

## Popularity

It has been reported that the compliance of the diet is difficult for CD patients who are thought to be rare. Gluten-free industry has grown explosively and the market is anticipated to increase 7.59 billion U.S. dollars by 2020 [18]. The reports showed that the 26% proportion of people choose GFD as a healthy option, whereas only 8% reported to contain gluten sensitivity [19]. Among normal population, the GFD has become popular as it is perceived as a healthy diet, especially in situations like nonspecific gastrointestinal symptoms and overweight or obesity [3]. Furthermore, a U.S. study using NHANES 2009 - 2014 reported that population with self-diagnosed gluten sensitivity is also increasing, which can be one of the main reasons for the popular trend [20]. Another study reported the association between socioeconomic factors and a GFD revealed that the popular Internet searches of a GFD were significantly associated with higher proportion of non-Hispanic white residents and higher household incomes in the U.S [1]. The study indicated that the prevalence of CD in the U.S. is high in Caucasian population, but this does not elucidate the high search rates because the occurrence is moderately increasing in white residents unlike the escalating popularity of the GFD.

## Gluten-free Industry

In the gluten-free industry, products are manufactured "gluten-free foods" based on the following criteria, i.e., a gluten content below 20 ppm or 20 mg/kg are allowed to be labeled as "gluten-free" and the content below 100 mg/kg, can be labeled as "very low gluten" based on the Codex Alimentarius and the European Union regulation [21,22].

From the last 3 decades, a gluten-free lifestyle has become popular among the people of United States and the country has spent over \$15.5 billion on retail sales of gluten-free foods in 2016 [23]. The reasons for the rapid growth of gluten-free market include the consumers who tend to recognize that gluten-free foods are healthier than gluten-containing foods due to the perception that gluten ingestion is harmful to health. The target consumers for the gluten-free foods include CD or gluten sensitive patients as well as health-conscious people. The medical journals' report on the benefits of gluten-free foods along with the well-being boom fueled by consumers spending on gluten-free foods due to aggressive marketing by food companies and the participation of celebrities [23]. Some athletes advocated a GFD in order to improve their athletic performance and stamina. In a study of athletes without CD including the Olympic medalists, 41% follow a GFD 50%~100% of the time in 2015 [24]. Of them, 57% were reported with self-diagnosed gluten sensitivity and they also attributed their fatigue to gluten ingestion. In addition, they indicated that they earn information and guidance for a GFD from online (28.7%), their trainer or coach (26.2%), and other athletes (17.4%) [23,24].

## Adequacy of GFD for a normal population

Health benefit of a strict gluten-free diet for people without coeliac disease remains inconclusive. Since avoiding whole grain can be detrimental for a normal population, cautious application of a GFD is needed for some reasons based on the previous literature, i.e. nutritional balance [25], exposure to heavy metals [19] and financial burden [1,4] etc. Generally, it has been reported that the gluten-free foods are frequently contain more carbohydrates, lipids and fewer micronutrients and fiber compared to their gluten-containing equivalents [5,23,26]. An Australian study reported that the nutritional quality of gluten-free foods was not superior to gluten-containing foods and any nutritional advantage was not found in gluten-free foods [27]. According to the study, lower protein content was detected in gluten-free foods across core food groups, in particular, pasta and breads. In the secondary analysis, no differences were reported between gluten-free and gluten-containing foods in terms of total energy, fiber content, saturated fats, total sugar, and sodium content [27]. Furthermore, exposure to heavy metals for consumers of a GFD was reported because they tend to consume more rice and fish instead of gluten-containing foods. A previous study indicated an almost 4-fold increase in blood mercury levels in patients who implemented a GFD [28]. Moreover, another report indicated that the rice grown in flooded fields can easily absorb inorganic arsenic [19]. The financial burden has also raised in order to maintain a GFD regardless of having CD or not [26]. A UK study related to the cost and nutritional quality of a GFD reported that GF products were 159% more expensive than regular foods [26]. Lastly, consumers are under the misapprehension with regard to weight loss benefit of a GFD. Weight loss effect of a GFD for the regular population has not been proved in spite of eager endorsements of celebrities [2]. Even some gluten-free foods have a greater energy than corresponding regular products, which means that GF products do not mean low-calorie foods [29].

### Future direction behind the popularity of a GFD

First of all, the health benefits and drawbacks of gluten are required to be informed to the general population to make a prudent decision. Unlike commercial advertisements for the gluten-free foods, gluten may be beneficial to the individuals with dyslipidemia and without CD. A randomized crossover study appeared that gluten attributes the reduction of serum triglyceride levels [30]. In addition, gluten may play a significant role in lowering blood pressure and also to boost the immune systems [2]. Besides the health benefits, gluten has an ability to retain air in the protein matrix, which improves the baking and processing of the products, thus has been frequently used by the food industries [5]. Consumers should be aware of evidence-based disadvantages or advantages of gluten rather than biased information through the grapevine or media and be smart enough to consume gluten-free foods according to the appropriate needs. For this purpose, nutrition experts should be involved in raising the consumer awareness and likewise appropriate standards and regulations at the government-level are required.

Secondly, reasonable assessment for a GFD should be performed and the nutritional properties of a GFD should be monitored to make a balanced and healthier GFD as per the public demands [5]. The prevalence of overweight or obesity in a population with CD has increased even though it is not clear whether the prevalence is associated with adherence to a GFD or not [5]. Nutritional evaluation to follow a balanced GFD is required by nutritionists for CD patients or normal followers to maintain their health [31]. Following strategies for a nutritional adequate GFD should also be taught by dietitians with experience on CD.

Thirdly, food companies have to develop and improve gluten-free foods that can meet consumers' expectation in the aspects of health and quality. Despite the high prices, gluten-free foods are chosen by consumers, therefore, manufacturers need to put their efforts on making better quality foods. Micronutrients fortified foods and mimicking the viscoelastic properties of gluten can be good examples. Furthermore, in the future, the gluten-free products need to reflect consumers' changing lifestyle such as involving the consumers in the process of developing and marketing gluten-free foods via market research [32].

Lastly, good alternative components for gluten-free products need to be developed in order to make them have good qualities. For instance, a study indicated that processed products containing amaranth, quinoa, and buckwheat have higher level of the protein, fat, fiber and minerals compared to rice and corn-based products [33]. In addition, gluten-free foods using teff, a cereal used as a stock in Ethiopia, have recently been developed. Teff is a gluten-free grain with higher nutritional value than wheat [34].

### Conclusion

A gluten-free diet became a popular diet embracing both populations with and without celiac disease. However, when we investigate thoroughly the actual advantages and disadvantages of gluten-free foods, the values may be over-estimated in particular for a normal population in spite of the expensive prices. Therefore, accurate knowledge and information based on scientific evidence need to be diffused for the implementation of a balanced GFD and this will be possible via expertized nutritional support and the collaboration of government and food industries.

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### Conflict of Interest

The authors declare that they do not have any conflict of interest regarding this original article.

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