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REVIEW

Recent strategies for tackling the problems in gluten-free diet and products

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ABSTRACT

The gluten-free food market is growing with the increases in the number of people who adhere to gluten-free diet. The noteworthy increase in the number of people following a gluten-free diet may be associated to the diagnosis of many silent and subclinical celiac disease cases, improved knowledge of celiac disease, gluten allergy or gluten sensitivity as well as to popular belief that gluten-free diet is healthier. Despite the increase in the number of people following a gluten-free diet, the lack of awareness and knowledge about gluten-free diet generates problems for non-celiac people who are considering that gluten-free products are healthier as well as for celiac people who have to follow gluten-free diet. Notwithstanding the increasing interest in adopting gluten-free diet, there are still important obstacles affecting the adherence to gluten-free diet. The limited availability, high price of products, insufficient labeling, cross-contamination risk, treatment burden, lack of knowledge and information about celiac disease and about gluten-free diet, psychological factors in celiac patients, the adverse effects of a gluten-free diet and quality defects of gluten-free products are among the major problems that faced by celiac patients. In this perspective, the aim of this review is to provide an overview of important challenges in the maintenance of a strict gluten-free diet that faced by celiac patients during the adherence to gluten-free diet and related approaches have been able for tackling the problems.

KEYWORDS

Celiac disease; gluten-free diet compliance; lack of awareness; high price of products; Insufficient labeling; the limited availability; cross-contamination risk; The adverse effects of a gluten-free diet; quality defects

Introduction

Celiac disease characterized by the life-long intolerance to gluten is a multi-symptom, autoimmune disorder. A lifelong and complete removal of gluten from the diet of patients is the only known treatment for patients with celiac disease and adherence to a strict gluten-free diet is likely to improve symptoms of patients (Mert, Sumnu, and Sahin 2016).

The noteworthy increase in the number of people following a gluten-free diet may be related to the diagnosis of many silent and subclinical celiac disease cases, improved knowledge of celiac disease, gluten allergy or gluten sensitivity as well as to the popular belief that gluten-free diet is healthier (Roman, Belorio, and Gomez 2019).

Despite the increase in the number of people following a gluten-free diet, the lack of awareness and knowledge about gluten-free diet generates problems for non-celiac people who are considering that gluten-free products are healthier as well as for celiac people who have to follow gluten-free diet. The significant relationship between knowledge of celiac disease and adherence to a gluten-free diet has also been shown. Although the prevalence of the celiac disease and the findings of persistent signs, symptoms, and small intestinal enteropathy are more common in patients than previously thought, long-term adherence to a gluten-free diet is poor in people with celiac disease. It has been found that over one-third of people diagnosed with celiac disease have never seen a dietitian (Halmos et al. 2018). The association between knowledge of celiac disease and the adherence to the diet as well as the relationship between knowledge of gluten-free diet in celiac patients and their adherence to the diet suggests the development of training programs for celiac patients (Paganizza et al. 2019). Gluten-free diet has also started to be self-initiated by a great number of people who are trying to lose weight or who are considering gluten-free diet as a fashionable lifestyle trend. However, it has been speculated that the consumption of gluten-free products can lead to weight gain unless bakery products are not changed with vegetables, fruits etc. since gluten-free products contain a higher amount of starch, fat etc. Furthermore, they have lower nutritional values. Consequently, the adherence of gluten-free diet due to the lack of awareness and knowledge of non-celiac people is continuing debate and thus the necessity of further research to define the effects of a gluten-free diet on non-celiac people has also been highlighted in many studies.

The positive effects of an increased level of awareness and knowledge toward celiac disease on compliance with a gluten-free diet have been highlighted in many studies. Celiac people have a higher level of knowledge about gluten-free diet as compared to non-celiac followers, but most of celiac patients following gluten-free diet still experience

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difficulties with food labeling due to the lack of patients' awareness and knowledge.

The number of people who adhere to a gluten-free diet and hence the gluten-free food market is growing rapidly. However, there are still important barriers affecting to adherence to gluten-free diet. The limited availability, the high price of products, the psychological factors in celiac patients, cross-contamination risk, and quality defects of gluten-free products are among the major problems faced by celiac patients. It has been reported that a high treatment burden for patients also creates difficulty in adherence to a gluten-free diet. Available evidence also suggests that there is an association between poor gluten-free diet adherence and self-reported depressive symptoms. The adverse effects of a gluten-free diet like low nutritional quality of a gluten-free diet and health problems potentially induced by the gluten-free diet are also challenges that faced by patients. The consumption of gluten, celiac patients' immune system generates antibodies against this protein resulting in damage to the tiny hairlike projections in the small intestine and hence malabsorption of macro and micro-nutrients. Furthermore, gluten-free products are incompetent with their gluten-containing counterparts in terms of nutritional characteristics. Therefore, nutrient deficiencies are another problem related to following a gluten-free diet. The studies also reflected the fact that gluten avoidance may be associated with adverse effects in patients without proven gluten-related diseases. For example, it has been speculated that the consumption of gluten-free products can lead to weight gain unless bakery products are not changed with vegetables, fruits etc. (Wild et al. 2010; Wu et al. 2015). It has also been stated that many adults as well as children with celiac disease are overweight or obese at diagnosis, or become overweight after treatment. Consequently, patients have a higher risk of developing nonalcoholic fatty liver disease. The observation prompted the hypothesis that modifications like decreasing a high-fat diet and a sedentary lifestyle can yield improvements in nonalcoholic fatty liver disease (Reilly et al. 2015). The studies also showed that long term dietary intake of gluten was not related to the risk of coronary heart disease. Thus, the promotion of gluten-free diets in order to prevent coronary heart disease among asymptomatic people without celiac disease should not be recommended. The new onset of constipation observed in patients after the introduction of a gluten-free diet may be related to a decrease in fiber intake due to gluten-free diet. Therefore, the studies suggest that it is essential to broaden the research to determine whether the gluten-free diet may be associated with adverse health problems in people.

Glutenin and gliadin are the major fractions of gluten. Thus, gliadin gives viscous properties and extensibility to a dough system, glutenin is, on the other hand, creates the elastic and cohesive characteristics of the dough. Since gluten is the primary structure-forming protein in flour, the removal of gluten leads to some quality defects in gluten-free products. Gluten-free products generally have low volume, firm texture, and stale rapidly. Furthermore, they are devoid of the unique taste and aroma contributed by distinct volatile compounds. Since consumer expectations for gluten-free products are greatly affected by traditional product features; manufacturers and scientists determine the quality attributes based on wheat-containing products. Therefore, another critical problem related to adherence to gluten-free diet is the quality defects of gluten-free products.

Numerous research papers and academic reviews have focused on the problems in the gluten free diet and possible approaches to improve the quality of celiac patients' life. The challenges related to quality defects of gluten-free products with particular emphasis on technological strategies to enhance quality parameters of gluten-free products have become another research topic, and in literature, there are some studies conducted on the quality of gluten-free products also. However, to the best of our knowledge, there is no work conducted on strategies for tackling the problems in gluten-free diet and products. Thus, the objective of this paper is to review important challenges in maintenance of a strict gluten-free diet that faced by especially celiac patients during the adherence to a gluten-free diet and related approaches that have been able to tackle the problems.

The prevalence of celiac disease and diagnosis problem

Celiac disease, also known as gluten-sensitive enteropathy, is a multi-symptom, autoimmune disorder. As a T cell-mediated autoimmune like disease, it is triggered by the ingestion of gluten proteins from wheat and related grains. The origin of this disease may be related to genetic factors (HLA and non-HLA genes). In genetically susceptible people, who express HLA DQ2 or DQ8 (positive antigen-presenting cell), T lymphocytes recognize gliadin through the antigen presentation process. Tissue transglutaminase interacts with gliadin proteins, leading to modification (deamidation) of certain glutamine residues. Deamidation improves the affinity of the peptide to the antigen-binding groove of HLA-DQ2 or HLA-DQ8. The deamidated gliadin peptide-tissue trans glutaminase complexes, which are presented by antigen presenting cells (B cells) trigger the increased activation of specific gluten-responsive T cells. The interaction between activated T cells and the B cell response together results in the stimulation of antibody-secreting cells and generate an inflammatory process that orchestrates the destruction of the intestinal mucosa (Gujral, Freeman, and Thomson 2012; Tye-Din, Galipeau, and Agardh 2018; Petersen et al. 2020; Wei et al. 2020). As a result of the inflammation, the small intestine is unable to absorb nutrients such as iron, calcium, folate, and B vitamins because of the loss of brush border proteins and enzymes. Rarely, life-threatening hypokalemia or hypomagnesemia may be observed. Lactose malabsorption, which is generally characterized by a deficiency of lactase, may also be occurred in celiac patients (See and Murray 2006).

Environmental factors are also found to be effective in celiac disease (Serena, Lima, and Fasano 2019). Since it is triggered by the inappropriate reaction of the body's immune system to prolamins present in wheat (gliadin), rye (secalin), barley (hordein), and their crossbreeds, the only available treatment for celiac patients is the permanent withdrawal of gluten from the diet of patients throughout their lifespan, and elimination of gluten from diet results in the reduction of symptoms (Mert, Sumnu, and Sahin 2016)

Although celiac disease is a common disease in the world and it is frequently misdiagnosed or undiagnosed. One of the possible reasons for misdiagnosis might be related to the complicated diagnosis procedure and the lack of awareness among physicians and patients. The symptoms of celiac disease indicate similarities with many common chronic intestinal disorders, such as irritable bowel syndrome, Crohn's disease and ulcerative colitis. Furthermore, wide variations in the sensitivity may also lead to misdiagnosis. For example, some celiac patients suffering from the disease do not manifest the symptoms or their complaints while some patients display very slight complaints, which are regarded as of secondary importance. Celiac disease may also show similarities with gluten sensitivity, which might be another reason for its misdiagnosis. It is often typical or even silent on clinical grounds that lead to the risk of long-term complications such as osteoporosis, infertility, and cancer; thus, it may also remain undiagnosed (Fasano and Catassi 2001; Van der Windt et al. 2010).

While it is difficult to calculate the true extent of celiac disease occurrence, the prevalence of it is estimated to be at least 1:133 in the United States and it is approximately present in 1:150–300 in Europe (McLoughlin et al. 2003). However, recent studies showed that celiac disease is more common than previously reported and it is increasing worldwide. The latest systematic review has shown the pooled global prevalence of celiac disease was 1.4% (Sing et al., 2018). The importance of use of simple, sensitive and specific serological screenings tests has been highlighted to determine the true prevalence of celiac disease. In order to determine the real incidence of celiac disease, the necessity of creating awareness among physicians about the onset of symptoms, associated disorders, and the use of serology testing especially in developing countries has been highlighted (Cataldo and Montalto 2007).

The importance of gluten-free diet

Rationale for the gluten-free diet

The sole treatment for celiac disease is to follow a stringent gluten-free diet through patients' life-span. In most patients with celiac disease, the strict adherence to gluten-free diet should lead to complete symptomatic and histologic resolution of the disease as well as decreases in the risk of complications (See and Murray 2006). Therefore, the overall aim of treatment for celiac disease should help to relieve the symptoms, heal the intestine, and reverse the consequences of malabsorption.

It is critical to motivate and educate celiac patients about the necessity of a strict gluten-free diet since such a diet has a protective role against morbidity and mortality caused by associated conditions, including infertility, skeletal disorders, and malignancy. Corrao et al. (2001) has shown the reverse relationship between mortality and compliance with a gluten-free diet. As compared to the general population, the mortality rate was not increased in patients adhering to a strict gluten-free diet. On the other hand, the mortality rate was 2-6 times higher in noncompliant patients. In the study of Biagi and Corazza (2010), it has been reported that the mortality rate in celiac patients seems to be associated with both the extent of lesions along with the small bowel and the quantity of gluten consumed before and after the diagnosis of celiac disease. The findings of the study showed that the mortality rate for celiac disease seems to be higher in Southern than in Northern Europe and this might be related to national gluten consumption. The authors proposed that the mortality rates may be linked to the amount of gluten consumed not only after but also before the diagnosis of celiac disease (Biagi and Corazza 2010). See and Murray (2006) found that elevated levels of mortality have been related to gastrointestinal malignancies, primarily intestinal lymphoma, which has been reported in 10%–15% of adult patients who have been noncompliant with the gluten-free diet. The risk of lymphoma decreased to closer than that of the general population in treated celiac patients. Osteoporosis has been reported as the main reason for morbidity in untreated celiac patients and the positive impact of a gluten-free diet on bone density, restoration of growth in children with celiac disease and glycemic control in diabetic patients has also been shown.

Nonresponsive celiac disease and gluten-free diet

After following a gluten-free diet, most celiac patients respond to a gluten-free diet and their histologic findings and symptoms normalize. Depending on the extent and duration of the disease, the full recovery may be obtained between 6 months and 2 years with strict exclusion of gluten from the diet. On the other hand, patients diagnosed with non-responsive celiac disease do not show any improvement in the symptoms (including lethargy, abdominal pain, and diarrhea) and this may be defined regarding persistent symptoms & signs, laboratory abnormalities, or histological changes of celiac disease despite 6–12 months of presumed adherence to a strict gluten-free diet (Penny et al. 2020).

Non-responsive celiac patients do not respond to a gluten-free diet. Some individuals initially respond to a diet, but then they develop symptoms despite ongoing adherence to a gluten-free diet. These patients may not tolerate even the trace amounts of gluten (even less than 20 parts per million). If any gluten ingestion is not detected by the assessments, the coexisting causes of symptoms such as pancreatic insufficiency, lactose or other food intolerance, irritable bowel syndrome, bacterial overgrowth, collagenous colitis, lymphoma, parasites, or other diseases should be identified (See and Murray 2006).

Nonresponsive celiac disease is mainly resulted by gluten contamination followed by coexisting associated disorder (Bharadia and Shivpuri 2012). Therefore, a very detailed dietary intake assessment to detect any sources of gluten as well as to determine any possible cross-contamination from the patients' diet is a critical point for the management of nonresponsive celiac disease (Dewar et al. 2012). Nonresponsive celiac people may have symptoms like continued diarrhea, malabsorption, and villous atrophy related to progressive malnutrition. In addition to diarrhea, abdominal pain, and weight loss were found to be the most common reasons for evaluation in cases of nonresponsive celiac disease (Abdulkarim et al. 2002). If patients have persistent villous atrophy despite adherence to a gluten-free diet and are diagnosed with celiac disease and also show persistent symptoms or enteropathy, they are defined as refractory celiac disease. Patients with refractory sprue should also follow a permanent gluten-free diet. Furthermore, they need intensive nutrition support. Leonard, Cureton, et al. (2017) highlighted the importance of the supervision of a dietitian who can monitor the patient's response and ensure nutritional adequacy.

Gluten-free diet in gluten-related disorders

The prevalence of gluten-related disorders is increasing, and hence the growing numbers of individuals are trying to follow a gluten-free diet. The gluten-free diet is recommended for patients having celiac disease, gluten-sensitivity as well as wheat intolerance. It may also be followed by people with irritable bowel syndrome, neurological disorder gluten ataxia, type 1 diabetes, and HIV-associated enteropathy. A substantial amount of research has shown that maintaining a strict gluten-free diet is likely to improve the symptoms of celiac patients. On the other hand, there is scanty data about the positive impacts of a gluten-free diet on conditions such as wheat intolerance, type 1 diabetes and HIV-associated enteropathy. Therefore, recent studies have attempted to address the question of whether gluten-free diet adherence affects these diseases (Bakker et al. 2013; Svensson et al. 2016; Valenti et al. 2017).

Non-celiac gluten sensitivity is characterized by symptom improvement after gluten withdrawal in the absence of celiac disease and wheat allergy. Even though the actual prevalence of non-celiac gluten sensitivity is still poorly defined due to the lack of validated biomarkers, it is thought to be more frequent than celiac disease (Leonard, Cureton, et al. 2017). Thus, there is a lack of evidence for the gluten-free diet, followed by people with non-celiac gluten sensitivity.

The mechanisms of non-celiac gluten sensitivity can not be identified clearly (Molina-Infante and Carroccio 2017; Skodje et al. 2018). In addition to gluten, wheat proteins (i.e. amylase- and trypsin- inhibitors) and fermentable monosaccharides, disaccharides and oligosaccharides, polyols (FODMAPs) have been defined as other generating factors in non-celiac gluten sensitivity. Since gluten containing foods also have fructans, a type of fermentable oligo-, di-, monosaccharides and polyols, Skodje et al. (2018) conducted to a study to determine the effects of gluten and fructans separately in individuals with self-reported gluten sensitivity. The findings of the study revealed that fructans were more likely to induce symptoms in people who reported having sensitivity to wheat, rye, and barley. Furthermore, the authors have hypnotized that their findings failed the use of the term "non-celiac gluten sensitivity" and increasing doubts about the need for a gluten-free diet in these patients.

Factors influencing gluten-free diet compliance

Many studies in literature indicated that adherence to gluten-free diet is correlated with different factors such as the awareness and knowledge of celiac patients/families about celiac disease, the knowledge and awareness about gluten-free diet, the perceptions of celiac patients about gluten-free products and the psychological factors in celiac patients. In other studies, the high price and limited availability of products, insufficient labeling, and cross-contamination risk of products are defined as other critical factors affecting adherence to the gluten-free diet (MacCulloch and Rashid 2014).

In case of children, concerns about the possibility of inadequate handling of food products in restaurants, the increasing independence from parents, the need to prepare meals for themselves, and the lack of understanding of the importance of a gluten-free diet adherence among family members and friends have also been stated as the factors having roles in the difficulties of keeping gluten-free diet (Ferster et al. 2015; Czaja-Bulsa and Bulsa 2018). The lack of availability of gluten-free products at schools is also another problem that should be faced by child patients daily, which in turn may result in non-adherence to the diet.

In this regard, team-based management of celiac patients, proper counseling and supervision of patients, industrial production of high-quality gluten-free products, improved gluten-free labeling system and following the international health organizations are highly recommended to improve the quality of life of children as well as adults who have celiac disease (Ferster et al. 2015).

Treatment burden

Although the prevalence of the celiac disease and the findings of persistent signs, symptoms, and small intestinal enteropathy are more common in patients than previously thought, long-term adherence to a gluten-free diet is poor in people with celiac disease. Shah et al. (2014) conducted a study to understand the burden of a gluten-free diet and the factors that affect adherence to the diet. For this purpose, the authors compared treatment burden and health state in celiac disease compared with other chronic illnesses (gastroesophageal reflux disease, irritable bowel syndrome, inflammatory bowel disease, hypertension, diabetes mellitus, congestive heart failure, and end-stage renal disease on dialysis). They also evaluated the relationship between the treatment burden and gluten-free diet adherence. Poor adherence, concern regarding food cost, eating outside the home, higher income, lack of college education, and time limitations in preparing food were defined as the factors related to a high treatment burden in celiac disease. It has been reported that a high treatment burden creates difficulty in adherence to a gluten-free diet. The results also reflected the fact that patients with celiac disease visit physicians less often as compared to patients having chronic medical conditions. Increased symptoms, low income, and low perceived importance of treatment were found to be the factors resulting in poor adherence. The importance of a need for non-dietary interventions as well as need for patients to regularly follow up with clinicians, dieticians, and other allied health professionals has been highlighted (Shah et al. 2014).

The lack of awareness and knowledge about gluten-free diet

The lack of knowledge of celiac and non-celiac people about gluten-free diet

The lack of awareness and knowledge of the general public about gluten-free diet creates problems for non-celiac people who are considering that gluten-free products are healthier as well as for celiac people who have to follow the gluten-free diet.

Although celiac people have a higher level of knowledge about gluten-free diet as compared to non-celiac followers, most of the celiac patients are also unlikely to consult health professionals about adopting a gluten-free diet (Silvester et al. 2016a). The study of Halmos et al. (2018) showed that over one-third of people diagnosed with celiac disease have never seen a dietitian. This finding reflected the critical role of the advice on diet practicalities, preferably from a dietitian with expertise in celiac disease on the adherence of a gluten-free diet.

Paganizza et al. (2019) conducted a study on a gluten-free diet adherence and potentially associated factors, focusing on the relationship between adherence and knowledge of the gluten content of foods and adherence and knowledge of celiac disease in Italy. Patients' knowledge regarding celiac disease as well as a gluten-free diet was found to be generally poor. Knowledge of celiac disease and a gluten-free diet was significantly related with adherence to a gluten-free diet. Silvester et al. (2016b) studied the relationship between self-reported adherence to a gluten-free diet and the ability to determine the appropriateness of particular foods in a gluten-free diet correctly. Most participants (55%) reported strict adherence, 18% reported intentional gluten consumption and 21% acknowledged rare unintentional gluten consumption. Participants could not correctly identify all foods (17 foods), while only 30% of participants could identify at least 14 foods correctly. The findings of this study reflected that people who believe they are following a gluten-free diet are not readily able to correctly identify foods (Silvester et al. 2016b). The association between knowledge of celiac disease and the adherence to the diet as well as the relationship between knowledge of gluten-free diet in celiac patients and their adherence to the diet suggests the development of training programs for celiac patients (Paganizza et al. 2019).

Self-prescription of a gluten-free diet without medical supervision

Recently, the gluten-free diet has also started to be self-initiated by a significant number of people due to public opinions suggesting that a gluten-free diet is a healthy diet option. Thus, such a diet has become a fashionable lifestyle trend among non-celiac patients also (Xhakollaria et al., 2019).

The studies showed that self-prescription of a gluten-free diet without medical supervision has become popular even though most of the people do not have any detailed knowledge about such a diet (Lis et al. 2013; Silvester et al. 2016a; Verrill, Zhang, and Kane 2013; Skodje et al. 2019). The study of Biesiekierski et al (2014) has revealed that 44% of participants self-initiated a gluten-free diet, while other participants were started to adopt a gluten-free diet by alternative health professionals (21%), dietitians (19%), and general practitioners (16%). Besides, only 27% of participants had detailed knowledge about a gluten-free diet.

The lack of knowledge of restaurant and food service staff about gluten-free diet

The lack of knowledge by the restaurant staff/food service staff regarding the gluten-free diet presents a social constraint for patients who want to eat away from home. Young and Thaivalappil (2018) conducted a systematic review that focused on global research on restaurant and food service establishment personnel knowledge, practices, and training related to food allergies and celiac disease. Most participants (65%) stated that they did not receive prior food allergy training. The improved declaration of food allergens on menus and risk communication practices in restaurants and other food service settings has been suggested to support food allergic people as well as celiac people to make informed decisions when eating out and to prevent possible allergen exposures.

A study conducted in the United Kingdom reflected the fact that approximately 80% of the chefs interviewed had not ever heard of celiac disease (Karajeh et al. 2005). In another study conducted in the USA, conversely, most chefs (77% of the chefs interviewed) claimed to have information about celiac disease; still they could not differentiate between gluten containing and gluten–free products (Simpson et al. 2011). Training of chefs to the improve chefs' knowledge of celiac disease as well as the use of clear statements on menus showing the presence or absence of gluten has been suggested (Olsson et al. 2009).

The lack of awareness and knowledge of celiac patients/families about celiac disease

Patients' awareness and knowledge about celiac disease affect their compliance with the gluten-free diet. Most of the studies have reflected that today many patients with celiac disease do not follow the gluten-free diet strictly. Strict adherence to gluten-free diet has been reported to vary between 36% and 96% for adults with celiac disease (Hall, Rubin, and Charnock 2009). While an increase in the number of children with celiac disease adhering to the gluten-free diet has been observed in recent years, today every one of four children having celiac disease are also not following gluten-free diet in Poland (Czaja-Bulsa and Bulsa 2018). It has been stated that younger children (up to 12) (8%) were found to be less likely to abandon gluten-free diet compared to teenagers (40%) (Czaja-Bulsa and Bulsa 2018). The study of Dowhaniuk et al. (2020) showed that while most children and families were considered to be adherent to the gluten-free diet; up to 40% of children with celiac disease were identified by a registered dietitian as still having ongoing gluten exposure in Canada.

The psychological factors in celiac patients

The significant correlation between adherence to a gluten-free diet and the psychological factors in patients has also been shown in several studies (Garg and Gupta 2014; Halmos et al. 2018; Sainsbury et al. 2018; Sainsbury and Marques 2018; Sainsbury and Marques 2018). Although the direction of the relationship between depression and adherence remains unclear, available evidence suggests that there is an association between poor gluten-free diet adherence and self-reported depressive symptoms (Sainsbury and Marques 2018). Halmos et al. (2018) examined the effects of patient factors including knowledge and psychological parameters on adherence to a gluten-free diet in Australia and New Zealand. 61% of 7393 patients were found to be adherent to a gluten-free diet. Poor knowledge of a gluten-free diet as well as psychological well-being were found to be independent predictors of adherence. Dietary adherence was associated with a better quality of life. Psychological distress was found to be common among celiac patients having difficulty in the following of a gluten-free diet. It has been highlighted that in the presence of psychological distress, the involvement of both a dietitian and mental health care professional may be necessary to improve adherence and health outcomes (Halmos et al. 2018).

Several studies were also assessed to identify the predictors of compliance to a gluten free diet in children with celiac disease. The studies revealed that child patients' and parents' attitudes about following a strict diet made a significant contribution to compliance. Other factors such as age at presentation, family, mother's education, and parents having a better knowledge of celiac disease were also found to be significantly associated with compliance in children (Garg and Gupta 2014). It has also been reported that child patients are facing some difficulties in maintaining gluten-free diet due to the need to better organize everyday life as well as the environmental pressure such as participating in birthday parties, summer camp, and eating out, etc. (Ferster et al. 2015; Czaja-Bulsa and Bulsa 2018).

The negative impact of psychological symptoms on quality of life and adherence suggests that management in celiac disease should include the provision of psychological coping skills and purely dietetic-based strategies to decrease gastrointestinal symptoms (Sainsbury, Mullan, and Sharpe 2013a). It has been reported that encouraging celiac patients to focus on the longer-term benefits of following a gluten-free diet, and the satisfaction and enjoyment that comes from being well may provide greater improvements in the maintenance of the gluten-free diet over time (Sainsbury et al. 2018).

Labeling of gluten-free products

Celiac people must read all food labels to understand the gluten-free status of a food product. Zarkadas et al (2012) stated that even though participants have been following a gluten-free diet over five years, more than three–quarters of them still experienced difficulties with food labeling. In the study of Halmos et al. (2018), the influences of food knowledge and psychological state of celiac patients on adherence to a gluten-free diet were evaluated. Patients with self-perceived poorer knowledge in reading labels were found to be more likely to identify gluten-free foods incorrectly. However, they could still identify gluten-containing foods. It has been stated that the inadequate adherence to a gluten-free diet might be related to over-restriction of diet caused by poor knowledge. Thus, to follow a gluten-free diet, referring to a dietitian was suggested for these patients.

Definition of an agreeable safe threshold for gluten

The definition of an agreeable safe threshold for gluten is one of the critical factors related to labeling. It has been stated that not only the minimum toxic dose but also the amount of gluten-free products consumed are important factors for the determination of threshold (Catassi et al. 2007). The sensitivity to trace intakes of gluten, which indicated a great interpatient variability is another important factor that should be considered for the implementation of a safe gluten threshold (Catassi et al. 2007). Therefore, the current evidence is not sufficient to establish a single definitive threshold, and the debate about a safe level of gluten in gluten-free products is still going. According to the study of Collin et al. (2004), the daily flour intake is even 300 g, a level of 100 ppm leads to 30 mg of gluten intake and thus, the threshold for gluten-contamination can safely be set at 100 ppm. On the other hand, the findings of the study of Catassi et al. (2007) suggested that 200 ppm is not a safe threshold. The findings indicated that even if gluten-free products are consumed at moderate levels (250 g/day), the gluten intake of patients can reach a harmful level (50 mg/day). Furthermore, it has been stated that the threshold of 100 ppm is also probably not a safe threshold, especially for the people living in the countries where a high amount of wheat (high as 500 g/day) is consumed. On the other hand, 20 ppm, which allows the intake of gluten below enough the amount of 50 mg/day has been suggested to provide a safe level for the variable gluten sensitivity and dietary habits of patients.

Definition of Gluten-Free foods

In the USA, Food and Drug Administration has determined a food-labeling term "gluten-free" to show that a food bearing this claim does not contain any of the following; (1) an ingredient that is a "prohibited grain," which includes any species of wheat (such as durum wheat, spelt wheat or kamut), rye, barley or their crossbred hybrids; (2) an ingredient (e.g., wheat flour) that is derived from a "prohibited grain" and that has not been processed to remove gluten; (3) an ingredient (e.g. wheat starch) that is derived from a "prohibited grain" that has been processed to remove gluten, if the use of that ingredient results in the presence of 20 ppm or more gluten in the food; (4) 20 ppm or more gluten (Food and Drug Administration HHS 2013).

Codex Alimentarius Commission (joint FAO/WHO Food Standards Programme) adopted gluten-free foods standards and defined food products for people intolerant to gluten. Thus, according to CODEX, a product may only be labeled as gluten-free if it contains no more than 20 ppm gluten. Products have more than 20 ppm, but less than 100 ppm gluten may be labeled as "very low gluten" (Codex Alimentarius Commission 2010). There is no international agreement on the types of grain foods that should be permitted in a gluten-free diet, as well as the amount of gluten in a food labeled as "gluten-free". For example, A Cochrane Review commissioned by Celiac Australia has indicated that a safe threshold level of gluten intake for people with celiac disease cannot be defined at present. Therefore, Australia New Zealand Food Standards (FSANZ) has defined gluten-free food as having no detectable gluten using the universally accepted most sensitive and specific testing method. Furthermore, food labeled as gluten-free must not contain oats or malt since the currently available testing methods cannot accurately detect gluten in these grains and their derivatives (Shepherd and Gibson 2006).

European countries have used the definition of gluten-free food similar to that designed by Codex Alimentarius. According to EU (European Union) regulation on the provision of food information to consumers (EU Regulation No. 1169/2011), information on potential allergens must be given to the consumer, even unpacked food presents to the consumers. In the case of packaged products, all foods ingredients such as gluten-containing ones should be labeled mandatorily. Furthermore, a scientifically proven allergenic or intolerance effect of these ingredients should also be given on the label. EU also harmonized the necessities for the provision of information to consumers in the absence or reduced presence of gluten in food (EU Regulation No. 828/2014). In the harmonized regulation, gluten-free labeling conditions such as "gluten-free" or "very low gluten" have been set out. Furthermore, additional requirements for food containing oats have been defined. In this regulation, the new rules apply to non-pre-packed foods like those served in restaurants have also been determined. Furthermore, it also provides information about how operators can inform gluten-intolerant consumers about the difference between naturally gluten-free foods and gluten-free formulated products. The information to consumers about specific rules for gluten-free food has been set out in another EU Regulation (EU Regulation No. 609/2013).

Consequently, the improvements in Codex Standard on Food Labeling, EU legislation and other national food labeling legislations have determined unknown gluten exposure resulted by the insufficient declaration of gluten-containing food additives in foodstuffs and hence resulting health hazard. An establishment of a definition for gluten-free with stable conditions for the use in food labeling will guarantee that people with celiac disease are provided with correct information and thus, they are not misled. Thus, a clearer and universal labeling system will ensure a better quality of life for the gluten-intolerant population.

Precautionary allergen labeling

Since a complete removal of gluten would be difficult, the definition of an agreeable safe threshold for gluten contamination in gluten-free products is also critical. Many studies have shown that gluten contamination in gluten-free products cannot be prevented. Mandatory labeling for the most common allergenic foods such as peanuts, tree nuts, milk, eggs, fish, crustacea/shellfish, soy, and wheat or cereals containing gluten, as well as ingredients derived from those foods has also been set by Codex Alimentarius Committee (1979). The use of "may contain" statements on the label as the potential for unintentional contamination of food with allergens during manufacture might be considered as a beneficial strategy to convey the risk of allergen cross-contamination. Allen et al. (2014) argued that "may contain" statements should be used to reflect the actual risk of cross-contamination following a risk assessment and intervention to minimize risk according to Good Manufacturing Practice (GMP). However, it has been stated that since this precautionary allergen labeling has been used as an alternative to allergen risk management by some manufacturers, this precautionary allergen labeling may also be caused to uncertainty over their meaning as well (Allen et al. 2014).

Foods and ingredients derived from gluten-free grains and their labeling

Gluten-free foods are also prepared from naturally gluten-free ingredients such as corn maltodextrin/dextrin, wheat maltodextrin/dextrin, soy products (including soy, soy lecithin, and hydrolyzed soy protein). Furthermore, oats and yeast extract can also be for the production of gluten-free foods. The ingredients derived from wheat such as wheat starch, glucose sirup from wheat, and wheat dextrose are also utilized in gluten-free formulations. Glucose sirups can also be used for sweetening mixtures and anti-crystallizing agents, in beverages, confectionary as well as in dairy products (Dostalek et al. 2009).

The food producers in the EU have to comply with the regulation on the indication of the ingredients present in foodstuffs (EU Regulation No. 2003/89) regarding the indication of allergenic ingredients present in foodstuffs. To give more comprehensive information to consumers suffering from food allergy/intolerances about the composition of foodstuffs, it should be obligatory to include all ingredients and other substances present in the foodstuff in the list of ingredients based on this regulation. This indication shall comprise the word "contains" followed by the name of the ingredient(s) concerned. However, an indication is not necessary when the ingredient is already included under its specific name in the list of ingredients or in the name (brand) under which the beverage is sold.

According to commission EU Directive (EU Regulation No. 2005/26) wheat starch-based glucose sirups including dextrose, wheat-based maltodextrins, glucose sirups based on barley, and cereals used in distillates for spirits are exempted from this labeling requirement. Although, the manufacturers may voluntarily declare that the product “may contain wheat” or “contains wheat ingredients” for people having wheat allergies, it has been reported that ingredients derived from wheat such as wheat starch, glucose sirup, and wheat dextrose may also cause misunderstanding. In the study of Dostalek et al. (2009), it has been stated that some manufacturers do not use the exemption, and they declare the presence of wheat whenever glucose sirups based on wheat are present. This may cause misunderstanding since celiac patients are not familiar with food legislation and do not know how to interpret the labeling. Consequently, the patients may not prefer to consume food containing glucose sirup even though they are safe.

There is a debate about the use of ingredients derived from gluten containing grains and their labeling. Shepherd and Gibson (2006) stated that most ingredients derived from gluten containing grains contain gluten even though the amount of gluten depends upon which component of the grain is used and how it is processed. The authors also reported that any ingredient derived from the protein component of gluten containing grain would contain gluten. Furthermore, the fiber component of gluten containing grains would also contain gluten. On the other hand, it has been reported that highly processed ingredients, particularly dextrose, glucose, glucose sirup, and color caramel does not have detectable gluten since high processing decreases residual gluten, which is present before processing.

Due the concern about wheat maltodextrin, The EFSA (European Food Safety Authority) published the Opinion of Scientific Panel on Dietetic Products, Nutrition and Allergies about the potential adverse reactions caused by maltodextrins based on wheat starch. The evidence showed that wheat-based maltodextrins are unlikely to cause an adverse reaction in people with celiac disease provided that the provisional value of gluten determined by Codex Alimentarius for gluten-free foods (currently 200 mg/kg) in not exceeded (The EFSA Journal 2004a, The EFSA Journal 2004b, The EFSA Journal 2007a, The EFSA Journal 2007b). The Panel was unable to predict the likelihood of adverse reactions in cereal allergic people based on the data provided by the applicant. Considering the levels of wheat proteins reported to cause allergic reactions in severe allergic people, the Panel decided that that the product will cause a severe allergic reaction in the majority of cereal allergic individuals. However, the necessity of further clinical information is stated to determine the effects of wheat-based maltodextrins in cereal allergy.

Other problems related to labeling include, but are not limited to mislabeling. It has been stated that many manufacturers may label products indicating ingredients such as starch, flavorings, and seasonings, as well as an extensive range of names for wheat such as couscous, faro, farina, filler, kamut, semolina, spelt and triticale instead of using clear statement whether a product contains wheat (Worosz and Wilson 2012). Thus, the labeling of products should provide a better understanding of the label of the product in which whether or not gluten-containing ingredients and/or additives are used and whether these ingredients and/or additives are obtained from gluten-containing cereals.

Gluten contamination in gluten-free products

Although food considered as “gluten-free” is defined in the Codex Alimentarius, gluten content of products may exceed the safe 20 ppm limit due to the possibility of gluten cross-contamination. Cross-contamination of gluten represents a health risk to not only people having celiac disease but also to people with non-celiac gluten sensitivity and gluten allergy. Therefore, a permanent complete exclusion of gluten from the daily diet is very difficult.

Inadequate procedures from the field to the milling and manufacturing steps, including shared production areas, unsuitable sanitation and inappropriate practices by industry/restaurant staff and improper storage conditions may be responsible for the cross-contamination of food with gluten.

Gluten contamination in gluten-free products

There are a large number of studies examining gluten contamination in different gluten-free products. It has been reported that gluten-free grains or flour may be contaminated with gluten containing grains or flours during harvesting, transportation or processing steps. The protein component of wheat can not be completely removed from its starch component and thus, the removal of gluten from gluten-free products is a challenging issue.

A study conducted to evaluate gluten contamination in beans served in self-service restaurants has shown that 16% of the samples were contaminated by gluten. Furthermore, 45% of the restaurants had at least one day of gluten contamination (Oliveira et al. 2014). The main reason for cross-contamination was stated as a lack of standardization. The necessity of public health actions to increase access to safe gluten-free products and hence to improve the quality of celiac patients’ life has also been highlighted (Oliveira et al. 2014). The study of McIntosh et al. (2011) indicated that gluten-free’ menu choices including ‘gluten-free’ notices, signs and menu choices and staff confidence did not guarantee risk-free dining. While the majority of attempts to purchase a ‘gluten-free’ meal on request in restaurants were successful, 10% of samples were found to be contaminated with gluten and two unsatisfactory samples were purchased from a so-called celiac-friendly restaurant in Ireland. The authors highlighted that these challenges could be best addressed by interventions that enhance the knowledge and awareness of chefs and managers. Further training, specifically for chefs and managers has been suggested.

In a systematic study, the prevalence of gluten contamination in gluten-free industrial and non-industrial products was evaluated (Falcomer et al. 2020). A contamination level was determined as 13.2% for industrial food products, while the prevalence of contamination was found to be higher (41.5%) for non-industrial food products. Despite the fact that the difference between contamination levels of industrial and non-industrial products was found to be insignificant, the lower percentage of gluten-contamination for industrial products was related to labeling of these products as gluten-free. On the other hand, it has been stated that foods labeled as "gluten-free" should not be considered safe for celiac patients since the information on the label showing only the presence/absence of gluten is not reliable (Falcomer et al. 2020). Thus, the findings of this systematic review have reflected the importance of understanding of gluten-free labeling.

Farage et al. (2017) investigated a study to assess the safety of gluten-free bakery products for consumption by celiac patients. The results showed that a total of 21.5% of contamination was found in bakery samples. Furthermore, it has been found that 64% of bakeries sold at least one contaminated product. Similarly, another study was designed to determine the concentrations of gluten in foods labeled "gluten-free" available in the United States (Lee, Anderson, and Ryu 2014). For this purpose, 78 samples, which were labeled as gluten-free, were analyzed. It has been found that 16 of 78 samples did not comply with gluten-free labeling standards established by the Codex Alimentarius. In another study, Colin et al (2004) analyzed 83 wheat starch-based gluten-free products in Finland in order to detect whether they contain gluten. It has been found that 24 of gluten-free products were found to not in compliance with gluten-free labeling standards established by the Codex Alimentarius and they contained gluten ranging from 20 to 200 ppm (Collin et al. 2004).

The most crucial step to avoid cross-contamination is to install separate production areas for gluten-free and gluten-containing products. In other words, the production line as well as equipment used from the field to storage steps should be different for gluten-containing and gluten-free products. The adoption of GMP and strict control of the standard processing steps are required to ensure the safety of products (Falcomer et al. 2020). It has been stated that even if requirements for GMP cannot be met, the implementation of control programs such as HACCP (Hazard Analysis and Critical Control Points) can be used to minimize the risk of cross-contamination (Farage et al., 2016). Furthermore, the prominence of an active policy of training and education for employees at food services about requirements for gluten-free diets has been highlighted in order to decrease the risk of gluten cross-contamination. Effective strategies such as training of employees, meeting with sanitary prerequisites and providing respective regulations and control measurements can be adopted to prevent cross-contamination (Farage et al., 2016).

Gluten contamination in oat products

Celiac patients should follow a strict gluten-free diet avoiding the prolamins of wheat, rye, and barley. However, there is a debate about whether the oat prolamin 'avenin' should be excluded from a gluten-free diet (Thomson, 2003). Although oats have been reported to be harmful since the early 1950s, no adverse effects associated with the regular consumption of moderate amounts of oats have been demonstrated in several studies. Some evidence has shown that people with celiac disease may tolerate small amounts of oats (50 g/day) (Janatuinen et al. 1995; Thompson 1997).

Although the positive impact of oats on the nutritional value of the gluten-free diets as well as adherence to a gluten-free diet has been shown, the use of oats in a gluten-free diet remains a controversial issue. The results of a recent systematic review and meta-analysis evaluating the safety of oats as part of gluten-free diets in celiac patients (adults and children) suggest that non-contaminated oats are tolerated by the great majority of patients (Pinto-Sánchez et al. 2017). Therefore, the previous conflicting results about oat containing gluten-free diet have been suggested to be caused by contamination risk. Fric, Gabrovska, and Nevoral (2011) examined the contamination risk for oat. It has been stated that the terms "100% oats," "pure oats," or "organic oats" do not guarantee that the product is free of contamination (Fric, Gabrovska, and Nevoral 2011). Thus, the selection of oat cultivars with low avenin content, evaluation of recombinant varieties of oats, development of assay methods to detect avenins in oat products and making guidelines for the agricultural processing of oats and manufacturing of oat products will provide safe oats for all celiac patients. The following up with celiac patients who consume oats will also be helpful (Fric, Gabrovska, and Nevoral 2011).

Limited availability and high prices of gluten-free products

The economic burden of the gluten-free diet and the limited availability of gluten-free products affect the quality of celiac patients' life. So, adhering to the gluten-free diet can be very challenging. In the study of do Nascimento et al. (2014), it has been stated that 71% of participants faced serious difficulty in the following of a gluten-free diet in Brazil. The factors contributing to not following gluten-free diet by celiac patients were defined as the lack of alternatives (38%); the necessity of to feel "normal" and better socialize or cravings (30%); the lack of knowledge about the fact that the product contained gluten (20%) and the high cost of products (12%). In another study, Araújo and Araújo (2011) reported that 67% of celiac patients consumed gluten due to the lack of availability of gluten-free products in Brazil. In another study conducted in the United States has shown that while the regular wheat-containing food can be available in all venues and all regions, the availability of gluten-free products is very limited. The availability of gluten-free products changes between the shopping venues and regular grocery stores in all five locations do not sell at least 2–3 gluten-free products (Lee et al. 2007). In the United Kingdom, the availability of gluten-free products also varies between store categories. As opposed to the findings of Lee et al. (2007), regular supermarkets had the largest number of gluten-free bread, which were followed by quality supermarkets and then health food shops in the UK (Singh and Whelan 2011).

In addition to the limited availability of gluten-free products, most people are also dissatisfied with the high prices of gluten-free products. The possible reasons for limited availability and hence the high cost of gluten-free products may be related to the expense of alternative grains used for replacement of wheat, the necessity of considerable food science expertise for the product development as well as the necessity & the costs of alternative additives. Furthermore, the distribution of products can be problematic since gluten-free products stale faster. High prices of gluten-free products may also result from lower supply and demand. Although the gluten-free food market has been growing, it has not resulted in the expected transformation in terms of accessibility of manufactured gluten-free products or decreases of prices of products (Hanci and Jeanes 2019). Today, gluten-free manufacturers are still much smaller than their main-market competitors and this may be another relevant factor affecting the costs of gluten-free products dramatically. The necessity of different production lines for gluten-free products to prevent cross-contamination risk may also play a role in the high prices of gluten-free products.

Many studies are available in literature reflecting the high prices of gluten-free products. Gluten-free foods at two grocery stores in Canada were found to be 180% more expensive compared to their standard counterparts (Stevens and Rashid 2008). Similarly, in the United States, gluten-free products markedly cost 240% more expensive than the conventional counterparts (Lee et al. 2007). Lee et al. (2019) conducted market basket study to determine the current cost and availability of gluten-free products and to make comparisons to the marketplace over a decade ago in the United States. As compared to wheat-based products, gluten-free products were found to be 183% more expensive in all regions and venues. Although the introduction of mass-market production of gluten-free products impacted both the cost and availability by venue, the result of the study showed that gluten-free products from mass-market producers were 139% more expensive than the wheat-based version of the same product. Therefore, even though the cost of gluten-free products decreased from 240% to 183% over the past 10 years, the finding of this study showed that the cost and availability of gluten-free products continue to be a burden for people who need gluten-free products.

The study conducted by Singh and Whelan (2011) also reflected the limited availability and high prices (76–518% higher than conventional products) of different gluten-free products in the United Kingdom. Another study was conducted to determine the perceptions of celiac patients about gluten-free products, their consumer behavior and which product is the most desired (do Nascimento et al. 2014). The price (26.5%) was found as the most considered factor for the selection of product after the sensory characteristics (33%). Lee et al. (2007) has demonstrated that geographic location between the states did not influence the prices of gluten-free products statistically except for bread and pasta. The cost was affected more by shopping venues rather than geographic location. Similarly, Hanci and Jeanes (2019) observed the significant differences between in costs of gluten-free products sold by different types of shopping venues in the United Kingdom. The costs of gluten-free products were generally found to be higher in regular supermarkets compared with premium supermarkets.

In order to access to gluten-free products as well as decrease the financial burden to celiac patients; subsidies such as tax reduction, cash transfer, food provision, and prescription can be used. Prescription prepayment certificate is used in some countries such as New Zealand, Canada, the Republic of Ireland and the United Kingdom (Pinto-Sanchez et al. 2015; Hanci and Jeanes 2019). It has been stated that even though the costs of gluten-free products are partially refunded by prescription, most of the celiac patients are still unable to afford the costs of gluten-free products. Furthermore, in several areas, prescribed gluten-free products are not available to celiac patients. Thus, patients with low-income are still facing the problem of the disproportionately high prices of gluten-free products.

The necessity of further research to determine the current and real-life economic problems concerning the following of a gluten-free diet by all population groups of celiac patients has been stated in different studies. It has been highlighted that an ideal balanced approach would include subsidizing gluten-free products by considering all population groups with celiac disease (Pinto-Sanchez et al. 2015; Hanci and Jeanes 2019).

The adverse effects of a gluten-free diet

Nutritional quality of a Gluten-Free diet

Most of the prepackaged gluten-free products are incompetent with their gluten-containing counterparts in terms of nutritional characteristics. Moreover, according to regulations, gluten-free flours are not enriched/fortified like refined wheat-based flours on mandatorily. They have more fat, sugar, or salt (depending on product type) as compared to the products containing gluten. Thus, the following of a gluten-free diet is not simple for celiac patients since such a diet may also cause nutrient deficiencies of some macro and micronutrients as well as lead to excess intake of saturated fats and carbohydrates. Consequently, most patients are more vulnerable to nutrient-related deficiencies such as osteoporosis, anemia, and failure to thrive (Elli et al. 2019). A metabolic imbalance may also be observed in celiac patients due to the lack of adequate consumption of essential fatty acids (Sen et al. 2019).

In literature, studies have assessed the nutritional quality and adequacy of a gluten-free diet. Many gluten-free foods were found to be deficient in several nutrients, including dietary fiber, folate, iron, niacin, riboflavin, and thiamin (Thompson 1999 and Thompson 2000). Taetzsch et al. (2018) performed a comprehensive comparison of gluten-free products with matched gluten-containing products. In this study, the nutrient intakes of celiac adults following a gluten-free diet were also compared with the control group who are following a gluten-containing diet. The results reflected the fact that gluten-free products are not nutritionally superior except for sodium, and in several respects are worse. Gluten-free products contained significantly lower protein, magnesium, potassium, vitamin E, folate, and sodium. Furthermore, they had lower calcium and higher fat content. The findings also indicated that a gluten-free diet was associated with higher energy and fat intakes and lower fiber and folate intakes compared to controls (Taetzsch et al. 2018). It has been highlighted that the ideal gluten-free diet should be nutrient-dense with naturally gluten-free foods, balanced with macro- and micronutrients as well as reasonably priced, and easily accessible (Theethira and Dennis 2015).

Health problems potentially induced by gluten-free diet

The nutrient deficiencies of the gluten-free diet. Celiac patients may also be prone to protein and dietary fiber deficiencies. Therefore, celiac patients adhering to a gluten-free diet should consume enough nutrient-dense foods to meet all nutritional recommendations. The nutrient deficiencies of the gluten-free diet were reviewed by Vici et al. (2016). It has been found that the exclusion of gluten from the diet results in histological recovery and normalization of iron, vitamin, and mineral levels in the majority of patients. Iron deficiency anemia, which is the most common extra-intestinal sign of celiac disease, is generally resolved with adherence to a gluten-free diet (Caruso et al. 2013). In case of folate and vitamin B12 deficiencies, the use of vitamin supplements is important for the correction of nutrient deficiencies. Similarly, in case of persisting bone disease or lactose intolerance, the use of calcium and vitamin D supplementation may be needed to normalize bone mineral density. Iron and vitamin supplements may also be necessary for the correction of nutrient deficiencies (Caruso et al. 2013). Each of the deficiency problems is dealt with in the following sections.

Fiber deficiency

The health benefits of dietary fiber have widely been reported in different studies (Elleuch et al. 2011; Turksoy et al. 2011; Mert 2020). The main health advantage of fiber may be related to its behavior in the gastrointestinal tract. In particular, they take roles in preventing obesity, diabetes, cardiovascular diseases, and various cancers. Besides, it has been stated that dietary fiber can also provide some functional roles such as improved water holding capacity, viscosity, oil holding capacity and swelling capacity to products (Turksoy et al. 2011; Mert 2020).

Gluten-free products are generally prepared with starches and/or flours containing a high amount of starch. They can also be produced with refined flours in which the outer layer of grains is removed from the remaining starchy inner part. Thus, one of the problems encountered with a gluten-free diet is often characterized by a lower intake of dietary fiber compared to a normal diet. In addition to the composition of gluten-free products, fiber deficiency may also be related to malabsorption linked to villi atrophy. In literature, a growing number of studies, which were conducted on the intake of fiber in the dietary pattern of celiac patients have shown lower intake of dietary fiber (Nishida et al. 2004; Wild et al. 2010; Martin et al. 2013).

Scientists and manufacturers have tried to overcome problems emanating with a lack of nutritional composition of gluten-free products by the reformulation of gluten-free products. The drawbacks associated with a low fiber content of gluten-free products have been overcome by the use of flours containing a higher amount of fiber such as pseudo-cereals like buckwheat, quinoa and amaranth, chestnut, tigernut, chickpea, corn, millet and possibly oat flour, etc. (Thompson 2000; Demirkesen et al. 2010a; Demirkesen, Sumnu, and Sahin 2013).

Dietary fibers derived from either grain, vegetables or fruits can also be incorporated in gluten-free formulations to compensate for the nutritional deficiencies of products. In literature, there are many studies also showing that gluten-free products can be reformulated with different bran types such as rice bran, corn bran, quinoa bran, etc. Although the use of such raw materials in gluten-free formulations as a commonly used technique, technological problems in terms of texture, volume, color, sensory, and shelf-life related to their usage can also be observed in gluten-free products. Thus, a substantial amount of research has successfully been completed by some authors in order to improve functional properties and physiological influences of dietary fiber by using different processing technologies such as traditional milling/grinding techniques and micro-fluidization. The functional properties of these fibers have been improved, and these fibers can also be used in gluten-free products (Mert 2020).

Food-by products such as pea hull, sugar beet, soy hull, carob fiber, flaxseed, apple fiber, citrus fiber, banana fiber, peanut hull, orange pomace, and psyllium husk have also been underutilized as potential fiber sources (Table 1). Cereal β-glucans as soluble dietary fiber has come to the attention of researchers due to their ability to reduce blood LDL-cholesterol levels and the postprandial blood glucose and insulin levels. The inclusion of β-glucans is also promising since it has the ability to act as a hydrocolloid and hence to improve the functional and nutritional properties of resulting products (Table 1). Inulin as a source of non-digestible polysaccharide and prebiotics is also used as dietary fiber in gluten-free products. Consequently, fibers intended to be used in gluten-free products are preferred to not only bring about a nutritional improvement of products but also enhance the quality attributes of the products (Table 1).

Vitamin and mineral deficiencies

Similar to fiber deficiency, vitamin and mineral deficiencies can also be observed in celiac patients because of the malabsorption associated with villi atrophy. Furthermore, gluten-free products are not enriched/fortified commonly; thus, a gluten-free diet may also contain inadequate levels of vitamins and minerals compared to gluten-containing counterparts.

Celiac patients are generally diagnosed with deficient in B group vitamins such as vitamin B2 (riboflavin), vitamin B3

Table 1. Different types of fiber sources used in gluten-free products.

Gluten-free Formulation	Fiber Source	Gluten-free Product Type	Observed Effects	Reference
Rice flour, corn starch, *MC	Orange pomace	Bread	Orange pomace improved volume, gave compact structure, decreased hardness during storage	O'Shea et al. (2013)
Corn starch, rice flour and HPMC	Wheat, maize, oat and barley fiber	Bread	The addition maize and oat fiber gave high loaf volume, softer crumb, an appealing darker crust and a more uniform and finely grained crumb texture.	Sabanis, Lebesi, and Tzia (2009)
Potato starch, rice flour, xanthan gum	$\beta-$glucan and inulin	Bread	The addition of $\beta-$glucan gave more elastic dough. Inulin gave higher volume, darker color and higher hardness. $\beta-$glucan decreased volume, gave lighter and softer texture.	Hager et al. (2010)
Corn starch, rice flour, rice starch, rice protein, HPMC, LBG, guar gum, maltogenic amylase	Psyllium and sugar beet fiber	Bread	Both fiber sources improved the workability of the doughs, but psyllium played a central role on gluten-free bread with antistaling effect, water-binding capacity.	Cappa, Lucisano, and Mariotti (2013)
Rice flour, HPMC	Chia seeds	Bread	The addition of chia reduced specific volume, increased the hardness of breads, minimized weight loss and gave a darker crust and crumb.	Steffolani et al. (2014)
Corn starch, potato starch, guar gum, pectin	Defatted blackcurrant and strawberry seeds	Bread	The addition of defatted blackcurrant and strawberry seeds significantly modified viscoelastic properties of dough. Higher volume and lower firmness after 24 h was obtained.	Korus et al. (2012)
Rice flour, guar gum, amyloglucosidase, glucose oxidase–peroxidase	Inulin and oat fiber	Cakes	Fiber sources gave improved specific volume and brighter color.	Gularte et al. (2012)
Rice flour	Flaxseed and chia gel	Cake	Chia or flaxseed gels gave higher moisture content, more uniform texture and better sensorial characteristics.	Hargreaves and Zandonadi (2018)
Rice flour	Apple, carrot, and orange pomace	Cake	Enrichment of dietary fiber content of gluten-free cakes was obtained without significant effect on specific volume and other quality characteristics.	Kırbaş, Kumcuoglu, and Tavman (2019)
Corn starch	Pumpkin seeds	Cakes	The chemical composition of cakes improved in terms of lipids, proteins, and dietary fibers giving more uniform structure.	Gorgônio, Pumar, and Mothé (2011)
Rice flour	Chia seeds	Pasta	The addition of chia seeds improved the nutritional profile of pasta, increased the slowly digestible starch fraction of rice flour.	Menga et al. (2017)

*HPMC: Hydroxypropyl methyl cellulose, LBG: Locust bean gum, MC: Methylcellulose

(niacin), vitamin B9 (folate), vitamin B12 (cyanocobalamin), vitamin D and less common Vitamin B6 (Pyridoxine) and Vitamin K. Furthermore, mineral deficiencies such as iron, calcium, magnesium, zinc, folate, phosphorus, and less common copper and selenium deficiencies can appear in patients (Vici et al. 2016).

In addition to malabsorption related to villi atrophy and composition of gluten-free products, calcium, phosphorus, and vitamin D deficiencies may also be related to a decreased intake of milk and dairy products because of the reduced lactase production by the damaged villi. The vitamin and mineral deficiencies detected in celiac patients have been proven in different studies (Thompson et al. 2005; Hallert et al. 2009; Wild et al. 2010; Caruso et al. 2013; Martin et al. 2013; Penagini et al. 2013; Samasca et al. 2014; Theethira, Dennis, and Leffler 2014). Therefore, the consumption of fish, meat, and fruits is recommended to meet the necessity of these micronutrients. On the other hand, the reformulation of gluten-free products to obtain gluten-free products with similar vitamin and mineral composition as their gluten-containing counterparts has also been suggested. Thus, manufacturers and scientists are recently producing gluten-free products enriched with vitamins and minerals because of the increasing concern on the nutritional quality of a gluten-free diet (Table 2).

Gluten-free flour sources richer in vitamins and minerals such as chestnut, teff, buckwheat, quinoa, and amaranth flour can also be used in diets to complement the micronutrient deficiency of gluten-free products. These studies showed that flours obtained from pseudocereals such as buckwheat (potassium, calcium, copper, zinc and manganese, vitamin E, vitamin B group), amaranth and quinoa (riboflavin, folic acid, vitamin C and vitamin E), chestnut (vitamin E, vitamin B group, potassium, phosphorous, and magnesium), teff (iron, zinc, calcium and copper), tigernut (phosphorus, potassium, iron and calcium, vitamins E and C) contains higher amount of vitamins and minerals as compared to wheat flour and other gluten-free flours such as rice and sorghum. Flaxseed, sunflower seeds, and a lesser extent, sesame, chia, poppy, or pumpkin seeds have also

Table 2. Different types of vitamin/mineral sources used in gluten-free products.

Gluten-free Formulation	Vitamin/Mineral Source	Gluten-free Product Type	Observed Effects	Reference
Corn starch, potato starch, pectin	Calcium caseinate and calcium citrate	Bread	The addition of calcium sources increased the specific volume, produced fine-colored and softer bread crust. Significant enrichment in calcium content was obtained. The desirable sensory attributes was observed in breads.	Krupa-Kozak et al. (2011)
Corn starch, potato starch, pectin	Calcium lactate, calcium citrate, calcium chloride and calcium carbonate	Bread	The addition of calcium carbonate and calcium citrate provoked an increase in dough consistency. The specific volume and texture parameters of gluten-free breads were improved. According to sensory evaluation, calcium carbonate followed by calcium citrate was the most recommended salt for obtaining calcium fortification of gluten-free breads.	Krupa-Kozak et al. (2012)
Soy flour, corn starch, guar gum, lecithin	Ferric pyrophosphate, Ferric pyrophosphate/emulsifiers, sodium iron EDTA, ferrous sulfate and elemental iron.	Bread	The addition of iron supplement gave firmer crumb texture and higher moisture.	Kiskini et al. (2012)
Refined and wholegrain buckwheat flour	Soaked flax seed and sesame seed	Cracker	Significantly higher total phenolics and tocopherols as well as favorable sensory properties were obtained from buckwheat crackers.	Sedej et al. (2011)
Buckwheat flour	Calcium hydroxide	Noodles	Tensile strength and cutting force of cooked buckwheat noodles increased. Release of amylose from the starch granules enhanced the formation of a compact and homogeneous buckwheat noodle. More compact and homogeneous, and less porous structure was obtained.	Han et al. (2012)

been used in gluten-free products in order to provide nutrients such as omega-6 and omega-3 essential fatty acids, fibers, antioxidants as well as vitamins & minerals (Roman, Belorio, and Gomez 2019).

Although the nutritional compositions of gluten-free products may also be improved with different supplements, many studies have especially focused on iron and calcium fortification (Table 2). Krupa-Kozak et al. (2011) supplemented gluten-free bread formulations with calcium and investigated their addition to the baking characteristics of a gluten-free formulation. Han et al. (2012) used calcium hydroxide in a buckwheat-based noodle formulation since buckwheat is a rich source of minerals but lacks calcium. Anemia is also commonly associated with celiac disease. Kiskini et al. (2012) stated that the development of fortified gluten-free products, which are rarely found in the market, would improve the quality of gluten-free diet. A successful fortification does not cause adverse effects on the quality characteristics of products especially on the sensory properties. Furthermore, a successful fortification requires commercial availability, higher bioavailability, higher stability and lower cost of micronutrients (Kiskini et al. 2012). Kiskini et al. (2012) analyzed the effects of different iron compounds (ferric pyrophosphate, sodium iron EDTA, ferrous sulfate and electrolytic (elemental) iron) on the physical and sensory characteristics of gluten-free bread formulation. Ferric pyrophosphate and sodium iron EDTA addition caused some quality defects. Among different iron compounds, electrolytic iron was found to be more stable in heat treatment and thus adverse changes to food by its addition were not noticed. Even though, it was usually poorly absorbed, the authors reported that the relatively low cost of electrolytic iron makes it economically feasible to incorporate the iron at a higher level to account for the lower bioavailability.

The other health problems potentially induced by the gluten-free diet. There is a rising trend in the adoption of a gluten-free lifestyle and the consumption of gluten-free foods. Even though emerging evidence suggested that gluten avoidance may be beneficial for some patients with gastrointestinal symptoms, such as those commonly encountered with irritable bowel syndrome; gluten avoidance may be associated with adverse effects in patients without proven gluten-related diseases.

The evidence at present has shown the life-long implementation of a strict gluten-free diet is the known medical treatment for celiac patients. Some studies have shown the adoption of a gluten-free diet may be an alternative treatment for people with autism spectrum disorders, but the evidence is still limited and anecdotal (Buie 2013; Mari-Bauset et al. 2014).

Self-prescription of a gluten-free diet without medical supervision has also become a popular fad diet in individuals who are trying to lose weight. However, there is not enough scientific evidence to suggest that a gluten-free diet is part of a healthier lifestyle or can be helpful to treat overweight or obesity (Leonard, Cureton, et al. 2017).

Gluten-free products contain a higher amount of starch. Moreover, these products generally can contain a higher saturated fat than their gluten-containing equivalents because adding extra fat is a common procedure in the gluten-free industry to obtain similar quality parameters with that of gluten-containing products (Demirkesen and Mert 2019). Thus, it has been speculated that the consumption of gluten-free products can lead to weight gain unless bakery products are not changed with vegetables, fruits etc. (Wild et al. 2010; Wu et al. 2015). A 3% increase in the prevalence of obesity among celiac children has been observed after the consumption of gluten-free products at least one year. It has been reported that because of gluten-free diets, patients, mostly children, can be exposed to an increased risk of overweight/obesity since they consume more bakery products like cakes, cookies, and biscuits (Demirkesen and Mert 2019). Increased obesity risk in celiac patients may also be related to the high glycemic index of the gluten-free diet (Norsa et al. 2013). Kabbani et al. (2012) evaluated the elevated body mass indexes (BMI) of celiac patients after following a gluten-free diet for three years. 15.8% of patients who are following the gluten-free diet move from a normal or low BMI class into an overweight BMI class, and 22% of patients overweight at diagnosis gain weight. Thus, the studies reflected the fact that people are more likely to be overweight and obese due to the following of the gluten-free diet (Wild et al. 2010; Kabbani et al. 2012; Norsa et al. 2013; Theethira and Dennis 2015). These results indicated that weight maintenance counseling should be an essential part of celiac dietary education.

Celiac patients were also found to be at an increased risk of nonalcoholic fatty liver disease, which is a common cause of chronic liver disease compared to the general population (Reilly et al. 2015). Excess risks were found to be the highest in the first year after celiac disease diagnosis but persisted through 15 years after diagnosis with celiac disease. It has also been stated that many adults as well as children with celiac disease are overweight or obese at diagnosis, or become overweight after treatment. Consequently, patients have a higher risk of developing nonalcoholic fatty liver disease. The observation prompted the hypothesis that modifications like decreasing a high-fat diet and a sedentary lifestyle can yield improvements in nonalcoholic fatty liver disease (Reilly et al. 2015).

Several studies have also attempted to identify whether a gluten-free diet was associated with coronary heart disease. Norsa et al. (2013) conducted a study to describe the cardiovascular disease risk factors in a population of children with celiac disease on a gluten-free diet. 14% of patients who were following a gluten-free diet were identified with cardiovascular disease risk factors such as body mass index, waist circumference, low density lipoprotein (LDL) cholesterol, triglycerides, blood pressure, and insulin resistance. High fasting triglycerides (34.8%), elevated blood pressure (29.4%), and high concentrations of calculated LDL cholesterol (24. 1%) were found to be the most observed cardiovascular disease risk factors. Furthermore, 3.5% of children had insulin resistance. Increased prevalence of borderline LDL cholesterol (24%) also occurred in children on a gluten-free diet. Moreover, trends toward rises in overweight (from 8.8% to 11.5%) and obesity (from 5.3% to 8.8%) were observed on a gluten-free diet (Norsa et al. 2013). The association of long-term intake of gluten with the development of incident coronary heart disease was also examined by Lebwohl et al. (2017). Although people with and without celiac disease may avoid gluten owing to a symptomatic response to this dietary protein, the findings showed that long term dietary intake of gluten was not related to the risk of coronary heart disease. The authors stated that the restriction of gluten may lead to a low intake of beneficial whole grains, which are associated with cardiovascular benefits. The authors highlighted that the promotion of gluten-free diets in order to prevent coronary heart disease among asymptomatic people without celiac disease should not be recommended. Similarly, Kim et al. (2017) stated that being on a gluten-free diet was not associated with decreased prevalence of metabolic syndrome or cardiovascular risk in gluten-free followers without celiac disease.

Constipation was observed in a considerable number of patients who had some diarrhea before diagnosis after the introduction of a gluten-free diet (Murray et al. 2004). The new onset of constipation after the introduction of a gluten-free diet may be related to a decrease in fiber intake of patients. Halmos et al. (2014) observed decreases in symptoms of irritable bowel syndrome with a diet low in the fermentable oligosaccharides, disaccharides, monosaccharides, and polyols (FODMAP). Rao, Yu, and Fedewa (2015) stated that natural fiber sources or dietary fiber supplements could be useful for the management of patients with chronic constipation and irritable bowel syndrome as well as FODMAP restricted diet has been recommended for irritable bowel syndrome, however more evidence is needed to determine its efficacy, compared with a regular Western diet (Halmos et al. 2014).

The findings of these studies suggest the importance of screening of obesity, cardiovascular disease, nonalcoholic fatty liver disease, chronic constipation, and irritable bowel syndrome risk factors in individuals both at diagnosis and during follow-up. Besides, dietary counseling over time, targeting these risk factors as well as monitoring adherence to a gluten-free diet in children and adolescents diagnosed with celiac disease may be warranted the success of management. The studies suggest that it is essential to broaden the research to determine whether the gluten-free diet may be associated with adverse health problems in people.

Quality problems of gluten-free dough/batter and resulting products

Rheological properties of gluten-free dough/batter and quality characteristics of resulting products

Glutenin and gliadin are the major fractions of gluten. Glutenin molecule, which is linked by intermolecular disulfide bonds, provides a network structure. On the other hand, the monomeric gliadin molecule is linked by intramolecular disulfide bonds forms a globular confirmation for the proteins (Tronsmo et al. 2002). Thus, gliadin gives viscous properties and extensibility to a dough system, glutenin is, on the other hand, creates the elastic and cohesive characteristics of the dough. Together, the two are responsible for the formation of a viscoelastic network capable of entrapment of gas formed during fermentation together with the early stage of baking as well as enclosing starch granules and fiber. Hence, the features of the protein-starch matrix affect the overall quality of products (Demirkesen et al. 2010b).

Since gluten is the primary structure-forming protein in flour, the removal of gluten leads to some quality defects in gluten-free products. Thus, the quality parameters of gluten-free products do not match that of gluten-based products. On the other hand, consumer expectations for gluten-free products are greatly affected by traditional product features; therefore, manufacturers and scientists determine the quality attributes based on wheat-containing products. However, gluten-free products generally have low volume, firm texture, and stale rapidly. Furthermore, they are devoid of the unique taste and aroma contributed by distinct volatile compounds.

Due to the lack of structure-building ability, the gluten-free dough is substantially less elastic and cohesive. Gluten-free dough formulation also tends to have a higher water level and so it looks like a cake batter rather than dough. Gluten-free dough is a sticker and more difficult to handle and hence dough can not be shaped like traditional wheat dough. Thus, in the case of gluten-free bread making, bulk fermenting and dividing are not necessary production steps. Gluten-free bread formulation also needs shorter proofing and baking times. The influence of mixing speed, mixing time, the type of mixing attachment and proofing time on gluten-free dough prepared with different water content was investigated by Gómez, Talegón, and De La Hera (2013). It has been demonstrated that since higher water content causes to batter-like consistencies, such dough system needs to the mixing regimes similar to that of cake batter. In other words, lower mixing speed but longer mixing time as well as using a whip wire mixing attachment are needed for the incorporation of more air bubbles into the batter. Longer mixing times lead to the formation of greater oxygenation, which permits yeast to reproduce under aerobic conditions. Furthermore, because of greater mixing times, amylase could produce maltose, which is the second main energy source for yeast after sucrose during proofing (Gómez, Talegón, and De La Hera 2013). In addition, longer proofing time is required for dough samples containing a higher amount of water. Demirkesen et al. (2010a, 2100b) also used similar conditions during the preparation of gluten-free bread formulations. In these studies, water absorption properties and mixing time are determined by some preliminary quality experiments such as volume, texture, and macro- or microstructural analysis of crumb instead of farinograph measurements. Since farinograph experiments can not be used for gluten-free dough due to its handling problems (Demirkesen et al. 2010a, 2010b).

When flour is hydrated, gluten creates a continuous 3-D protein network, which is responsible for entrapment of gas produced during fermentation and oven rise of wheat counterparts. In the case of gluten-free dough, the structure formed mainly by starch gelatinization and this is not enough to give resistance to shear and entrapment of CO_2. He and Hoseney (1991) determined higher release in the gluten-free dough (22 μmol/min) compared to the wheat dough in which the rate of CO_2 release was determined as only 5 μmol/min at 23 °C. Thus, in the absence of gluten functionality, products have some quality defects such as a crumbling texture, low volume, poor color, and short shelf life. Consequently, most gluten-free products are formulated by using some additives (e.g., starches, hydrocolloids, emulsifiers, enzymes, protein, fat and/or fiber sources) in order to mimic the viscoelastic properties of gluten as well as to provide some nutritional advances (Demirkesen et al. 2010b).

Another concern regarding gluten-free formulations is the development of gluten-free pasta. Gluten forms a 3-D viscoelastic protein network responsible for avoiding the dissolution of the pasta during cooking. In other words, a strong protein network formed by gluten prevents the disintegration of pasta during cooking. On the other hand, because of low starch gelatinization, a high cooking loss associated with a high level of solids in the cooking water is observed in gluten-free pasta formulations (Padalino et al. 2011). Susanna and Prabhasankar (2013) revealed that the best-cooked pasta features with the lowest cooking loss, soft texture and higher protein content was obtained when pasta samples were formulated with protein sources and hydrocolloids.

In the case of cookie or biscuit formulations, since gluten-free cookie or biscuit formulations (except for semi-sweet biscuits which may need gluten network) do not require extensive gluten network formation like breads, the quality problems observed in bread-making are rarely encountered during the manufacture of short dough products.

Similar to gluten-free cookie or biscuit type of products, the full development of gluten is also not required during the cake making. However, it should be highlighted that although gluten has a more limited role in cakes compared to breads, its interaction with proteins as well as starch has a critical role in the development of the structure. In other words, proper starch gelatinization prevents the collapse of the cake during cooling offering high volume, a fine grain, and a moist & tender crumb.

do Nascimento et al. (2014) studied the perceptions of celiac patients about gluten-free products considering the consumer behavior as well as the product choice. It has been stated that while 73.6% of the participants followed the gluten-free diet, interestingly, 18.7% of patients reported that they sometimes consume gluten (1 time/10–15 days or 1/a month). 6.6% confirmed that they more frequently consume gluten (at least once a week), and 1.1% stated that they ate gluten without restriction. The sensory characteristics (33%) were found to be the most considered factor for the selection of product followed by the price (26.5%), nutritional characteristics (17%), brand (16%), packaging (4.6%) and publicity (2.7%). These findings have suggested that perception rather than knowledge about diet may be the primary contributor to following of gluten-free diet. Olsson et al. (2009) also addressed this issue and the quality of gluten-free products was found to be the main reason for the weak adherence to the gluten-free diet. In another study, the sensory properties of gluten-free food were found to be effective not only celiac patients but also non-celiac consumers' compliance with the gluten-free diet (de Magistris, Xhakollari, and Munoz 2015).

Cereal sources for gluten-free products

In order to compensate for the lack of gluten protein and hence to counteract the technological problems, several additives such as hydrocolloids, emulsifiers, enzymes, dairy proteins, etc. have been employed in gluten-free formulations. Apart from designing of formulation, the adaptation of novel technologies for gluten-free product development considering of flour components present and the interactions among them may also be necessary. In literature, numerous studies have been attempted for enhancing the quality of gluten-free bakery products by utilizing the interaction of many additives as well as by using different production methods.

Finding suitable alternatives for gluten also presents a formidable problem for manufacturers and scientists. These alternative flours are selected considering special attributes such as their functional roles, economic cost as well as nutritional and quality characteristics of the resulted products. Recently, rice, corn, sorghum, chickpea, maize and soybean flour and pseudocereals such as buckwheat, amaranth and quinoa have been used as alternative flour types to wheat flour (Tables 1-4).

Rice flour is the most used flour for preparing gluten-free products because it is natural, hypoallergenic, colorless, and has a bland taste. Furthermore, it has a very low amount of protein, sodium, and fat but it is rich in easily digested carbohydrates. Because it has a bland taste, it can also be easily combined with other types of gluten-free flours such as chestnut, chia, quinoa, corn, sorghum flour, etc. However, similar to other gluten-free flours, it can not form a viscoelactic structure due to its hydrophobic nature. Many studies have investigated to show the potential use of rice flour in gluten-free formulations (Sivaramakrishnan, Senge, and Chattopadhyay 2004; Rosell and Collor 2007; Demirkesen et al. 2010a, 2010b).

Chestnut flour has become being a popular because of its several noteworthy characteristics such as having high-quality proteins with essential amino acids (4–7%), a relatively high amount of sugar (20–32%), starch (50–60%), dietary fiber (4–10%), a low amount of fat (2–4%), some important vitamins, minerals and phenolic components. In addition to its health and nutritional benefits, chestnut flour may provide some functional properties to the products. It has been shown that the quality problems related to using only rice flour have been overcome by the use of rice and chestnut flour together in gluten-free formulations. The fiber content of chestnut flour provides stabilizing, texturizing, and thickening characteristics to the dough, while the sugar in chestnut flour has positive roles on color and flavor features of products when chestnut flour used until a certain level (Paciulli et al. 2019).

As the storage prolamine of corn, zein can not create a viscoelastic dough at room temperature. However, it offers cohesive, stretchable, and extensible dough above its glass transition temperature (approximately 35 °C) when it is hydrated (moisture contents is higher than 20%). Thus, corn flour has also widely been used in gluten-free product formulations (Ozturk and Mert 2018a, 2018b).

Sorghum flour is also considered as a safe cereal-based flour alternative for celiac patients since its protein is more closely related to maize rather than wheat, rye, and barley. Furthermore, as compared to maize, sorghum has slightly lower protein (11–12%) and starch digestibility. Its neutral flavor and the light color like rice flour make it a suitable alternative to be combined with other gluten-free flours. Although the protein content of sorghum does not have a big role in creating structure, it can form cross-links with themselves or with other constituents during processing and baking, which improves functional properties of the dough (Hamaker and Bugusu 2003).

There has been a lot of research dealing with the potential use of pseudocereals in gluten-free formulations. Pseudocereals (buckwheat, amaranth, and quinoa) and their seeds have similar functional roles and composition with true cereals even though they do not have gluten proteins. They are also rich sources of good-quality protein with adequate levels of essential amino acids, which provide nutritional and functional properties. They have an excellent nutritional value because of their high amount of dietary fiber and lipids rich in unsaturated fats, adequate levels of important minerals and vitamins, and significant amounts of other bioactive components. Such properties of pseudocereals have encouraged researchers to enhance the structural properties of them for the preparation of high-quality and healthy gluten-free products. Among pseudocereals, special prominence has also been put on the inclusion of buckwheat into gluten-free formulations. Buckwheat proteins are composed mainly of the water-soluble globulins and albumins, having high levels of the essential amino acid lysine and arginine and thus, it has a high biological value (Conte et al. 2019). It has minor nutrients such as minerals (potassium, calcium, copper, zinc, and manganese), vitamins (B group and E), and phenolic compounds (hyperin, quercitrin, and quercetin). Apart from buckwheat flour, amaranth and quinoa flours have also been used recently. Amaranth and quinoa have higher protein contents (14–15% and 13–14%, respectively) compared to buckwheat (12%). They have high levels of the essential amino acids lysine and methionine. Similar to buckwheat, they are rich in many macro and micronutrients such as fiber, folate, riboflavin, ascorbic acid, tocopherol, calcium, magnesium, iron, potassium, zinc and phenolic compounds (Conte et al. 2019).

Teff flour has also been used in gluten-free formulations. The protein content of teff (8.7–11%) is close to that of true cereals. It has a well-balanced amino acid composition but relatively lower lysine and isoleucine contents. It contains a high amount of fiber (9.8% dry basis) and considerable

Table 3. Different types of hydrocolloids and/or emulsifiers used in gluten-free products.

Gluten-free Formulation	Hydrocolloids and/or emulsifiers	Gluten-free Product Type	Observed Effects	Reference
Chestnut flour, chia	Guar gum, *HPMC and tragacanth gum	Bread dough	The presence of chia and hydrocolloids modified significantly the rheological properties of doughs.	Moreira, Chenlo, and Torres (2013)
Rice flour, corn flour, soy flour	Carrageenan, alginate, xanthan gum, CMC and gelatin	Bread	The addition of hydrocolloids improved batter consistency and gave higher specific volume to breads. Overall, xanthan gum was the hydrocolloid that most improved gluten-free bread quality.	Sciarini et al. (2010)
Rice flour, buckwheat flour	Xanthan gum and propylene glycol alginate	Bread	The addition of both hydrocolloids significantly enhanced rheological properties of dough. Higher improvement in terms of increased specific volume and decreased crumb firmness and crumb structure was obtained especially with the addition of propylene glycol alginate.	Peressini, Pin, and Sensidoni (2011)
Rice flour	Xanthan gum, guar gum, LBG, HPMC, pectin, xanthan–guar blend and xanthan–LBG blend and emulsifier Purawave™ and emulsifier DATEM	Bread	Rheological measurements showed that emulsifiers in addition to gums were necessary to obtain the desired physical properties in dough formulations. Xanthan, xanthan–LBG and xanthan–guar gum mixture were observed to be the most effective gums in improving dough structure. The desired firmness, volume and sensory results could be obtained for all bread samples containing DATEM as an emulsifier.	Demirkesen et al. (2010b)
Brown rice flour	Xanthan, guar, LBG, agar, MC, CMC, HPMC and xanthan–guar blend and xanthan–LBG blend	Bread	The crumb structure of breads prepared with MC and agar gave heterogeneous structure with a lot of void spaces. The addition of xanthan, CMC, xanthan–guar, xanthan–LBG and HPMC provided finer texture of these crumbs.	Demirkesen et al. (2014)
Chestnut flour, rice flour	Xanthan–guar blend and xanthan–LBG blend and emulsifier DATEM	Bread	Gum blend and emulsifier addition were necessary to obtain the desired physical properties in dough formulations. The breads containing chestnut/rice ratio at 30/70 with addition of the blends of xanthan–guar and emulsifier had the best quality parameters in terms of hardness, specific volume, color and sensory values.	Demirkesen et al. (2010a)
Tigernut flour, rice flour	Xanthan–guar blend and emulsifier DATEM	Bread	Substitution of tigernut flour at certain amount significantly improved the quality of gluten-free rice breads with the use of xanthan–guar gum blend and emulsifier DATEM.	Demirkesen, Sumnu, and Sahin (2013)
Chickpea flour, tigernut flour	Xanthan gum, emulsifier CITREM and emulsifier sucrose fatty acid esters.	Bread	When chickpea protein and emulsifier were added in the formulation, shortening increased elastic moduli values of dough and specific volume of breads, and reduced initial crumb firmness of breads. Bread elaborated with both chickpea and tigernut flour maintained its baking characteristics even when shortening and/or emulsifier were reduced or eliminated.	Aguilar et al. (2015)
Rice flour, corn flour, corn starch	Cress seed gum, xanthan gum and DATEM	Bread	Hydrocolloid had positive effect on crumb color during storage. Hydrocolloid by forming thick layer influenced the stability of gas cells and caused more regular and solids pores in gluten-free bread.	Naji-Tabasi et al. (2016)
Rice, maize, buckwheat flour	HPMC and xanthan gum	Bread	The effect of the hydrocolloids on the gluten-free model systems of this study varied according to the raw materials used. HPMC had a positive linear effect on volume of teff and maize breads but a negative linear effect on rice breads, while the volume of buckwheat bread did not change. HPMC addition reduced crumb hardness of all breads. Xanthan addition reduced loaf volume of all breads. Xanthan increased the crumb hardness of teff and buckwheat breads. Crumb hardness values of maize breads were reduced by xanthan addition.	Hager et al. (2013).
Amaranth flour	Guar gum, gum acacia and gum tragacanth	Pasta	Guar gum was found to be best in terms of improving all aspects of gluten free pasta quality.	Chauhan et al. (217)

*HPMC: Hydroxypropyl methyl cellulose, LBG: Locust bean gum, MC: Methylcellulose, CMC: carboxymethylcellulose, DATEM: Diacetyl tartaric acid esters of mono-diglycerides, CITREM: citric acid esters of mono and diglycerides.

Table 4. Technological approaches used in gluten-free products.

Gluten-free Formulation	Gluten-free Product Type	Technological Approach	Application Purpose	Reference
		Changing flour functionality through particle size classification	Functionalization of protein content or amylose/ amylopectin ratio of starch, other features through milling	
Rice flour	Bread	Milling		de la Hera, Martinez, and Gómez (2013a) Park et al. (2014) de la Hera, Rosell, and Gomez (2014)
Maize flour	Bread	Milling		de la Hera et al. (2013b)
Wholegrain oat flour	Bread	Milling		Hüttner, Dal Bello, and Arendt (2010a)
Rice flour	Cake	Milling		de la Hera et al. (2013c)
Rice flour and buckwheat flour	Cookie	Milling		Torbica, Hadnađev, and Hadnađev (2012)
		Microfluidization	Functionalization of the structures through microfluidization and then utilization of these finely separated structures with enhanced physical properties in gluten-free formulations	
Corn gluten meal	Bread			Ozturk and Mert (2018a) Ozturk and Mert (2018b)
		Hydrothermal treatments	Modification of the functionality of starch-based ingredients by hydrothermal treatments	
Sorghum flour	Bread and Cake			Marston, Khouryieh, and Aramouni (2016)
Rice flour and corn flour	Bread			Bourekoua et al. (2016)
Rice flour	Noodle			Cai et al. (2016)
		Extrusion cooking	Providing starch gelatinization, breakage of the amylose and amylopectin chains, denaturation of proteins, enzyme (in)activation and maillard reactions.	
Rice flour	–			Martínez, Marcos, and Gómez (2013)
Rice flour	–			Martínez, Calviño, et al. (2014)
Rice flour	Bread			Sánchez et al. (2008)
Rice flour	Bread			Clerici and El-Dash (2006)
Rice flour	Bread			Clerici, Airoldi, and El-Dash (2009)
Rice flour	Bread			Martínez, Oliete, et al. (2014)
Rice flour	Cake			Jeong, Kang, and Shin (2013)
Extruded soy protein	Bread and Biscuit			Aly et al. (2015)
		High pressure assisted structure formation	Creating new structures and textures by modifying functional properties of biopolymers such as proteins and starches, inducing starch swelling and gelatinization	
Oat flour	–			Hüttner, Dal Bello, and Arendt (2010b)
Oat batter	–			Hüttner et al. (2009)
Barley starch	–			Stolt et al. (2001)
Sorghum flour	Bread			Vallons et al. (2010)
Buckwheat, white rice and teff batters	–			Vallons, Ryan, and Arendt (2011)
Sorghum starch	–			Vallons and Arendt (2009)
Basmati rice slurries	–			Ahmed et al. (2007)
		Sourdough fermentation	Enhancement of rheological properties of gluten-free dough and the quality of breads in terms of volume, texture, crumb structure, flavor and nutritional value. Retardation of the staling process and protecting gluten-free bread from mold and bacterial spoilage.	

(*continued*)

Table 4. Continued.

Gluten-free Formulation	Gluten-free Product Type	Technological Approach	Application Purpose	Reference
Buckwheat flour				Moroni et al. (2011)
Sorghum flour				Schober, Bean, and Boyle (2007)
Sorghum flour				Galle et al. (2012)
brown rice flour, buckwheat flour (Doves Farm Foods Ltd, Berkshire, UK), cornstarch (National Starch and Chemical Ltd, USA), soya flour, (Brown rice flour, corn starch, buckwheat flour and soya flour				Moore et al. (2007)
Brown rice flour, corn starch, buckwheat flour and soya flour				Moore, Dal Bello, and Arendt (2008)
	Cake	*Oleogel application*	Replacement of solid fats with these structured solid-like materials and reduction of saturated fats	
Rice flour	Bread			Demirkesen and Mert (2019)

Table 5. Technological approaches for adherence of gluten-free diet.

Technological Approach	Application Purpose	Reference
Gluten immunogenic peptides	Determination of gluten peptides in stool and urine for verification of diet compliance	de Lourdes Moreno et al. (2017) Cebolla et al. (2018) Gupta et al. (2019) Ruiz-Carnicer et al (2020)
SPR biosensor	Determination of gluten peptides in urine	Soler et al. (2016) Peláez et al (2020)
Nima gluten sensor	Determination of gluten in food	Taylor et al. (2018)
Online intervention	Interactive online intervention to improve gluten free diet adherence	Sainsbury et al (2013)

levels of vitamins. It is a good source of iron, calcium, and zinc. It has a high amount of unsaturated fatty acids (72.46%, oleic acid and linoleic acid). However, in literature, many studies have been conducted on the use of teff flours in traditional wheat-containing breads rather than in gluten-free formulations (Conte et al. 2019).

The positive impact of oats on the nutritional value of the gluten-free diets as well as adherence to gluten-free diet has also been shown (Størsrud, Hulthen, and Lenner 2003). However, there has long been doubt about the necessity of excluding oats from a gluten-free diet (Garsed and Scott 2007). In the study of Peräaho, Collin et al. (2004), it has been found that patients appreciated the taste, the ease of use, and the low costs of oats. Furthermore, 94% of patients believed that oats diversified the gluten-free diet; while 15% of celiac patients and 28% of dermatitis herpetiformis patients had stopped eating oats. The same authors also studied the impact of an oats-containing diet on quality of life and gastrointestinal symptoms of patients (Peräaho, Kaukinen, et al. 2004). The findings of study, conversely, showed that the oats-containing gluten-free diet led to more intestinal symptoms compared to the traditional gluten-free diet. Although mucosal integrity was not disturbed, more inflammation was observed in the oats consuming people. Therefore, the authors suggested that oats provide an alternative in the gluten-free diet, but patients with celiac disease should be aware of the possible increase in intestinal symptoms. Garsed and Scott (2007), on the other hand, suggested that the previous conflicting results about the use of oat in gluten-free diet may have been partly due to contamination of oats by wheat.

Gluten-free products can also be produced with the combination of alternative flour and flour& starch types. Starches can be used in gluten-free products. They provide better hydrolysis and improved gelatinization behavior with. Rice, corn, potato, cassava, sorghum, and tapioca have been widely used as starches types in gluten-free formulations. The recent and ongoing studies have demonstrated that gluten-free products can also be formulated with flours obtained from different sources such as nuts (tigernut, almonds, hazelnuts, walnut, cashew nut), seeds (flax seeds, chia seeds, pumpkin seeds) and tubers (arrowroot, tapioca, jicama, taro, potato, etc.), food by-products (green banana flour, orange pomace, strawberry seed, pumpkin seed, blackcurrant seeds, apple) in order to increase their nutritional and functional values with low costs. Furthermore, the use of such agro by-products can also help to obtain value-added novel ingredients creating sustainable food system opportunities (Tables 3–5).

Ingredients and additives to improve the quality of gluten-free baked products

In order to mimic wheat protein functionality, the use of ingredients such as hydrocolloids, enzymes, emulsifiers, protein and/or fiber sources have also been used for manufacturing of gluten-free products. Hydrocolloids (xanthan gum, guar gum, locust bean gum (LBG), hydroxypropylmethylcellulose (HPMC), and carboxymethylcellulose (CMC)) have commonly been used as gluten substitutes in order to assist viscoelastic properties, moisture retention properties and gas holding ability to dough/batter, to modify gelatinization of starch and hence to enhance texture and to retard starch retrogradation (Table 3). Emulsifiers are another of the most frequently used additives in gluten-free formulations. They are used to help blending and emulsification of ingredients to improve the properties of the shortening. They also enhance handling, hydration and gas retention ability of dough and hence the overall quality of products. Mono and diglycerides of fatty acids, DATEM (Diacetyl tartaric acid esters of monodiglycerides), sodium stearoyl-2-lactylate (SSL) and lecithin are some of the used emulsifiers in gluten-free bakery products (Table 3). The synergic interaction between hydrocolloids and emulsifiers has also been highlighted by some studies (Table 3).

The incorporation of enzymes such as amylase, cyclodextrin glycosyltransferases (CGT), transglutaminase (TG), glucose oxidase (GO), lactase, and proteases has also been established in the gluten-free baking industry. They can help to the formation of a 3-D network through the formation of intra- and intermolecular cross-links between the polypeptide chains. Thus, they can enhance water binding, handling and gas retaining ability of dough and consequently improve texture, volume, and shelf life of products.

Dairy protein with low lactose has also been incorporated into the gluten-free baking industry. The incorporation of dairy-based protein provides not only the functional properties but also the nutritional quality of products (Conte et al. 2019). Lactose intolerance can be noticed among celiac patients due to the lack of the lactase enzyme, which could not be generated by their damaged intestinal villi. Thus, the selection of dairy-based protein that will be used in gluten-free products is important. Supplementation of gluten-free products with high lactose-content powders is not suitable for celiac patients and dairy powders having a high protein/low lactose content (sodium caseinate, milk protein isolate) are preferred to be used in gluten-free formulations (Conte et al. 2019).

Technological approaches to improve gluten-free diet adherence

Technological approaches to improve the quality of gluten-free baked products

In order to meet the rising demands of celiac patients for high-quality products, apart from formulation emphasized methodology, technologies for gluten-free product improvement such as sourdough fermentation, high pressure-assisted structure formation, the functionalization of starch-based ingredients through hydrothermal treatments and functionalization cereal by-products through microfluidization as well as reducing of solid fats amount with oleogel technology have also been applied as potential production methods to meet the growing requests of celiac patients for high-quality products (Table 4).

Novel approaches for gluten-free diet compliance

The available diagnostic tests for celiac disease contain a series of blood tests as well as a small bowel biopsy. Serological tests may be used for management of celiac disease. In literature, many attempts conducted on development of standard reference materials for gluten were found to be unsuccessful and hence there is no consensus reference material for gluten. Thus, gluten detection in food is still challenging issue (Cebolla et al. 2018). Although various gluten-free diet adherence markers are available, they have significant limitations and are inadequately sensitive to identify occasional transgressions that may impede full gut mucosa recovery. Recent developments in analytical methods for detection of gluten is reviewed by Scherf and Poms (2016).

Celiac disease is triggered by the certain gluten immunogenic peptides (GIP) which are resistant to gastrointestinal digestion and can interact with the immune of patients to generate an autoimmune response against tTG and other antigens (Gupta et al. 2019). The improvement in the scientific knowledge and pathology of celiac disease has allowed to detect and identify gluten peptide sequences that activate the immunological response by T-cell activations in celiac patients and also the most immunodominant among them. Determination of gluten immunogenic peptides (GIP) in urine has recently been suggested to verify of diet compliance (Table 5). A proportional fraction of the GIP absorbed in the gastrointestinal tract is found to be excreted in urine. Thus, GIP can be detectable and quantifiable in very different environments including hydrolyzed food and beverages, excreted in stool and urine providing the simple and objective means to evaluate adherence to gluten-free diet. It may be a suitable method to measure recent gluten exposure in celiac patients and appears to accurately predict the absence of histological lesions (Ruiz-Carnicer et al., 2020).

In the study of de Lourdes Moreno et al (2017), GIP were sensitively detected in human urine samples in positive correlation with the amount of gluten intake. Thus, GIP allowed to distinguish gluten consumers from non-consumers by a quantitative lateral flow test using anti-α-gliadin monoclonal antibodies. Thus, the combination of more easy-to-handle samples such as urine and user-friendly biosensors has been used for the development of portable and simple devices for the diet compliance of celiac patients. The study of Soler et al. (2016) reflected that SPR biosensor was proposed for detecting gluten peptides in urine and gluten consumers could be differentiated from nonconsumers by measuring several urine samples from both normal diet and gluten-free diet (Table 5). Recently, a gluten sensor device (Nima) has developed a portable gluten detection device intended for use by gluten-intolerant consumers

(Table 5). Furthermore, Nima was evaluated against the existing ELISA methods with respect to its accuracy, sensitivity, and specificity. Even though the portable, handheld Nima gluten sensor functions reliably detected gluten residues at appropriate levels in a range of different foods, the limitations of the gluten-sensing device such as the need for the following of the instructions for its proper use, the need for small sample size and the necessity of the homogenized sample as well as the detection problem of gluten residues in fermented and hydrolyzed products should be identified (Taylor et al. 2018).

Another approach for gluten-free diet adherence is the use of interactive online intervention. Sainsbury, Mullan, and Sharpe (2013b) tested the effectiveness of an interactive online intervention to improve gluten free diet adherence in adults with celiac disease (Table 5). The findings of study showed that the intervention group evidenced significantly enhanced gluten free diet adherence, and gluten free diet knowledge following the treatment period relative to the waitlist control group. The online program was found to be effective in improving adherence and represents a promising resource for celiac patients who are trying to follow gluten free diet.

Conclusion

The gluten-free food market is growing with the increases in the number of people who adhere to a gluten-free diet. On the other hand, the lack of awareness and knowledge about a gluten-free diet creates difficulties for the general public following the gluten-free diet. The positive effects of an increased level of awareness and knowledge toward a gluten-free diet have been highlighted in many studies. Although celiac people have a higher level of knowledge about gluten-free diet as compared to non-celiac followers, most of the celiac patients adhere to the gluten-free diet still experience difficulties. The limited availability, the high price of products, lack of information and knowledge about celiac disease, lack of information and knowledge about the gluten-free diet, treatment burden, insufficient labeling, cross-contamination risk, treatment burden, lack of knowledge and information about celiac disease and gluten-free diet, psychological factors in celiac patients, the adverse effects of a gluten-free diet and quality defects of gluten-free products are among the major problems faced by celiac patients. In order to overcome treatment burden, the importance of a need for non-dietary interventions as well as need for patients to regularly follow up with clinicians, dieticians, and other allied health professionals has been highlighted. The association between knowledge of celiac disease and the adherence to the diet as well as the relationship between knowledge of gluten-free diet in celiac patients and their adherence to the diet suggests the development of training programs for celiac patients. The negative impact of psychological symptoms on quality of life and adherence suggests that management in celiac disease should include the provision of psychological coping skills and purely dietetic-based strategies to decrease gastrointestinal symptoms.

Inadequate producing steps during the harvesting, milling, transportation and processing steps may be responsible for the cross-contamination of food with gluten. In order to avoid cross-contamination, the importance of the use of separate production areas for gluten-free and gluten-containing products and the use of more precise and universal labeling system and understanding of gluten-free labeling have been highlighted. An ideal balanced approach, such as subsidizing gluten-free products considering all population groups with celiac disease, can be helpful in order to access different gluten-free products as well as decrease the financial burden to celiac patients. The nutritional compositions of gluten-free products may be improved with the reformulation of products as well as with the use of technological approaches. The drawbacks associated with the low fiber of gluten-free products have been overcome by the use of alternative flours. Furthermore, dietary fibers derived from either grain or from vegetables or fruits can also be incorporated in gluten-free formulations to compensate for the nutritional deficiencies of products. Food-by products have also been underutilized as potential fiber sources. Different gluten-free flour sources richer in vitamin and minerals can also be used to complement the micronutrient deficiency of gluten-free products.

In order to counteract quality defects such as low volume, firm texture, short shelf life, and lack of unique taste and aroma; alternative flour and/or starches can be used. These alternative flours and/or starches are selected considering special attributes such as their functional roles, economic cost as well as nutritional and quality characteristics of the resulted products. Several additives such as hydrocolloids, emulsifiers, enzymes, dairy proteins, etc. have also been employed in gluten-free formulations to mimic wheat protein functionality. Apart from designing of formulation, the adaptation of novel technologies such as sourdough fermentation, high pressure-assisted treatment, hydrothermal treatments, microfluidization, oleogel technology for gluten-free product development considering of flour components and the interactions among them can also be used. Novel approaches such as determination of gluten immunogenic peptides, a gluten sensor device (Nima) and interactive online intervention may also be used to verify of diet compliance.

Disclosure statement

No potential conflict of interest was reported by the authors.

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