The Pharma Innovation Journal 2022; SP-11(6): 2371-2382

www.ThePharmaJournal.com

The Pharma Innovation

ISSN (E): 2277-7695
ISSN (P): 2349-8242
NAAS Rating: 5.23
TPI 2022; SP-11(6): 2371-2382

www.thepharmajournal.com
Received: 03-03-2022
Accepted: 06-04-2022

Domma Pavan
Department of Food Technology and Nutrition, School of Agriculture, Lovely Professional University, Phagwara, Punjab, India

Anaghasree
Department of Food Technology and Nutrition, School of Agriculture, Lovely Professional University, Phagwara, Punjab, India

Putti Satish
Department of Food Technology and Nutrition, School of Agriculture, Lovely Professional University, Phagwara, Punjab, India

Doddi Chaitanya
Department of Food Technology and Nutrition, School of Agriculture, Lovely Professional University, Phagwara, Punjab, India

Yadagiri Pooja
Department of Food Technology and Nutrition, School of Agriculture, Lovely Professional University, Phagwara, Punjab, India

Corresponding Author
Domma Pavan
Department of Food Technology and Nutrition, School of Agriculture, Lovely Professional University, Phagwara, Punjab, India

Gluten-free diet: Challenges faced by celiac disease patients

Domma Pavan, Anaghasree, Putti Satish, Doddi Chaitanya and Yadagiri Pooja

Abstract
Celiac disease (CD) is an immune-mediated disease in which gluten causes damage to the small intestinal mucosa in genetically sensitive people. It can show in a variety of ways, from classic gastrointestinal or extra intestinal symptoms to asymptomatic variants. To date, the only treatment for CD is a strict, lifetime gluten-free diet (GFD). According to the findings, as little as 50 mg gluten per day (equivalent to a few breadcrumbs) can cause significant mucosal damage in CD patients. In CD patients, poor adherence to a GFD is related to anaemia, osteoporosis, infertility, secondary autoimmunity, cancers, and death.
However, because gluten is a major part in most diets, sticking to a GFD can be incredibly difficult. Several investigations have shown that CD patients' adherence to the GFD is poor. Understanding the GFD and food labelling, as well as the cost and availability of GF foods, all have a significant impact on GFD adherence. To ensure long-term dietary adherence, CD patients must be given accurate and thorough information on the GFD and monitored by a healthcare expert on a regular basis. Celiac disease (CD) is only treated with a lifelong gluten-free diet (GFD), which can be difficult. The goal of this study was to learn more about how patients felt about the GFD in terms of challenges, disease-specific symptoms, adherence, and information sources.

Keywords: Gluten-free diet, celiac disease, challenges, treatment, gluten-free flours

1. Introduction
Celiac disease is an autoimmune disease of the small intestine that is triggered and maintained by consuming storage proteins. (Gluten) (Kahaly *et al*., 2018) [1]. It is characterised by immune-mediated enteropathy, which causes malnutrition and vitamin malabsorption (Holtmeier & Caspary, 2006) [2]. Gluten is the main storage protein of wheat grains and it is made up of hundreds of related but distinct proteins, the most common of which are gliadin and glutenin. Secalin in rye, hordein in barley, and avenins in oats are all similar storage proteins that are generally referred to as "gluten."(Biesiekierski. 2017) [3]. Newer celiac disease diagnostic methods, such as serologic tests for antibodies against tissue transglutaminase and deamidated gliadin peptide, make diagnosis much easier. In some clinical situations, tests for celiac- permissive human leukocyte antigen (HLA-DQ2) and (HLA-DQ8) molecules are more useful. Histopathologic evaluation of duodenal biopsy specimens is used to detect celiac disease. In some cases, especially in children, a diagnosis can be made without a biopsy, according to recent controversial guidelines. Adherence to a gluten-free diet can reduce symptoms, mortality, and the risk of cancer (Kelly *et al*., 2015) [11]. Small intestinal adenocarcinoma, refractory sprue, and enteropathy-associated T-cell lymphoma are complications of celiac disease that must be ruled out when alarming symptoms such as abdominal pain, diarrhea, and weight loss develop despite a strict gluten-free diet (Green & Cellier, 2007) [20]. Treatment of celiac disease involves a gluten-free diet (i.e., a diet with no wheat, rye, or barley proteins). Gluten-free wheat substitutes are available for celiac disease patients in a variety of forms like fruits, vegetables, meat and dairy products. it is a low-nutritional value protein that can be substituted with other dietary proteins. However, patients who follow a gluten-free diet tend to consume lower nutrients than they should, particularly fibers, iron, calcium, and folate (Fasano & Catassi, 2012) [6]. Adherence to gluten-free diet, the best standard in the treatment of celiac disease, plays an important role in alleviation of clinical symptoms, prevention of long-term celiac disease-related complications, improvement of nutritional status and quality of life. Iron, folic acid, calcium, and vitamin D, as well as B vitamins and zinc, are all deficient in gluten-free diets that aren't properly balanced (Marciniak *et al*., 2021) [8].

This review focuses on celiac disease and their symptoms, causes, treatment and also nutritional challenges of celiac patient. Health benefits of Gluten-free diet and gluten-free flours. Chemical composition, nutritional and anti-nutritional content of gluten free flours, various challenges encountered in consuming gluten-free food. as well as a variety of gluten-free flour- based food products, has also been discussed in the review to provide a brief overview to the readers.

2. Celiac disease

Celiac disease (CD) is a multigenetic autoimmune illness caused by gluten consumption in people who are genetically predisposed to it (Guandalini & Discepolo, 2022) [17]. CD is a complicated illness with both hereditary and environmental components. Various genetic polymorphisms within the HLA region (those producing the HLA-DQ2/DQ8 heterodimers) were the only reliably recognised genetic variables contributing to CD risk for a long period (Cenit *et al*., 2015) [18]. Celiac disease was once thought to be an uncommon childhood malabsorption illness, however it is now largely a disease that affects adults (Green & Jabri, 2006) [19]. Because celiac disease can strike at any age and has a low absolute mortality rate, it's natural to assume that the disease's prevalence would be higher among the elderly people (Lebwohl *et al*., 2015) [20]. Celiac disease is described by small-intestinal mucosal injury and nutritional loss in genetically predisposed people as a result of dietary consumption of wheat gluten and related proteins found in barley and rye. Celiac disease is linked to genes that code for HLA-II antigens, primarily from the DQ2 and DQ8 classes. And also the Celiac disease is more common in some at-risk groups and can be linked to other autoimmune disorders such type 1 diabetes or thyroiditis (Rodrigo, 2006) [21].

2.1 History and origin

Samuel Gee originally identified celiac disease in 1888, but it wasn't until 1953 that the role of gluten in the pathology's development became obvious (Parzanese *et al*., 2017) [22].

Aretee de Cappadoce, a Greek physician, was the first to describe the symptoms of CD in the first century. However, the involvement of gluten peptides in CD triggering was discovered only in 1950. William Dicke was the first physician to recommend a gluten-free diet as a cure for celiac disease symptoms, and it is still the only effective treatment for the disease in 2014. Margot Shiner published a pathologic description of the particular lesions seen in CD in 1957. The discovery of highly specific and sensitive antibodies in the early 1990s revolutionised the disease's diagnostic circumstances (Cerf-Bensussan *et al*., 2015) [23].

CD's current high frequency is only the final link in a sequence of events that began around 10,000 years ago with wheat domestication and spread from the Middle East.

2.2 Epidemiology

Celiac disease was once assumed to be limited to (or predominant in) Northern and Western Europe, however it is now known to affect people all over the world. A systematic assessment of global celiac disease prevalence indicated a seroprevalence rate of 1.4 percent, with prevalence varied by continent from 1.3 percent (11 research in South America) to 1.8 percent (11 studies in Europe) (Asia, 20 studies) (Lebwohl & Rubio-Tapia., 2021) [24]. Celiac disease is common in families, with homozygous twins having an 80% concordance rate (Ludvigsson, & Murray., 2019) [25]. When compared to people residing in the south, people living at latitudes of 35 north or higher have a higher prevalence of CD. Although little is known about the global incidence of CD, in Olmsted County, Minnesota, a growing incidence in both men and women has been convincingly observed over the last 30 years. Between 2000 and 2010, the adjusted incidence of CD was 17.4 per 100,000 person-years. However, when compared to placebo, adjusting the timing of gluten introduction or the amount of gluten in the diet did not lessen the overall risk of CD. Surprisingly, the prevalence of typical CD among incident patients hasreduced over time, whereas those with nonclassic symptoms has grown (Oxentenko & Rubio- Tapia., 2019, December). The condition is more common, with considerable differences between series in so-called high-risk populations such type 1 diabetes (1–12%), Thyroid autoimmunity (which affects 2–6% of people), Down syndrome affects 2–6% of people, 3–7% of people have auto-immune hepatitis, Turner syndrome affects 4–5% of people. Members of CD's first-degree family (10–20%) Individuals with iron deficiency anaemia (3–15%), osteoporosis patients (1–3%), and a variety of other clinical problems (Ben Houmich & Admou., 2021) [27].

2.3 Symptoms and causes

Diarrhoea, vomiting, stomach pain and distention, and malabsorption are all common symptoms of CD. After gluten-containing foods are introduced to the diet, these symptoms commonly develop between the ages of 6 and 24 months. Irritability, poor growth, and inability to flourish are common in young children (Durhaa & Temples, 2018) [28]. There are no indications or symptoms of malabsorption in non-classic celiac disease. Reflux, dyspepsia, abdominal pain, vomiting, bloating, constipation, or extraintestinal manifestations such as fatigue, anaemia, dental enamel hypoplasia, osteoporosis/osteopenia, vitamin deficiencies, hypertransaminasemia, dermatological, gynaecological, neurological, or psychiatric conditions are all common in this type of patient. This type appears later in childhood or in adulthood (Domsa *et al*., 2020) [29].

Problems with growth and failure to thrive (in children). This is due to their inability to absorb nutrition. Gluten-induced damage to the small intestine results in nutritional absorption surface area decrease in celiac disease (Owen & Owen, 2018) [30]. Changes in behaviour, such as short- term memory loss, anxiety, depression, sleep difficulties, cognitive impairment, psychosis, and attention-deficit disorder, are one of the most fascinating yet poorly understood clinical manifestations of celiac disease (Fasano, 2017) [31]. Obesity was found to be common among celiac patients in recent investigations. Almost half of all adult celiac disease patients have a BMI of 25 or above; however, because obesity is more common in celiac children, it is vital to test for celiac disease in obese children. Obesity and weight gain may occur from the high calorie content of commercially accessible GF foods. Furthermore, damage to the villi of the intestine can cause problems with food digestion and absorption, leading to obesity (Hosseini *et al*., 2018) [32].

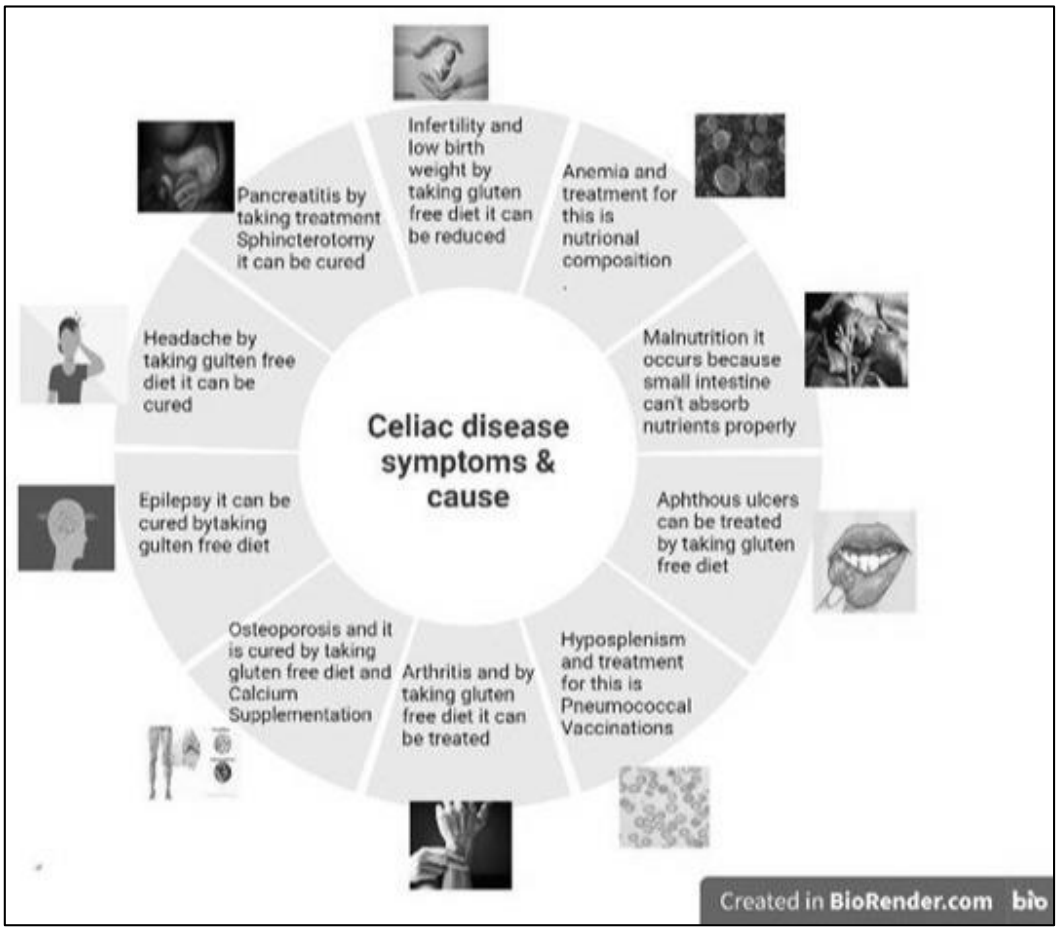

Fig 1: Symptoms and Causes

3. Treatment

3.1 Gluten free diet

CD is now treated solely with a gluten-free diet that must be followed for the rest of one's life. Gluten can be tolerated by CD patients in amounts ranging from 10 to 50 mg per day (Durham& Temples, 2018) [28]. The gluten-free diet is the foundation of all celiac disease treatment and should be prescribed to all patients once a proper diagnosis has been obtained. Gluten-free eating entails avoiding wheat, rye, barley, and all closely related cereals, such as spelt (a wheat variant). Although isolated incidences of oat intolerance have been reported, oats are a related cereal that is accepted by almost all celiacs. Many commercially available oat products are contaminated with other grains. Maize, rice, sorghum, and tef are among the cereals that are permitted. And Vegetables, salads, legumes, fruits, nuts, meat, fish, poultry, cheese, eggs, and milk are all natural foods that can be taken without restriction on a Gluten free diet (Lionetti & Catassi, 2011) [33].

3.2 Supplemental Therapy

As previously stated, the majority of untreated CD patients have several nutritional deficits. Because few gluten-free goods are enhanced or fortified in nutrients, the GFD may exacerbate these deficiencies. As a result, deficient nutrients like iron, calcium, zinc, magnesium, and other vitamins (particularly the B complex) should be supplemented in these patients' dietary plans (Chand & Mihas, 2006) [34].

3.3 Immunotherapeutic

3.3.1 NexVax2

Nexvax2 is an unique gluten tolerizing vaccine candidate made up of three patented peptides that aims to restore long-term gluten tolerance in Celiac Disease patients' immune systems via immunotherapy desensitisation methods. Nexvax2 was created to protect patients with Celiac disease from the negative effects of inadvertent gluten consumption by reprogramming gluten- responsive T-cells, allowing them to resume their usual diet and quality of life (Asri *et al*. 2020) [35].

3.4 Treatment of celiac disease for children

Treatment with a gluten-free diet (GFD) is advised for all symptomatic children with celiac disease-like intestinal histopathologic abnormalities (CD). Children with recurrent diarrhoea and low weight growth due to CD have completely resolved symptoms when treated with a GFD, according to clinical experience. Treatment with a GFD has been shown to reverse impaired bone mineralization in children with CD and lower the prevalence of spontaneous abortions and low-birth-weight babies in adult women with CD. According to epidemiological studies, CD therapy can reduce the incidence of some intestinal malignancies and lower death rates compared to the general population. Early CD therapy does not seem to prevent the emergence of other autoimmune illnesses. Within days or weeks of commencing a GFD, the clinical response of children with CD might be noted. The small intestinal mucosa takes longer to heal histologically following GFD, however children recover considerably faster and completely than adults (Mearin, 2007) [10].

3.5 Treatment of celiac disease for adults

Celiac crisis has a significant morbidity rate and, while being seldom reported, occurs in adults with a definite triggering event. Patients with severe unexplained diarrhoea and

malabsorption should be examined for celiac disease, and systemic steroids or oral budesonide may be investigated as therapy options. In the near term, nutritional assistance is frequently necessary, although most patients eventually react to gluten restriction (Jamma *et al*., 2010) [11]. Celiac illness can only be treated by following a gluten-free diet for the rest of one's life (Leffler *et al*., 2007) [12].

3.6 Treatment of celiac disease for pregnant women

Celiac disease can influence a woman's reproductive life, including delayed puberty, infertility, amenorrhea, and early menopause. Female celiac disease patients had a greater incidence of spontaneous abortions, low birth weight babies, and shorter nursing periods, according to clinical and epidemiological research. There are no good data on the risk of birth abnormalities in the offspring of celiac disease patients; nonetheless, celiac disease causes malabsorption and lack of key organogenesis components such as iron, folic acid, and vitamin K. Overall, data shows that celiac disease patients are especially vulnerable to reproductive toxins; nevertheless, the pathophysiology of celiac disease-related reproductive problems is yet unknown. At the moment, like the other diseases connected with celiac disease, the only way to avoid or treat reproductive repercussions is to follow a gluten-free diet for the rest of your life (Stazi & Mantovani, 2000). In pregnancies with CD, we feel that patient-specific customised care is critical, as is nutritional control, for improved pregnancy outcomes. In the treatment of CD pregnancies, low-molecular-weight heparin (LMWH) and low-dose corticosteroids (LDC) appear to be beneficial (Beksac *et al*., 2017).

4. Pathogenesis

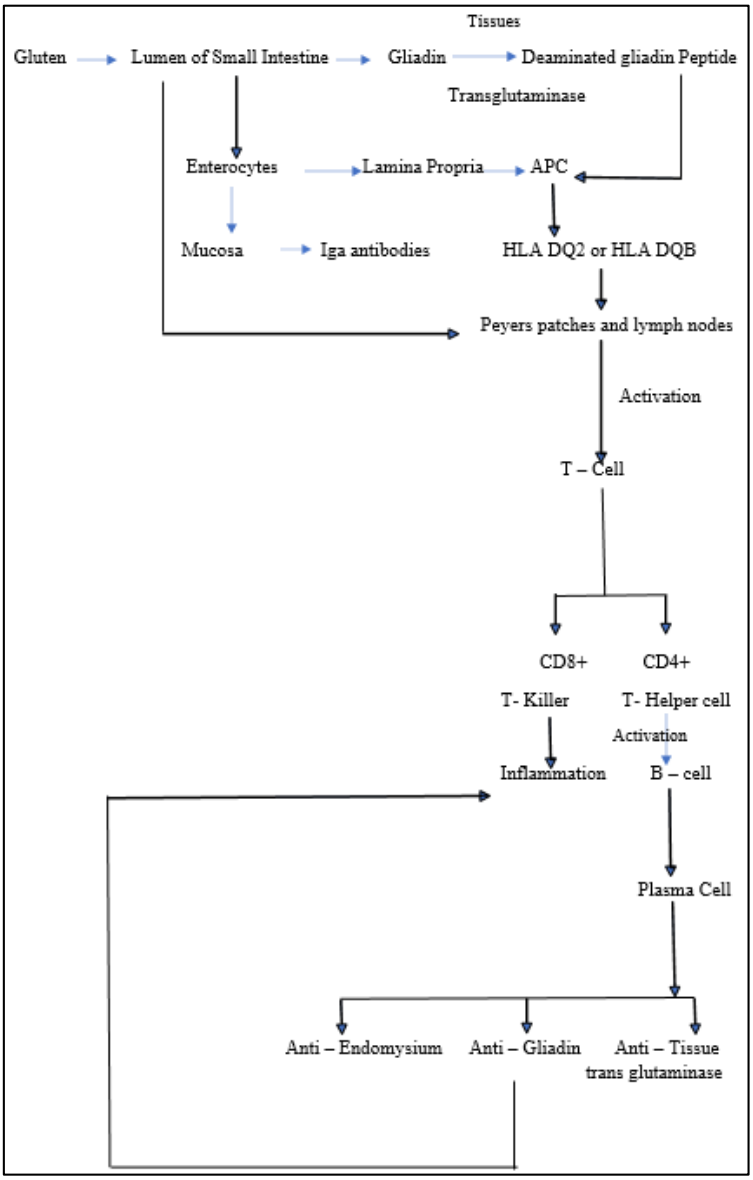

Fig 2: Pathogenesis of Celiac disease

5. Nutritional Challenges of Celiac Patient

Gluten free products are often lacking in B vitamins, calcium, vitamin D, iron, zinc, magnesium, and fibre. There are few gluten-free goods that are supplemented or fortified, increasing the risk of vitamin shortages. patients who have just been diagnosed or who have had inadequate treatment have symptoms like low bone mineral density, uneven macronutrients, low fibre consumption, and micronutrient deficiencies. The increased incidence of obesity reported in people with celiac disease who adopt a gluten-free diet is also

concerning. A trained dietician must be part of the health care team that examines the patient's nutritional status and compliance on a frequent basis due to the nutritional concerns associated with celiac disease (Kupper, 2005) [15].

Classic celiac disease is marked by malabsorption, weight loss, and vitamin/mineral deficiency. The nutritional condition of the participants, as well as serum concentrations of folic acid, vitamin A, B6, B12, and (25-hydroxy) D, zinc, haemoglobin (Hb), and ferritin, were assessed (before prescribing gluten free diet). Almost all CD patients (87%) had at least one value below the recommended lower limit. Vitamin A deficiency was found in 7.5 percent of patients, 14.5 percent for vitamin B6, 20 percent for folic acid, and 19 percent for vitamin B12. Similarly, 67 percent of CD patients exhibited zinc deficiency, 46 percent had low iron storage, and 32 percent had anaemia. Overall, 17 percent of the patients were malnourished (weight loss of more than 10%), 22% of the women were underweight (BMI of less than 18.5), and 29% were overweight (body mass index (BMI) of more than 25). With the exception of vitamin B12, vitamin deficits were barely visible in healthy controls. Contrary to popular belief, vitamin/mineral shortages were not linked to a (higher) grade of histological intestine damage or (impaired) nutritional status. In conclusion, even if the prevalence of obesity at initial diagnosis is rising, vitamin/mineral deficiencies are still widespread in newly "early diagnosed" CD-patients (Wierdsma *et al*., 2013) [16].

Between 20% and 38% of celiac patients have nutritional inadequacies, with 12 percent to 69 percent having iron deficiency and 8% to 41% having Vitamin B12 deficiency. Furthermore, damaged villi in celiac patients induce lactose intolerance due to reduced lactase production, resulting in phosphorus, calcium, and Vitamin D deficiency (Hosseini *et al*., 2018) [32]. Gluten in the range of 50–100 mg per day appears to be safe for most celiac disease patients. Due to low levels of contamination in international trade bulk food goods and the usage of gluten in the food industry, a completely gluten-free diet is difficult to obtain (Sollid & Lundin, 2009) [36].

6. Gluten free diet

Gluten is also a nutritional term for certain cereal prolamins, which are ethanol-soluble proteins found in wheat, rye, barley, and their cross-bred grains, as well as possibly oats (El Khoury *et al*., 2018) [37]. This is due to the fact that the majority of popular gluten-free (GF) raw materials are mineral-deficient. Despite the fact that GFD is becoming increasingly popular, data on minerals in GF products is still scarce. Even more importantly, data access is even more restricted. As a result, the paper examines the Ca, Fe, Mg, and Zn content of hundreds of grain- free products sold around the world. The glutenfree diet, touted by celebrities for weight loss and athletes for improved performance is virtually impossible to avoid hearing about. Between 2004 and 2011, the market for glutenfree products grew at an annual rate of 28% (Jones, 2017) [96]. A gluten-free diet (GFD) is undeniably important in the treatment of celiac disease and other gluten-related disorders. Strict GFDs, on the other hand, frequently result in nutritional imbalances and, as a result, deficiencies. An insufficient amount of Ca, Fe, Mg, and Zn is one of the most common deficiencies caused by a GFD. This is due to the fact that the majority of popular gluten-free (GF) raw materials are mineral-deficient. For more than a decade, the gluten-free diet (GFD) has been the most popular elimination diet. The number of people following a GFD is steadily rising (Rybicka, 2018) [38]. Celiac disease can only be treated with a lifelong glutenfree diet (GFD) (CD). For most people with CD, changing lifelong eating habits and adapting to the new gluten-free (GF) lifestyle can be a huge challenge for a variety of reasons. Many studies have looked into the impact of celiac disease and a GFD on quality of life in adults1– 5 and children6,7, with mixed results (Case, 2005) [39]. However, it has been studied as a potential treatment for other medical conditions such as dermatitis herpeticformis irritable bowel syndrome, neurologic disorders, rheumatoid arthritis, and diabetes mellitus, despite the lack of evidence. People who want to lose weight have become increasingly interested in following a gluten-free diet in recent years. The global GF product market is expected to become enormously valuable in the near future, as one clear example of the boom in this type of diet (Simon *et al*., 2014) [40]. When a patient first starts eating gluten-free, there is often a lot of anxiety and confusion about what foods are allowed and which are not. Many foods, such as quinoa, are gluten-free. Fresh, frozen, or canned fruits; milk, butter, and cheese fresh meats, fish, poultry, eggs, beans, and vegetables seeds, nuts, corn, and rice are a few examples. Gluten is the most common allergen. It's in breads, cereals, and pastas, but it's also in seasonings, sauces, marinades, soy sauce, and other foods. Soups, salad dressings, and flavoured rice in convenient packages (Niewinski, 2008) [42].

6.1 Benefits of gluten free diet

One of the most significant advantages of a gluten-free diet is that it aids in the rapid improvement of energy levels. Gluten intolerance comes in a variety of forms and degrees of severity, but it has no negative consequences (2). A gluten-free diet can also help you manage your Autism symptoms. Autism is a mental disorder that typically affects children under the age of two.

6.2 Negative of gluten free diet

According to research, a gluten-free diet is thought to have insufficient fibre in the overall diet, which can lead to constipation. Gluten is abundant in whole wheat and foods derived from it, and these are also the primary sources of fibre. Gluten-free food, on the other hand, consists of potato, tapioca, and white rice, which do not contain enough fibre to meet the needs of the human body. Fiber in the diet, despite being indigestible, plays an important role in reducing constipation. (Khayrullin *et al*., 2019) [41].

6.3 History and origin

The gluten-free diet was first mentioned in a report on the dietary treatment of CD written by paediatrician and scientist Willem Karl Dicke in 1941.

The diet is still used and researched today for a variety of other health conditions, including NCGS, IBS, diabetes, DH, inflammation, and obesity.

For many years, there has been an increase in research interest in the gluten-free movement, in addition to the clinical and practical applications of the diet. The current trends, attitudes, and knowledge surrounding the gluten-free diet, as well as its nutritional adequacy, will be discussed in the sections that follow. Furthermore, the gluten-free diet's effects on glutenrelated illnesses, diabetes, and other autoimmune diseases, as well as weight loss (Joye *et al*., 2018) [37].

Table 1: Nutritional and anti-nutritional content of gluten free flours

Sr. No:	Flour	Energy (kcal/100g)	Protein (g/100g)	Fat (g/100g)	Fibre (g/100g)	CH 2O (g/100g)	Vit A (g/100g)	Vit B1 (g/100g)	Vit B2 (g/100g)	Vit B3 (g/100g)	Vit B6 (g/100g)	Vit B12 (g/100g)	Ca (g/100g)	Fe (g/100g)	P (g/100g)	Mg (g/100g)	Mn (g/100g)	Reference
1.	Rice Flour	347	48.6	1.70	4.91	33.8	1.5	0.13	0.13	1.81	0.35	1.1	37	11.6	102.60	8.17	47.0	Shih and Daigle (2000) [43] Santelli *et al*. (2006) [4]
2.	Ragi Flour	430	6.45	1.14	3.80	76.18	ND	0.42	0.29	N D	0.38	ND	182.15	9.10	193	114	4.50	Verma and Mishra (2019) [45] Desai *et al*. (2010) [44]
3.	Coconut Flour	335.28	9.90	0.87	11.14	78.46	0.1	0.43	0.11	0.47	0.30	0.40	63.4	0.10	0.41	0.23	75	Gunathilake *et al*. (2009) [7] Makinde and Eyitayo (2019) [59] Ramya and Anitha (2020) [46]
4.	Cassava Flour	338.28	1.60	2.04	1.21	79.50	ND	0.25	0.04	N D	N D	ND	15.77	3.50	242.85	51.77	13.4	Klang *et al*. (2020) [47] Kristantia and Herminiati (2019) [49]
5.	Oat Flour	420	4.8	3.5	17.2	82.4	ND	0.25	0.04	0.72	0.10	ND	40.3	5.49	290.89	133	3.72	Rybika And Gliszczy Nska (2017) [50] Dan Yang *et al*. (2017) [62]
6.	Chickpea Flour	387	23.7	4.8	14.8	61.1	ND	0.37	0.12	1.64	0.17	ND	91.8	4.30	320	120	2.70	Rybika And Gliszczy Nska (2017) [50] Iga and Anna (2017) [9] Sreerama *et al*. (2012) [51]
7.	Acorn Flour	506	5	8.5	11.5	75	0.5	0.02	0.13	N D	0.03	0.6	164	18.61	29.2	54.2	3.65	RYBIKA and GLISZCZY NSKA (2017) [50] Iga and Anna (2017) [9] Martins *et al*. (2020) [52]
8.	Amaranth Flour	389	12.81	8.9	3.15	63.8	0.2	0.01	0.04	<0.01	0.69	0.1	93.5	5.96	597.93	205	2.56	Rybika And Gliszczy Nska (2017) [50] Iga and Anna (2017) Morals *et al*. (1987)
9.	Buckwheat Flour	301	14.91	2.31	10.69	54.23	ND	0.37	0.22	3.16	0.33	ND	3.2	8.24	328.44	157	2.11	Rybika And Gliszczy Nska (2017) [50] Iga and Anna (2017) [9] Culetu *et al*. (2021) [53]
10.	Teff Flour	356	11.89	2.48	8.31	73	ND	0.60	0.13	3.24	0.12	ND	83.7	9.79	402.30	137	4.02	Rybika And Gliszczy Nska (2017) [50] Iga and Anna (2017) [9] Culetu *et al*. (2021) [53]
11.	Millet Flour	333.3	9.98	3.95	7.79	70	0.1	0.40	0.20	6.02	0.90	0.01	14.1	3.14	309.87	107	0.97	Rybika and Gliszczy Nska (2017) [50] Iga and Anna (2017) [9] Culetu *et al*. (2021) [53] Nazni and Shobana (2016) [55] Tumwine *et al*. (2019) [56]
12.	Maize flour	298.04	7.25	2.16	7.30	20.58	0.2	1.5	1.5	14.9	2.0	0.002	4.28	1.19	95.83	47.33	0.55	Culetu *et al*. (2021) [53] Aini *et al*. (2016) [54] Pachon *et al*. (2018) [71]

7. Health Benefits of Gluten free flours

Pseudo cereals are high in starch, fibre, proteins, minerals, vitamins, and phytochemicals with potential health benefits such as saponins, polyphenols, phytosterols, phytosteroids, and betalains. Pseudocereals are a good source of fibre (Martínez-Villaluenga, *et al*., 2020) [57].

Other gluten-free cereals, such as sorghum, millet, and teff, as well as pseudo cereals like buckwheat and quinoa, have stimulated the interest of researchers due to their various potential health benefits (Bauer, *et al*., 2015) [58].

Table 2: Health benefits of some gluten free flours

Gluten free flour	Various health benefits and mechanism	References
1. Coconut flour	The viscose and fibrous structure of dietary fibres can control the release of glucose in the blood over time, helping in the proper control and management of diabetes mellitus and obesity. Consumption of an antioxidant-rich diet has been shown to reduce the risk of cardiovascular disease and some cancers. Vitamin E (alpha-tocopherol), which is abundant in coconut, is one of the most prominent natural antioxidants.	(MAKINDE *et al*., (2019) [59] (Rajchasom, *et al*., (2019) [60]
2. Brown rice	GBR contains a number of bioactive compounds, which is not absorbed in the small intestine but instead enters the large intestine and is fermented. This helps promote colon health and may help to reduce the risk of diet-related diseases such as obesity, type 2 diabetes, and colorectal cancer This flour helps to reduce cholesterol level and also promotes growth.	(Sirisoontaralak, *et al*., (2018) [61] (Saleh, Wang *et al*., (2019) [62]
3. Oat flour	Insulin resistance (IR) is a common pathophysiological condition in which a higher-than-normal insulin concentration is required to maintain normal glycemia and adequate glucose consumption in insulin target tissues. Type 2 diabetes (T2D) is a metabolic disorder characterized by chronic low-grade inflammation and abnormal expression and production of multiple inflammatory mediators such as tumour necrosis factor (TNF)	(Zhu, Dong, *et al*., (2020) [63]
4. Almond flour	Almonds are high in protein, calcium, and bioactive compounds, as well as dietary fibre, iron, and zinc almond flour helps in decrease in risk of chronic diseases	(Martinescu, *et al*, (2020) [64](Siqueira *et al*., (2015) [65]
5. Rice flour	Rice flour is high in protein, contains more B vitamins, calcium, potassium, thiamine and niacin, iron, fibre, improves blood sugar and cholesterol levels, and also helps in weight loss, decrease the chances of diventricular disease, colon disease, type 2 diabetes, and hypertension.	(Martinescu, *et al*, (2020) [64] (Kupkanchanakul, *et al*., (2019) [66]
6. Arrowroot flour	Related to the digestive system, frequently used to diagnose diarrhoea and relieve stomach pain Arrowroot flour is high in potassium, contains minerals like iron, manganese, phosphorus, magnesium, and zinc, and has a low-calorie count. It is also a great source of protein and does not contain gluten, making it perfect for celiac disease people suffering. Since it is easily digestible, it is commonly used in children's bread and biscuits.	(Martinescu, *et al*, (2020) [64] (Amante, *et al*., (2020) [67]
7. Sorghum flour	Sorghum is high in antioxidants, which provide numerous health benefits and may help in the prevention of chronic diseases that plague the world today. Sorghum is more than just a wheat substitute; it is also high in soluble prebiotic fibre.	(Zhao, *et al*., (2021) [68]

7.1 Uses of different gluten free flours

7.1.1 Coconut flour

Coconut flour is made from dried coconut meat, which is naturally sweet and has a mild coconut flavour. It has high fat content and the highest fibre content as compared to any other flour. Coconut flour is a good option for those with nut and gluten allergies. (Goyal *et al*., 2022) [74]

7.1.2 Oat flour

Grinding whole-grain oats produces oat flour. It contains beta-glucan, a type of soluble fibre with numerous health advantages. Oat flour adds flavour, texture, and structure to cookies, breads, and other baked products thanks to its high fibre, protein, and nutritional content. Make sure you use oats or oat flour if you have celiac disease or gluten allergy. (Pang *et al*., 2012) [75]

7.1.3 Tapioca flour

The liquid extracted from the cassava root is turned into tapioca flour. It's a starchy white powder used to thicken soups and sauces, as well as bread recipes. It should be used in conjunction with other flours, since using too much can result in a dense or gluey recipe chevalier. Tapioca flour is high in fibre, protein, and minerals, in addition to carbohydrates. (Roberfroid *et al*., 2000) [76]

7.1.4 Corn flour

Corn meal is formed from the entire corn kernel, including the bran, germ, and endosperm, and is known in India as Makkai. It's a thickening for liquids that can also be used to produce tortillas and breads. It has a nutty flavour to it. Fiber, manganese, magnesium, riboflavin, niacin, folate, iron, and thiamin are all found in corn flour. (Vaughan *et al*., 2020). [77]

7.1.5 Buckwheat flour

Buckwheat is not a wheat grain and does not contain gluten, despite its name. The plant's little seeds are processed into flour, which has a deep, earthy flavour that goes well with quick breads and yeast breads. This flour is high in B vitamins, manganese, fibre, copper, magnesium, and other minerals, as well as balanced protein and eight important amino acids. It comes in three different shades: light, medium, and dark. (Moreno *et al*., 2014). [78]

7.1.6 Chickpea flour

Dried chickpeas are used to make chickpea flour, also known as gramme or garbanzo flour. It is high in protein, fibre, and important nutrients, as well as having excellent binding characteristics. Because of its gritty texture, it can be used as an egg substitute. Tortillas, crepes, and flatbreads can all be made using it. (Picascia *et al*., 2015) [79]

7.1.7 Brown rice flour
This flour is created from ground rice flour or white rice flour, as the name implies. This flour is whole-grain since it includes the bran, germ, and endosperm. Essential amino acids, dietary fibre, protein, and a range of other vitamins and minerals are abundant in this flour. When used as a thickening ingredient in soups, sauces, or gravies, brown rice flour can be replaced 1:1 for wheat flour. It has a subtle nutty flavour and is used in the preparation of noodles, breads, cakes, and pastries. (Churruca *et al*. 2015) [40]

7.1.8 Amaranth flour
The seeds of the Amaranth plant are used to make amaranth flour. It's a healthy flour for baking tortillas, bread, and pie crusts because it's high in protein and fibre. It includes phytochemicals with strong antioxidant properties. Vitamin A, iron, B vitamins, potassium, vitamin C, calcium, and manganese are all abundant in this superfood. It can replace 25% Page 1 of 2 of wheat flour in baking but should be blended with other flours. (Dhankar *et al*., 2013) [80]

7.1.9 Almond flour
Almond flour is typically produced from blanched almonds that have had their skins removed. It's typically used to replace wheat flour in baked goods at a 1:1 ratio. Magnesium, copper, iron, calcium, potassium, and manganese are all abundant in this sort of flour. It has a low carbohydrate content, a high fibre content, and a high protein content. (Bauman *et al*., 2018) [81]

8. Different challenges encountered in using gluten free food
Gluten-free products are finding an increased demand since the incidence of celiac disease or other gluten-associated allergies. The replacement of gluten becomes a necessity to avoid the occurrence of any such disorder. (Newinski, 2008) [42] Eliminating gluten however appears in the face of a technological challenge as it aims to minimize the prevalence of any disease causing condition on the one hand, and gives rise to products with compromised quality on the other hand. (Curiel *et al.*, 2014) [82] Attempts are thus made to adopt methods that could produce cereal based gluten-free products with technological properties comparable to their gluten containing counterparts and minimum compromises with quality. (Farah *et al.*, 2017) [83].

Celiac disease is a severe autoimmune illness that can damage the lining of the small intestine and create a variety of symptoms, some of which are connected to malabsorption and inflammation in the intestine, and others which are extraintestinal in nature. (Hollén *et al.*, 2003) [84] A considerable number of patients may experience no symptoms, and there is a modest, but not insignificant, chance of developing intestinal lymphoma or possibly small intestine cancer in the long run. The presence of a specific genetic genotype (HLA-DQ2 and/or HLA-DQ8 genes) and highly specific autoantibodies, such as IgA tissue transglutaminase antibodies (IgAt), antiendomysial antibodies (IgA EMA), and/or deamidated gliadin peptide (IgG) antibodies, are the keys to diagnosing celiac disease. (Fasano *et al*., 2008) [85]. The IgAt antibody is usually used for screening, while the IgA EMA antibody is utilised for confirmation. Gluten, an antigen found in the environment, causes the condition. (Barker *et al*, 2008) [86] Gluten is a protein made up of prolamins and glutenins that can be found in wheat, barley, rye, and spelt. These proteins are high in prolines and glutamines, and intestinal enzymes can only partially digest them. (Sapone *et al.*, 2012) [72]

Food malabsorption may result, resulting in children's failure to thrive, extensive vitamin and protein deficits, discomfort, and impairment. Early detection of certain serum antibodies, particularly IgAt, is critical for early diagnosis and avoidance of the harmful immunological cascade (Woodward *et al.*, 2017) [87]. It's also important to remember that gluten triggers this sequence, and the amount of gluten necessary in certain cases can be quite minimal. (Lerner *et al.*, 2019) [88] Unfortunately, if the patient is already on a gluten-free diet, the antibody titer, which should be at least two times greater than the upper limit of normal, begins to decline and may become undetectable, delaying diagnosis. (Simpson *et al.*, 2011) [89] Long-term harm and the possibility of various extraintestinal issues can occur if gluten avoidance is insufficient or if the patient is extremely sensitive to very small levels of gluten. (Fric *et al.*, 2011) [90]

8.1 Nutritional deficiencies
Nutritional deficits affect 20% to 38% of celiac patients, with iron insufficiency affecting 12%– 69% and Vitamin B12 deficiency affecting 8%–41%. Furthermore, damaged villi in celiac patients induce lactose intolerance due to reduced lactase synthesis, resulting in phosphorus, calcium, and vitamin D deficiency. (Saturni *et al.*, 2010) [70]

Inadequate fibre intake is caused by the use of starches and processed flours with low fibre content in GF foods. In the United States, anaemia was observed to affect 4% of newly diagnosed celiac patients. Glutened foods have more folate than gluten-free foods. As a result, it's critical to add folate to gluten-free food. GF vitamins and minerals should be introduced to the patient's diet in therapeutic levels as soon as a deficiency in these or other micronutrients is diagnosed, based on individual factors such as laboratory test results, age, overall eating habits, and GFD compliance. (Kupper, 2005) [15]

To increase iron absorption, patients should be encouraged to consume foods high in vitamin B12 (meat, milk, fish, and poultry), folate (dried beans and legumes, flax seeds, dark leafy greens, and citrus fruit), heme iron (lean meats, poultry, and seafood), nonheme iron (legumes, seeds, and nuts), and vitamin C-rich foods. Amaranth, buckwheat, and quinoa are pseudocereals that are high in iron, fibre, and B vitamins. (Kiskini *et al.*, 2007) [94]

8.2 Obesity
Obesity was found to be common among celiac patients in recent investigations. (Tucker *et al.*, 2012) [13] Almost half of all adult celiac disease patients have a BMI of 25 or above; however, because obesity is more common in celiac children, it is vital to test for celiac disease in obese children. (Venkatasubramani *et al.*, 2010) [91] Obesity and weight gain may occur from the high calorie content of commercially accessible GF foods. (Theethira *et al.*, 2015) [95] Furthermore, damage to the villi of the intestine can cause problems with food digestion and absorption, leading to obesity.

8.3 Bone disease
Calcium- and vitamin-D-rich meals should be advised to patients throughout their lifetimes, especially those with osteopenic bone disease. (Catassi *et al.*, 1994) [14] Milk, cheese, and calcium- fortified beverages like orange or apple

juice, as well as enhanced, gluten-free soy, almond, or rice milk, GF yoghurt, sardines, or tinned salmon with bones, are all calcium-rich foods. Patients should be encouraged to expose their skin to sunlight during late spring, summer, and early fall. Vitamin D-rich foods include fatty fish and fish oils, egg yolk, liver, Vitamin D- fortified milk, and some GF enriched beverages; additionally, patients should be encouraged to expose their skin to sunlight during late spring, summer, and early fall. (Krupa-Kozak *et al*., 2019) [92]

A common problem for celiac is bloating, gas, and diarrhea; these may indicate lactose intolerance. Lactose consumption should be avoided and limited for one or more months until lactase enzyme synthesis is restored in this condition. Lactose-reduced or lactose-free goods, such as Lactaid milk, aged cheese, and GF yoghurt with live and active cultures, enhanced dairy-free/GF beverages, such as soy, almond, or rice milk, and supplementation with GF lactase enzyme supplements are some of the recommended techniques. (Krupa-Kozak *et al.*, 2019) [92]

8.4 Technological challenges

Gluten is responsible for dough's elasticity and extensibility, as well as the volume of the loaves. Cereal goods baked with different gluten-free cereals (excluding oats) have been proven to have reduced volume, poor physical texture, and a slower staling rate than wheat-based samples. In the creation of GF products, many additives such as hydrocolloids, emulsifiers, starch, eggs, and other ingredients have been employed as improvers. (Hager 2012) [93].

9. Various food products made by gluten free- flours

Flour can be found in a variety of meals, including breads, sweets, and noodles. It's also frequently used to thicken sauces and soups.

The majority of the goods are produced with white or wheat flour. These two varieties of flour should not be consumed by those with celiac disease, non-celiac gluten sensitivity, or those who avoid gluten for other reasons.

Fortunately, there are many gluten-free flours on the market, each with its own flavor, texture, and nutritional profile.

Only a few whole grains contain gluten, whereas the remainder are gluten-free by nature.

When buying whole grains, it's crucial to read the labeling. Gluten contamination can occur even in gluten-free whole grains, especially if they are produced in the same facility as gluten- containing goods (Jnawali *et al*., 2016) [69].

Furthermore, important food products such as most breads, biscuits, and cakes are affected. Pasta, cakes, pastries, breakfast cereals, bagels, and soups all contain wheat; eliminating all of them would necessitate a full dietary change. a lifestyle that may not be suitable for everyone The demand for gluten-free products has risen as a result of all of these issues (Jnawali *et al*., 2016) [69].

9.1 Naturally Gluten-Free Grains & Starches

- Rice
- Quinoa
- Millet
- Oats
- Cassava
- Sorghum
- Teff
- Corn
- Buckwheat
- Amaranth
- Potatoes and potato flour

Gluten is a protein that can be found in cereals like wheat, rye, and barley. It provides flexibility and wetness to help food keep its shape. It also helps the bread rise and has a chewy texture (Biesiekierski, 2017) [3].

Although gluten is generally healthy for most individuals, persons with celiac disease or gluten sensitivity should avoid it to avoid negative health consequences (Leonard *et al*. 2017) [72]. Many foods include gluten-containing substances, therefore people who are unable to ingest it should carefully read ingredient labels.

9.2 Gluten free foods

- Whole grains
- Fruits and vegetables
- Dairy products
- Fats and oils
- Beverages
- Spices, sauces, and condiments

10. Conclusion

Celiac disease is an inflammatory condition that develops in those who are vulnerable to wheat protein gluten, especially the protein gliadins. Celiac disease is characterised by stomach pain, bloating, diarrhoea, and stinking faeces, which is essentially a fascist anaemia weight loss, and failure to flourish, particularly in children and adolescents. However, celiac disease can also appear asymptomatically with a 1/3 habit. It's crucial to remember that if someone has diarrhoea, weight loss, or anaemia, it might be an iron deficit or vitamin B 12 insufficiency. Autoantibodies to transglutaminase, endomysin, and gliadin, which are present in celiac disease, may be tested with serological testing. Finally, endoscopy may be used to diagnose celiac disease, and it is the gold standard. A gluten-free diet implies avoiding gluten-containing foods, which may be recalled using the acronym brow: B is for barley, R is for rye, O is for oats, and W is for wheat. These four items all contain a lot of gluten and should be avoided. Supplements such as calcium, iron, and other vitamin supplements can also be given if malabsorption is a problem. During moments of celiac disease exacerbation, often known as celiac crisis, prompt treatment is critical. Celiac disease is a life-threatening illness. People who appear with inexplicable diarrhoea, significant malabsorption, and passive emesis are unusual.A family history of celiac disease, autoimmune thyroid disease, type 1 diabetes, IGA deficiency, and inflammatory bowel disease are all risk factors. Anemia, higher chance of developing certain cancers, anaemia, hyposplenism, osteoporosis, neuropathy, and dermatitis herpetiformis are all consequences of celiac disease. Cow milk sensitivity, food sensitive enteropathies, Crohn's disease colitis, GIT lymphoma, whipple's disease, Giardia lambia infection, and irritable bowel syndrome are among the celiac disease differential diagnoses.

11. Acknowledgement

The authors are thankful to Lovely Professional University for providing the necessary facilities, which were used for the preparation of manuscript.

12. References

1. Kahaly GJ, Frommer L, Schuppan D. Celiac disease and

glandular autoimmunity. Nutrients. 2018;10(7):814.
2. Holtmeier W, Caspary WF. Celiac disease. Orphanet journal of rare diseases. 2006;1(1):1-8.
3. Biesiekierski JR. What is gluten?. Journal of gastroenterology and hepatology. 2017;32:78-81.
4. Santelli RE, de Almeida Bezerra M, de SantAna OD, Cassella RJ, Ferreira SLC. Multivariate technique for optimization of digestion procedure by focussed microwave system for determination of Mn, Zn and Fe in food samples using FAAS. Talanta. 2006;68(4):1083-1088.
5. Green PH, Cellier C. Celiac disease. New England journal of medicine. 2007;357(17):1731-1743.
6. Fasano A, Catassi C. Celiac disease. New England Journal of Medicine. 2012;367(25):2419-2426.
7. Gunathilake KDPP, Yalegama C, Kumara AAN. Use of coconut flour as a source of protein and dietary fibre in wheat bread. Asian Journal of Food and Agro-Industry. 2009;2(3):382-391.
8. Maciejewska K, Bednarkiewicz A, Marciniak L. NIR luminescence lifetime nanothermometry based on phonon assisted Yb 3+–Nd 3+ energy transfer. Nanoscale Advances. 2021;3(17):4918-4925.
9. Rybicka IGA, Anna Gliszczyńska-Świgło. Minerals in grain gluten-free products. The content of calcium, potassium, magnesium, sodium, copper, iron, manganese, and zinc. Journal of food composition and analysis. 2017;59:61-67.
10. Mearin LM. Celiac disease among children and adolescents. Curr Probl Pediatr Adolesc Health Care. 2007;37(3):86-109.
11. Jamma S, Rubio–Tapia A, Kelly CP, Murray J, Najarian R. Celiac crisis is a rare but serious complication of celiac disease in adults. Clinical Gastroenterology and Hepatology. 2010;8(7):587-590.
12. Abdallah H, Leffler D, Dennis M, Kelly CP. Refractory celiac disease. Current gastroenterology reports. 2007;9(5):401-405
13. Tucker E, Rostami K, Prabhakaran S, Dulaimi DA. Patients with coeliac disease are increasingly overweight or obese on presentation. Journal of Gastrointestinal & Liver Diseases. 2012, 21(1).
14. Gabrielli O, Carloni I, Catassi C, Natalini G, Coppa GV, Giorgi P. Stratton-Parker syndrome: Confirmation of a new entity. American journal of medical genetics. 1994;49(3):333-336.
15. Kupper C. Dietary guidelines and implementation for celiac disease. Gastroenterology. 2005;128(4):S121-S127.
16. Wierdsma NJ, Bokhorst-De Van Der Schueren V, Marian AE, Berkenpas M, Mulder J, Van Bodegraven A.A. Vitamin and mineral deficiencies are highly prevalent in newly diagnosed celiac disease patients. Nutrients. 2013;5(10):3975-3992.
17. Guandalini S, Discepolo V. Celiac disease. Textbook of pediatric gastroenterology, hepatology and nutrition, 2022, 525-548.
18. Cenit MC, Olivares M, Codoñer-Franch P, Sanz Y. Intestinal microbiota and celiac disease: cause, consequence or co-evolution?. Nutrients. 2015;7(8):6900-6923.
19. Green PH, Jabri B. Celiac disease. Annu. Rev. Med. 2006;57:207-221.
20. Lebwohl B, Ludvigsson JF, Green PH. Celiac disease and non-celiac gluten sensitivity. Bmj, 2015, 351.
21. Rodrigo L. Celiac disease. World journal of gastroenterology: WJG. 2006;12(41):6577.
22. Parzanese I, Qehajaj D, Patrinicola F, Aralica M, Chiriva-Internati M, Stifter S. Celiac disease: From pathophysiology to treatment. World journal of gastrointestinal pathophysiology. 2017;8(2):27.
23. Garnier-Lengliné H, Cerf-Bensussan N, Ruemmele FM. Celiac disease in children. Clinics and research in hepatology and gastroenterology. 2015;39(5):544-551.
24. Lebwohl B, Rubio-Tapia A. Epidemiology, presentation, and diagnosis of celiac disease. Gastroenterology. 2021;160(1):63-75.
25. Ludvigsson JF, Murray JA. Epidemiology of celiac disease. Gastroenterology Clinics. 2019;48(1):1-18.
26. Oxentenko AS, Rubio-Tapia A. Celiac disease. In Mayo Clinic Proceedings. 2019, December;94(12):2556-2571. Elsevier.
27. Ben Houmich T, Admou B. Celiac disease: Understandings in diagnostic, nutritional, and medicinal aspects. International journal of immunopathology and pharmacology. 202;35:20587384211008709.
28. Durham J, Temples HS. Celiac Disease in the pediatric population. Journal of Pediatric Health Care. 2018;32(6):627-631.
29. Domsa EM, Berindan-Neagoe I, Para I, Munteanu L, Matei D, Andreica V. Celiac disease: a multi-faceted medical condition. J Physiol Pharmacol. 2020; 71(1):3-4.
30. Owen DR, Owen DA. Celiac disease and other causes of duodenitis. Archives of Pathology & Laboratory Medicine. 2018;142(1):35-43.
31. Fasano A. Celiac disease, gut-brain axis, and behavior: cause, consequence, or merely epiphenomenon?. Pediatrics. 2017, 139(3).
32. Hosseini SM, Soltanizadeh N, Mirmoghtadaee P, Banavand P, Mirmoghtadaie L, Shojaee-Aliabadi S. Gluten-free products in celiac disease: Nutritional and technological challenges and solutions. Journal of research in medical sciences: The official journal of Isfahan University of Medical Sciences, 2018, 23.
33. Lionetti E, Catassi C. New clues in celiac disease epidemiology, pathogenesis, clinical manifestations, and treatment. International reviews of immunology. 2011;30(4):219-231.
34. Chand N, Mihas AA. Celiac disease: current concepts in diagnosis and treatment. Journal of clinical gastroenterology. 2006;40(1):3-14.
35. Asri N, Rostami-Nejad M, Rezaei-Tavirani M, Razzaghi M, Asadzadeh-Aghdaei H, Zali MR. Novel therapeutic strategies for celiac disease. Middle East Journal of Digestive Diseases. 2020;12(4):229.
36. Sollid LM, Lundin KEA. Diagnosis and treatment of celiac disease. Mucosal Immunology. 2009;2(1):3-7.
37. El Khoury D, Balfour-Ducharme S, Joye IJ. A review on the gluten-free diet: Technological and nutritional challenges. Nutrients. 2018;10(10):1410.
38. Rybicka I. The handbook of minerals on a gluten-free diet. Nutrients. 2018;10(11):1683.
39. Case S. The gluten-free diet: how to provide effective education and resources. Gastroenterology. 2005;128(4):S128-S134.
40. Miranda J, Lasa A, Bustamante MA, Churruca I, Simon E. Nutritional differences between a gluten-free diet and a diet containing equivalent products with gluten. Plant

foods for human nutrition. 2014;69(2):182-187.
41. Kulushtayeva B, Rebezov M, Igenbayev A, Kichko Y, Burakovskaya N, Kulakov V. Gluten-free diet: positive and negative effect on human health. SCOPUS IJPHRD CITATION SCORE. 2019;10(7):889
42. Mary Niewinski M. Advances in Celiac Disease and Gluten-Free Diet. 2008;108(4):661-672.
43. Shih FF, Daigle KW. Preparation and characterization of rice protein isolates. Journal of the American Oil Chemists' Society. 2000;77(8):885-889.
44. Desai AD, Kulkarni SS, Sahoo AK, Ranveer RC, Dandge PB. Effect of supplementation of malted ragi flour on the nutritional and sensorial quality characteristics of cake. Advance Journal of Food Science and Technology. 2010;2(1):67-71.
45. Verma S, Mishra S. Organoleptic properties and acceptability of ragi flour to prepare noodles. Journal of Pharmacognosy and Phytochemistry. 2019;8(6):213-216.
46. Ramya HN, Anitha S. Development of muffins from wheat flour and coconut flour using honey as a sweetener. Int. J Curr. Microbiol. App. Sci. 2020;9(7):2231-2240.
47. Klang JM, Tene ST, Kamdem FEM, Boungo GT, Womeni HM. Optimization using response surface methodology (RSM) of the energy density of flour-based gruels of sweet cassava (*Manihot esculenta* Crantz) flour: Effect of the addition of two new sprouted rice varieties produced under optimal conditions (Nerica 3 and Nerica L56). NFS journal. 2020;19:16-25.
48. Suzauddula M, Hossain M, Farzana T, Orchy TN, Islam M, Hasan M. Incorporation of oat flour into wheat flour noodle and evaluation of its physical, chemical and sensory attributes. Brazilian Journal of Food Technology, 2021, 24.
49. Kristanti D, Herminiati A. Physicochemical properties of pudding powder as a complementary food fortified with the essential mineral. In AIP Conference Proceedings AIP Publishing LLC. 2019, November; 2175(1):020053.
50. Rybicka I, Gliszczynska-Swiglo A. Gluten-Free flours from different raw materials as the source of vitamin B1, B2, B3 and B6. Journal of nutritional science and vitaminology. 2017;63(2):125-132.
51. Sreerama YN, Sashikala VB, Pratape VM, Singh V. Nutrients and antinutrients in cowpea and horse gram flours in comparison to chickpea flour: Evaluation of their flour functionality. Food Chemistry. 2012;131(2):462-468.
52. Beltrão Martins R, Gouvinhas I, Nunes MC, Alcides Peres J, Raymundo A, Barros AI. Acorn flour as a source of bioactive compounds in gluten-free bread. Molecules. 2020;25(16):3568.
53. Culetu A, Duta DE, Papageorgiou M, Varzakas T. The role of hydrocolloids in gluten-free bread and pasta; rheology, characteristics, staling and glycemic index. Foods. 2021;10(12):3121.
54. Aini N, Prihananto V, Wijonarko G, Sustriawan B, Dinayati M, Aprianti F. Formulation and characterization of emergency food based on instan corn flour supplemented by instan tempeh (or soybean) flour. International Food Research Journal, 2018, 25(1).
55. Nazni P, Shobana DR. Effect of processing on the characteristics changes in barnyard and foxtail millet. Journal of Food Processing and Technology. 2016;7(3):1-9.
56. Tumwine G, Atukwase A, Tumuhimbise GA, Tucungwirwe F, Linnemann A. Production of nutrient-enhanced millet-based composite flour using skimmed milk powder and vegetables. Food Science & Nutrition. 2019;7(1):22-34.
57. Martínez-Villaluenga C, Peñas E, Hernández-Ledesma B. Pseudocereal grains: Nutritional value, health benefits and current applications for the development of gluten-free foods. Food and Chemical Toxicology. 2020;137:111178.
58. Missbach B, Schwingshackl L, Billmann A, Mystek A, Hickelsberger M, Bauer G. Gluten-free food database: the nutritional quality and cost of packaged gluten-free foods. Peer J. 2015;3:e1337.
59. Makinde F, Eyitayo AO. The evaluation of nutritional composition and functional and pasting properties of wheat flour-coconut flour blends. Croatian journal of food science and technology. 2019;11(1):21-29.
60. Vuthijumnonk J, Rajchasom S. Total Dietary Fiber in Coconut Powder Cookies and Their Antioxidant Activity: A Healthy Snack Potentiality. International Journal of Food Engineering, 2019, 5(1).
61. Sirisoontaralak P, Nakornpanom NN, Koakietdumrongkul K, Panumaswiwath C. Development of quick cooking germinated brown rice with convenient preparation and containing health benefits. LWT-Food Science and Technology. 2015;61(1):138-144.
62. Saleh AS, Wang P, Wang N, Yang L, Xiao Z. Brown rice versus white rice: Nutritional quality, potential health benefits, development of food products, and preservation technologies. Comprehensive Reviews in Food Science and Food Safety. 2019;18(4):1070-1096.
63. Zhu Y, Dong L, Huang L, Shi Z, Dong J, Yao Y. Effects of oat β- glucan, oat resistant starch, and the whole oat flour on insulin resistance, inflammation, and gut microbiota in high-fat-diet-induced type 2 diabetic rats. Journal of Functional Foods. 2020;69:103939.
64. Martinescu CD, Sârbu NR, Velciov AB, Stoin D. Nutritional and sensory evaluation of gluten-free cake obtained from mixtures of rice flour, almond flour and arrowroot flour. Journal of Agroalimentary Processes and Technologies. 2020;26:368-374.
65. Siqueira APS, Pacheco MTB, Naves MMV. Nutritional quality and bioactive compounds of partially defatted baru almond flour. Food Science and Technology. 2015;35:127-132.
66. Kupkanchanakul W, Yamaguchi T, Naivikul O. Gluten-Free Rice Breading Using Composited Rice Flour and Pre-Germinated Brown Rice Flour for Health Benefits. Journal of nutritional science and vitaminology. 2019;65(Supplement):S206-S211.
67. Amante PR, Santos ECZ, Correia VTDV, Fante CA. Benefits and Possible Food Applications of Arrowroot (*Maranta arundinaceae* L.). Journal of Culinary Science & Technology. 2021;19(6):513-521.
68. Xu J, Wang W, Zhao Y. Phenolic Compounds in Whole Grain Sorghum and Their Health Benefits. Foods. 2021;10(8):1921.
69. Jnawali P, Kumar V, Tanwar B. Celiac disease: Overview and considerations for development of gluten-free foods. Food Science and Human Wellness. 2016;5(4):169-176.
70. Saturni L, Ferretti G, Bacchetti T. The gluten-free diet: safety and nutritional quality. Nutrients. 2010;2(1):16-34.

71. Pachón H. Wheat and maize flour fortification. In Food Fortification in a Globalized World. Academic Press. 2018, 123-129.
72. Leonard MM, Sapone A, Catassi C, Fasano A. Celiac Disease and Nonceliac Gluten Sensitivity: A Review. JAMA. 2017 Aug 15;318(7):647-656.
73. Hujoel IA, Reilly NR, Rubio-Tapia A. Celiac disease: clinical features and diagnosis. Gastroenterology Clinics, 2019;48(1):19-37.
74. Goyal A, Tanwar B, Sihag MK, Sharma V. Sacha inchi (*Plukenetia volubilis* L.): An emerging source of nutrients, omega-3 fatty acid and phytochemicals. Food Chemistry. 2022;373:131459.
75. Pang Y, Ahmed S, Xu Y, Beta T, Zhu Z, Shao Y, Bao J. Bound phenolic compounds and antioxidant properties of whole grain and bran of white, red and black rice. Food Chemistry. 2012;240:212-221.
76. Roberfroid MB. Chicory fructooligosaccharides and the gastrointestinal tract. Nutrition. 2000;16(7-8):677-679.
77. Vaughan MM, McCormick SP, Brown JA, Bakker MG. Sarocladium zeae is a systemic endophyte of wheat and an effective biocontrol agent against Fusarium head blight. Biological Control. 2020;149:104329.
78. Moreno Amador MDL, Comino Montilla IM, Sousa Martín C. Alternative grains as potential raw material for gluten–free food development in the diet of celiac and gluten–sensitive patients. 2014.
79. Picascia S, Mandile R, Auricchio R, Troncone R, Gianfrani C. Gliadin-specific T-cells mobilized in the peripheral blood of coeliac patients by short oral gluten challenge: clinical applications. Nutrients. 2015;7(12):10020-10031.
80. Dhankhar P, Tech M. A study on development of coconut based gluten free cookies. International Journal of Engineering Science Invention. 2013;2(12):10-19.
81. Baumann A, Windhab EJ. Tailoring rice flour structure by rubbery milling for improved gluten-free baked goods. Food & function. 2018;9(5):2951-2961
82. Curiel JA, Coda R, Limitone A, Katina K, Raulio M, Giuliani G. Manufacture and characterization of pasta made with wheat flour rendered gluten-free using fungal proteases and selected sourdough lactic acid bacteria. Journal of Cereal Science. 2014;59(1):79-87.
83. Naqash F, Gani A, Gani A, Masoodi FA. Gluten-free baking: Combating the challenges-A review. Trends in Food Science & Technology. 2017;66:98-107.
84. Hollén E, Holmgren Peterson K, Sundqvist T, Grodzinsky E, Högberg L, Laurin P. Coeliac children on a gluten-free diet with or without oats display equal anti-avenin antibody titres. Scandinavian journal of gastroenterology. 2006;41(1):42-47.
85. Fasano A, Araya M, Bhatnagar S, Cameron D, Catassi C, Dirks M, Phillips A. Federation of International Societies of Pediatric Gastroenterology, Hepatology, and Nutrition consensus report on celiac disease. Journal of pediatric gastroenterology and nutrition. 2008;47(2):214-219.
86. Barker JM, Liu E. Celiac disease: pathophysiology, clinical manifestations, and associated autoimmune conditions. Advances in pediatrics. 2008;55(1):349-365.
87. Woodward J, Gkrania-Klotsas E, Kumararatne D. Chronic norovirus infection and common variable immunodeficiency. Clinical & Experimental Immunology. 2017;188(3):363-370.
88. Lerner A, O'Bryan T, Matthias T. Navigating the gluten-free boom: the dark side of gluten free diet. Frontiers in pediatrics. 2019;7:414.
89. Simpson S, Lebwohl B, Lewis SK, Tennyson CA, Sanders DS, Green PH. Awareness of gluten-related disorders: A survey of the general public, chefs and patients. e-SPEN, the European e-Journal of Clinical Nutrition and Metabolism. 2011;6(5):e227-e231.
90. Fric P, Gabrovska D, Nevoral J. Celiac disease, gluten-free diet, and oats. Nutrition Reviews. 2011;69(2):107-115.
91. Venkatasubramani N, Telega G, Werlin SL. Obesity in pediatric celiac disease. Journal of pediatric gastroenterology and nutrition. 2010;51(3):295-297.
92. Krupa-Kozak U. Technological and nutritional challenges, and novelty in gluten-free breadmaking: A review. Polish Journal of Food and Nutrition Sciences, 2019, 69(1).
93. Hager AS, Wolter A, Jacob F, Zannini E, Arendt EK. Nutritional properties and ultra-structure of commercial gluten free flours from different botanical sources compared to wheat flours. Journal of Cereal Science. 2012;56(2):239-247.
94. Kiskini A, Argiri K, Kalogeropoulos M, Komaitis M, Kostaropoulos A, Mandala I. Sensory characteristics and iron dialyzability of gluten-free bread fortified with iron. Food Chemistry. 2007;102(1):309-316.
95. Theethira TG, Dennis M. Celiac disease and the gluten-free diet: consequences and recommendations for improvement. Digestive Diseases. 2015;33(2):175-182.
96. Jones AL. The gluten-free diet: fad or necessity?. Diabetes Spectrum. 2017;30(2):118-123.