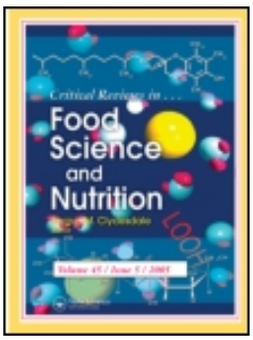

Critical Reviews in Food Science and Nutrition

ISSN: 1040-8398 (Print) 1549-7852 (Online) Journal homepage: http://www.tandfonline.com/loi/bfsn20

Wheat Allergy and Intolerence; Recent Updates and Perspectives

Imran Pasha, Farhan Saeed, Muhammad Tauseef Sultan, Rizwana Batool, Mahwash Aziz & Waqas Ahmed

To cite this article: Imran Pasha, Farhan Saeed, Muhammad Tauseef Sultan, Rizwana Batool, Mahwash Aziz & Waqas Ahmed (2016) Wheat Allergy and Intolerence; Recent Updates and Perspectives, Critical Reviews in Food Science and Nutrition, 56:1, 13-24, DOI: 10.1080/10408398.2012.659818

To link to this article: https://doi.org/10.1080/10408398.2012.659818

Accepted author version posted online: 02 Sep 2013.
Published online: 02 Sep 2013.

Critical Reviews in Food Science and Nutrition, 56:13–24 (2016)

ISSN: 1040-8398 / 1549-7852 online
DOI: 10.1080/10408398.2012.659818

Taylor & Francis
Taylor & Francis Group

Wheat Allergy and Intolerence; Recent Updates and Perspectives

IMRAN PASHA,[1] FARHAN SAEED,[1] MUHAMMAD TAUSEEF SULTAN,[2] RIZWANA BATOOL,[1] MAHWASH AZIZ,[1] and WAQAS AHMED[1]

[1]National Institute of Food Science and Technology, University of Agriculture, Faisalabad
[2]Department of Food Sciences, Bahauddin Zakariya University, Multan

The current review paper highlights the complicacies associated with communities relying on wheat as their dietary staple. Although, wheat is an important source of nutrients but is also linked with allergenic responses in genetically susceptible subjects. The wheat proteins especially α-amylase inhibitors, ω-5 gliadins, prolamins, nonprolamin, glucoprotein, and profilins are of significance importance. The allergenic responses are further categorized into IgE-mediated and non-IgE-mediated reactions. Conjugation and degranulation of the IgEs with the allergens results in release of several mediators. In contrary, non-IgE-mediated wheat allergy depends on immune complexes formed by food and food antibodies and cell-mediated immunity. As results, different diseases tend to occur on the completion of these reactions, i.e., celiac disease, baker's asthma, diarrhea, atopic dermatitis, and urticaria. This instant paper highlighted the concept of food allergy with special reference to wheat. The models are developed that are included in this paper showing the wheat allergen, their possible routes, impact on human health, and indeed possible remedies. The paper would provide the basic information for the researchers, common man, and allied stakeholders to cater the issue in details. However, the issue needs the attention of the researchers as there is a need to clarify the issues of wheat allergy and wheat intolerance.

Keywords Wheat allergens, immune cells, celiac disease, baker's asthma, atopic dermatitis

INTRODUCTION

Provision of adequate and balanced food is important for vitality of life. However, adverse reactions on foods are extremely common and some of them are described as allergic that imply an immune mechanism (Guandalini and Newland, 2011). In this regard, Food allergy is defined as an undesirable response of the immune system against proteins. Generally, foods that induce rhinitis, sinusitis, bronchitis, asthma, intestinal cramps, diarrhea, hives, angioedema, eczema, and migraines are said to be "allergenic." There have been increasing reports of food allergy to a wide range of foods but cow's milk, egg, peanut, wheat, soy, tree nuts, fish, and shell-fish are of critical significance (Sampson, 2004). These foods generally account for nearly 90% of the food-allergic reactions. However, the prevalence of apparent food hypersensitivity varies (1.4–19.1%) among different communities. These wide variations can also be attributed to differences in the diagnostic criteria, study design and population, etc. (Crespo and Rodriguez, 2003). In general, about 1.5% of adults and 5–8% of growing children suffer from food allergies (Sampson, 2000). The estimated percentage of allergies caused by different foods is 0–3% for milk, up to 1.7% for egg, 0.2–1.6% for peanut, and 1–10.8% for other foods (Zuidmeer et al., 2008). The allergies due to consumption of cereals are another major problem in many countries where they cereals are habitually consumed (Battais et al., 2008). In Japan, wheat is third commonest food causing allergy in children following eggs and cow's milk (Imai and Likura, 2003). Though allergies to cow's milk and egg can be tolerated by elimination, wheat allergy can't be controlled through elimination. In Pakistan, self-reported frequency of allergy varied from 1.2 to 17% for milk, 0.2–7% for egg, 0–2% for peanut and fish, 0–10% for shellfish, and 3–35% for other foods (Rona et al., 2007).

Food allergy is also dependent upon genetic factors, cultural and dietary habits, and exposure to allergenic products. For instance, peanut allergy is common in UK, France, and

Address correspondence to Rizwana Batool, National Institute of Food Science and Technology, University of Agriculture, Faisalabad. E-mail: rizwana_uaf@yahoo.com

Color versions of one or more of the figures in the article can be found online at www.tandfonline.com/bfsn

Switzerland but rare in Italy, Singapore, and Israel (Dalal et al., 2002). Food allergies have augmented considerably in the past decade. At the onset, food intolerance must be separated from food allergies and, furthermore, these allergies should be categorized into an IgE, Non-IgE, or a mixed response. The clinical features differ from life-threatening anaphylaxis to milder IgE-mediated reactions, atopic dermatitis (AD), and gastrointestinal symptoms (Heratizadeh et al., 2011; Wang et al., 2011). As far as IgE-mediated wheat allergy is concerned, specific IgE are developed in the absence of oral tolerance (OT). IgE are related to high affinity specific Fc receptors FCЄRI present on the mast cells, fixed cells present in the mucosa and skin, and basophils circulating in the blood (Pizzuti et al., 2011). These cells have various cytoplasmic granules mainly including histamine in which preformed mediators are stored. When the allergenic proteins are captivated in the gut they contact with specific IgEs linked to mast cells/basophils. The conjugation of the IgEs with the allergens triggers these cells to degranulate, thus releasing immuno-mediators in the surrounding microenvironment (Sotkovsky et al., 2011). Consequently, different mediators such as prostaglandins, leukotriens, and cytokines are also released. An abrupt reaction follows few minutes after making contact with the allergen essentially due to the histamine release. At the base of the reaction, there is vasodilation, tissue fluid exudation, smooth muscle contraction, and mucous secretion. A late-phase response follows the instant reaction which begins 4–6 hours after contact with the allergen and continues for several days. This response is caused by chemotactic mediators released at the same time as the immediate reaction which promote selective conscription of inflammatory cells, mainly eosinophils and neutrophils. These cells infiltrate the tissues produce inflammation lasting for a period of 4–5 days. However, in order to predict IgE mediated allergy, the two clinical elements are required, i.e., presence of IgE specific antibodies and a proven relationship between ingestion of the food and the appearance of the symptoms (Cabrera-Chávez and de-Barca, 2009).

On the other hand, non-IgE-mediated food allergy consists of immune reactions that are dependent upon presence of antibodies other than IgE (e.g., IgG, IgM, and IgA) and immune complexes (food, food antibodies, and cell-mediated immunity). It is important to remember that there is no verification to support the affiliation between the allergenic food and a reaction to non-IgE antibodies in any allergic disease. However, in normal individuals, there is an increase in IgG food antibodies after ingestion of the food. Likewise, there is no solid evidence about the responsibility of cell-mediated immunity (Paganelli et al., 1987).

Strategies for the prevention of allergy have been proposed including the utilization of product with extensively reduced allergenicity. A perfect history is vital in approaching the administration (Wantanabe, 1993). Structural proteins are imperative determinants of the sternness of the reactions and may often foresee the natural history and cross reactivity. Indicative work up must be directed by the clinical history. Skin testing and food-specific IgE done by standard methods are very helpful, while OT may be specified in some circumstances (Ramesh, 2008).

WHEAT ALLERGY

Wheat is widely consumed cereal all over the world and its potential to cause allergenic responses is a matter of great interest for clinical practitioners and nutritionists. Despite the large consumption of wheat all over the world, there are few reports about clinical aspects of wheat food allergy in controlled adults. Wheat is amongst the most ordinary reasons of food-related allergies and intolerances that are linked with its ingestion or inhalation (Yacoub et al., 2011). Wheat, like all other foods, contains a number of proteins (more than 100), of which, some have been identified as allergens. The type and extent of proteins in a cereal have a major impact in determining the quality and end use properties of the cereal (Shewry and Halford, 2002). Wheat food allergy is frequent in children and infants and indeed is listed as one of the six most commonly implicated food allergens (FAO, 1995). The wheat allergy has been confirmed by the large number of double-blind, placebo-controlled food challenges performed in subjects over the globe (Palosuo et al., 2001).

On the basis of solubility, wheat proteins can be characterized as water-soluble, salt-soluble, alcohol-soluble, and alcohol-insoluble (Pomeranz, 1988). According to the type of wheat, proteins (albumin, globulin, and gluten) vary in proportion and this variability results in nonconsistent reactions in different wheat products (Joneja, 1998). Among gluten protein, gliadins (28–42%), the major prolamin protein in wheat is soluble in 70–90% alcohol whereas glutenins (42–62.5%), the major glutelin proteins in wheat is soluble in dilute acid or alkali solutions (Armentia et al., 1993). Wheat proteins are subdivided into the water/salt-soluble (including albumins and globulins) and insoluble (containing gliadins and glutenins) fractions. The latter represent about 80% of all wheat proteins. Mono-meric gliadins mainly exhibit intramolecular disulfide linkages, thus being compressed and of round shape. The different gliadin subunits share amino acid sequence and three-dimensional structure homologies (Bietz, 1977). Several wheat salt-soluble proteins (albumins and globulins), alpha-amylase/trypsin inhibitors, peroxidase, thioredoxin, nonspecific lipid transfer protein, serine proteinase inhibitor, and thaumatin-like protein-as well as salt-insoluble storage proteins (prolamins, namely, gliadins and glutenins) act as allergens (Salcedo et al., 2011). Recently, thaumatin-like protein, and lipid transfer protein 2G are also responsible for allergenic responses resulting due to wheat ingestion. Gluten proteins especially its gliadin fraction is the major aspect in triggering celiac disease, a common enteropathy, linked with intake of wheat gluten proteins and related prolamins from oat, rye, and barley (Mamone et al., 2011). Gliadin is known as a presumptive major allergen by immunoblotting

and RAST inhibition test (Morita et al., 2001). Previously, Palosuo et al. (2001) have identified ω-5 gliadin, which had been reported g-gliadin-like protein in their preceding report (Palosuo et al., 1999) as a major allergen in children with wheat-dependent exercise induced anaphylaxis (Palosuo et al., 2001). Wheat proteins belonging to both the soluble and insoluble fractions can act as allergens in sensitized individuals. In this regard, the soluble proteins seem to be responsible for respiratory allergy, such as baker's asthma arising from flour inhalation.

By characterization, gluten is found only in wheat, although the term is commonly used to refer to any similar prolamin protein in any grain (Thompson, 2000). The percentages of different types of prolamin found in various cereals have been given in Table 1. Because the type and proportion of prolamin proteins in these grains vary, the kind of reaction (if any) they are expected to cause also varies (Fasano and Catassi, 2001). An elevated IgE in gliadin-intolerant patients is indicated in some studies (Varjonen et al., 2000), however, little is known about cellular mechanisms involved in such conditions. The generation of specific IgE against gliadin in atopic patients suggested that IgE dysregulation is related to gliadin intolerance (Giannotti et al., 2001). The IgE production by human β-lymphocytes is mainly controlled by interleukin (IL)-4 (De Vries et al., 1991) produced by TH2-lymphocytes, mast cells, or basophils (Arock et al., 1993) and by CD40–CD40 ligand interactions between β and T-lymphocytes (Vercelli, 1995). IL-4 is upregulated during gliadin intolerance (Troncone et al., 1998) that further modulates the phenotype and function of β- and T-lymphocytes and monocytes/macrophages (Dugas et al., 1990). In β cells and monocytes/macrophages, IL-4 induces CD23-expression which amplifies IL-4-induced IgE production. In addition to these immunological mechanisms, it is shown that cellular redox status also controls this production (Benngtsson et al., 2001). Indeed, the redox metabolism is responsible for controlling dendritic cell functions (Alderman et al., 2002), and thus it mediates the protective immunity (Bachmann and Kopf, 2002). Gliadin can induce a redox imbalance in gastro-intestinal epithelial cells and macrophages probably due to overproduction of free radicals. According to a study, it was evaluated that native gliadin and gliadin lysates (Glilys) showed the regulatory effects on the spontaneous and the IL-4-induced IgE production by normal human peripheral blood mononuclear cells. Although, enzymatic (Cu/Zn-superoxide dismutase) and non-enzymatic (thiols) antioxidants can perform pharmacological roles under such conditions (Ribavene et al., 1999) but imbalance in redox potential results in severity of allergenic responses. IgE-mediated hypersensitivity reactions for ingested foods have been an important health problem. Several hypersensitivity reactions have been reported that are concerned with orally ingested wheat (Sampson, 1983). It is hypothesized that IgE from AD patients react with wheat and other cereal allergens. Number of patients suspected of AD owing to wheat ingestions is increasing in Japan. Multiple findings recommended that some wheat proteins (salt-soluble and salt insoluble fractions) are reactive to IgE in AD patients (Miyakawa et al., 1988).

Table 1 Percentages of prolamin type in different cereals

Cereals	Prolamin type	Amount (%)
Wheat	Gliadin	69
Corn	Zein	55
Barley	Hordein	46–52
Sorghum	Kafirin	52
Rye	Secalinin	30–50
Millet	Panicin	40
Oats	Avenin	16
Rice	Orzenin	5

Generally, food allergic reactions to wheat can give way to an array of clinical manifestations that can range from immediate to delayed, and their strictness can vary from mild to life-threatening. Typical immediate symptoms include erythema, pruritus, eczema, gastrointestinal reactions, oropharyngeal symptoms, urticaria, angioedema, AD, rhinitis, asthma, and anaphylaxis (Bock, 1986; Heffler et al., 2011). Investigators have confirmed that IgE antibodies specific to wheat albumins and globulins are present in the serum from children with wheat allergy and patients with baker's asthma (Jones et al., 1995; Cho et al., 2011).

In infants and young children, the symptoms associated with wheat allergy usually arise after weaning. In children, gastrointestinal problems are more evident including abnormal stools, abdominal distension and pain, flatulence, nausea, vomiting, and intestinal malabsorption (Alderman et al., 2002). Children are also suffered by irritability, apathy, loss of appetite, weight loss, poor weight gain, short stature, muscle wasting, hypotonia, general failure to thrive, poor school performance, bone and joint pains, and occasionally rickets (Varjonen et al., 2000).

In older children and adults, the symptoms may quite vary ranging from severe weight loss, diarrhea, and bulky, offensive stools to less severe symptoms. Subtle complaints of abdominal bloating, cramping, flatulence, and constipation are often mistakenly attributed to irritable bowel syndrome. Some individuals suffer from only anemia-related fatigue and have no gastrointestinal symptoms. Other manifestations of the disease include osteopenic bone disease, infertility, tetany, ataxia, and neurologic disorders. Recent studies show the presence of ataxia in persons with serological evidence of gluten sensitivity but without overt gastrointestinal symptoms or evidence of small-bowel inflammation (Joneja, 1998). The details of wheat allergens and various allergenic disorders are discussed in detail herein (See Fig. 1).

WHEAT ALLERGENS

Several wheat proteins have been described as allergens on the molecular level. Amongst, α-amylase inhibitors, acyl-coenzyme, oxidase, fructose-biphosphate aldolase, and wheat-flour peroxidase and ω-5 gliadin are of significance importance.

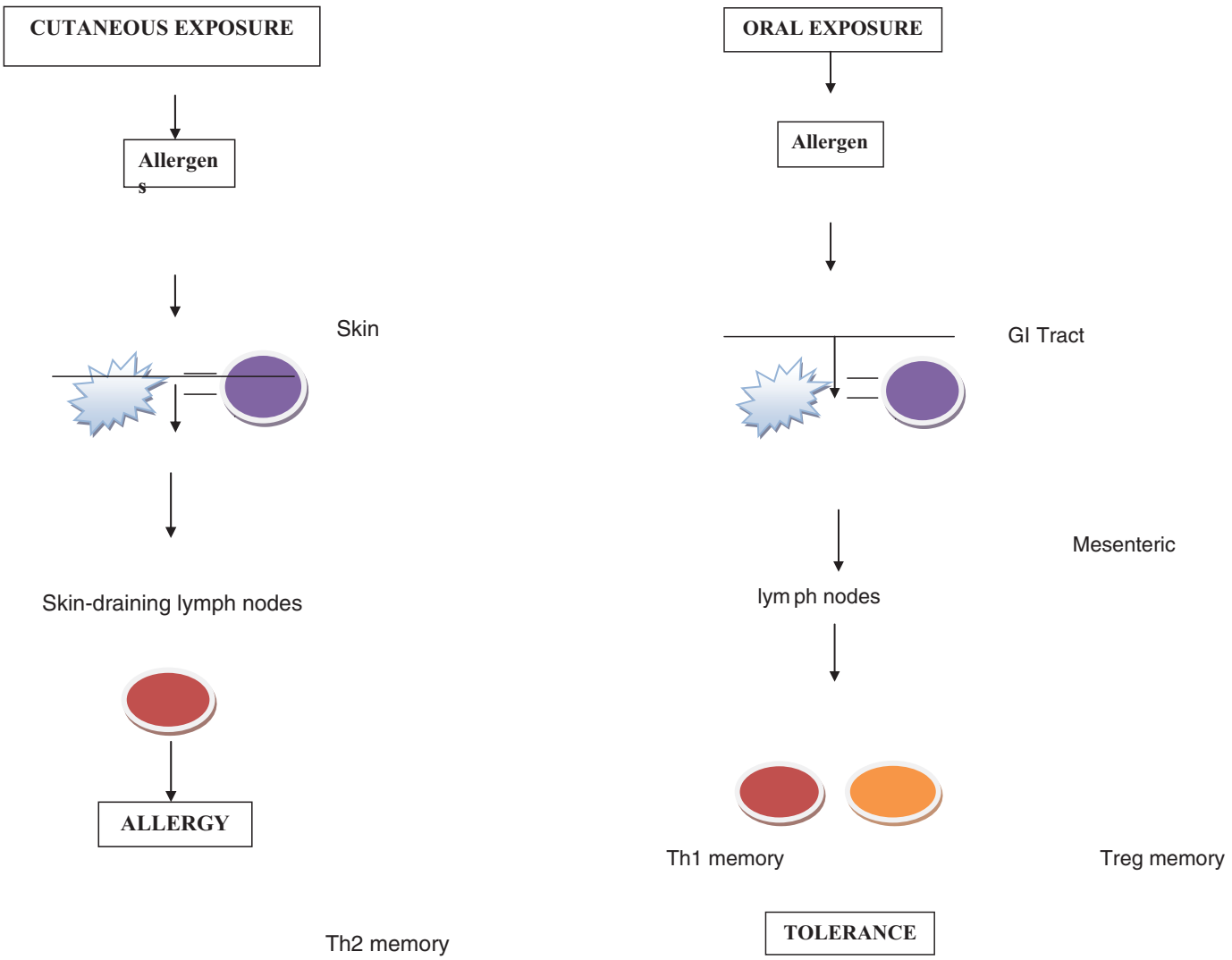

Figure 1 Mechanism of wheat allergy (Lack, 2008).

α-Amylase Inhibitors

Several groups of investigators have reported that some of the wheat allergens responsible for baker's asthma are members of a family of wheat α-amylase inhibitors (Sandiford et al., 1995). A 16 kDa wheat protein, a glycosylated subunit of the wheat tetrameric α-amylase inhibitor, has been identified and confirmed as an important allergen. Using IgE immune-blotting, Pfeil et al. (1990) identified major α-amylase inhibitor with molecular weights of 15 and 17 kDa. In similar investigations, Sandiford et al. (1995) identified 15 and 12 kDa α-amylase inhibitor in patients with baker's asthma. In another study, Jones et al. (1995) showed 20 and 47 kDa wheat proteins as potential allergens in children with confirmed wheat hypersensitivity. Ikezawa et al. (1994) found 33–98 kDa IgE-binding wheat proteins with AD patients sera in the salt-insoluble fraction by immunoblotting. In contrast, Ikezawa et al. (1994) reported that salt-soluble proteins with molecular masses of about 14 kDa bound IgE in AD patients sera, and these might be the same proteins considered to be major allergens of baker's asthma. Likewise, James et al. (1997) identified a subunit of the wheat dimeric α-amylase inhibitor which binds IgE in patients with hypersensitivity reactions to ingested wheat proteins. In another study, Gomez et al. (1990) revealed that CM3 (14 kd), one of the subunits of α-amylase inhibitors, binds to IgE sera from AD patients. The single allergen sensitization profiles obtained with 17 recombinant wheat flour allergens while two CCDs revealed no major allergen for German bakers. The highest frequencies were found for α-amylase inhibitors and CCDs (Sander et al., 2011).

Walsh and Howden, (1989) using an epitope mapping method, have recently identified a putative allergenic peptide in the NHz-terminal amino acid sequence of protein (0.28). It was further considered as a new wheat monomeric inhibitor of heterologous α-amylases. Similarly, a major allergen with activity against insect α-amylase has been also characterized in barley flour (Barber et al., 1989; Tordesillas et al., 2011). Both aforementioned proteins have around 14 kDa, and belong to the

same protein family in cereals, which includes trypsin inhibitors and subunits of monomeric, dimeric, and tetrameric inhibitors of heterologous α-amylases.

Prolamins

Prolamins, the second major type of protein are alcohol-soluble and water-insoluble storage proteins of cereal grains (Shewry and Halford, 2002). In addition, they often have unusual amino acid compositions, being particularly rich in proline and glutamine (Shewry and Tatham 1999). The prolamins themselves are immensely diverse in structure, with the major prolamins of maize (a-zeins) and closely related panicoid' cereals (millets and sorghum) forming an apparently distinct group. In addition, wheat prolamins have also been implicated in dietary allergy, with symptoms including AD and exercise-induced anaphylaxis (Varjonen et al., 1997). Consequently; the prolamin currently forms the largest and most widely distributed group of plant food allergens.

ω-5 Gliadins

The function of gliadin and its derived peptides in educing the unfavorable reactions in celiac disease is still far from being entirely elucidated. Gliadins proteins are further divided into subunits, i.e., α-, β-, γ-, and ω-gliadins. Whilst, ω-gliadins are further subdivided into $\omega 1$, $\omega 2$, and $\omega 5$ components on the basis of sequences and mobility (Kasarda et al., 1983). Amongst, α-, β-, and γ-gliadins are toxic to persons with celiac disease (CD) and ω-gliadins is nontoxic to persons with CD (Pomeranz, 1988).

Wheat ω-5 gliadin has been identified as the major allergen in wheat-dependent, exercise-induced anaphylaxis (WDEIA) (Staden et al., 2007). More lately, it has been reported that IgE to ω-5 gliadin is also highly predictive of immediate allergy to ingested wheat in children, with increased levels correlating with positive oral wheat challenge results (Bauer et al., 1999). More than 80% of children with immediate symptoms to wheat reportedly had IgE anti-bodies to ω-5 gliadin. The findings of Lauriere et al. (2006) and Patriarca et al. (2006) showed that sera from patients allergic to hydrolyzed wheat proteins with immediate skin reactions and from patients with WDEIA exhibited distinct patterns of reactivity. Similarly, Niggemann et al. (2006) have shown that different profiles of wheat antigens are known by patients with IgE-mediated wheat allergy and celiac disease (Palosuo et al., 2001; Tanaka et al., 2011). Amongst, w5-gliadins induced release of histamine from the basophils of patients with WDEIA but not from those of controls (Lehto et al., 2003).

Fast ω-gliadin (contains ω-5 gliadin) is a major allergen in wheat-dependent exercise-induced anaphylaxis and IgE against fast ω-gliadin cross-reacts to other gliadins. $\omega 5$-gliadin has been identified as a major allergen in adults having WDEIA (Palosuo et al., 1999; Morita et al., 2003; Matsuo et al., 2004).

Nonprolamin

Nonprolamins consist of water-soluble albumins and salt-soluble globulins (Singh and Skerritt, 2001). Few studies on nonprolamins have been carried out so far as compared to gliadins and glutenins. Glutenins are composed of high molecular weight subunits and low molecular weight subunits. In fact, nonprolamins possess multiple functions during growth and development of wheat. For instance, albumins and globulins include enzymes and inhibitors of enzymes that regulate development at different stages. The relative amounts of essential amino acids such as aspartate, threonine, lysine, and tryptophan for humans are more abundant in albumins and globulins, but less adequate than in storage proteins.

Glycoproteins

Glycoproteins are proteins that contain oligosaccharide chains (glycans) covalently attached to polypeptide side-chains. The carbohydrate is attached to the protein in a cotranslational or posttranslational modification that is known as glycosylation. In proteins that have segments extending extracellularly, the extracellular segments are often glycosylated. Glycoproteins are often important integral membrane proteins, where they play a role in cell–cell interactions. Glycoproteins also occur in the cytosol, but their functions and the pathways producing these modifications in this compartment are less well-understood (Funakoshi and Suzuki, 2009). The major food allergens identified as class 1 allergens are water-soluble glycoproteins that are 10–70 kDa in size and fairly stable to heat, acid, and proteases (Sampson, 1999). According to Robert et al. (2006), monosaccharides commonly found in eukaryotic glycoproteins are given in Table 2.

Table 2 Monosaccharides present in eukaryotic glycoproteins

Sugar	Type	Abbreviation
β-D-glucose	Hexose	Glc
β-D-galactose	Hexose	Gal
β-D-mannose	Hexose	Man
α-L-fucose	Deoxyhexose	Fuc
N-acetylgalactosamine	Aminohexose	GalNAc
N-acetylglucosamine	Aminohexose	GlcNAc
N-acetylneuraminic acid	Aminononulosonic acid (Sialic acid)	NeuNAc
Xylose	Pentose	Xyl

Profilins

Profilins play a major role in the regulation of polymerization of actin filaments as well as consist of a large portion of the class 2 allergens and frequently show cross-reactivity between pollen and food (Breiteneder and Ebner, 2000). Patients often become sensitized to the inhaled pollen and, because of the cross-reactivity with profilins in the fruit or vegetable, experience oral, and pharyngeal symptoms when ingesting the raw fruit or vegetable (i.e., the pollen-food allergy or oral allergy syndrome). The majority of these class 2 allergens are presumably comprised of conformational epitopes and therefore highly heat labile, susceptible to enzymatic degradation and difficult to isolate, often giving unsatisfactory standardized extracts for diagnostic purposes.

Derivative Allergies

Proteins are made of a chain of dehydrated amino acids. When enzymes cut proteins into pieces they add water back to the site at which they cut, called enzymatic hydrolysis, for proteins, it is called proteolysis. The initial products of this hydrolysis are polypeptides, and smaller products are called simply peptides; these are called wheat protein hydrolysates. These hydrolysates can create allergens of wheat proteins that previously did not exist by the exposure of buried antigenic sites in the proteins.

When proteins are cut into polypeptides, buried regions are exposed to the surface, and these buried regions may possibly be antigenic. Such hydrolyzed wheat protein is used as an additive in foods and cosmetics. The peptides are often 1 kDa in size (9 amino acid residues in length) and may increase the allergic response (Akiyama et al., 2006). These wheat polypeptides can cause immediate contact urticaria in susceptible people (Laurière et al., 2006).

COMMON DISEASES

Celiac Disease

The occurrence of CD is about 1: 100 (Europe, USA) and higher than supposed earlier (Jankowiak et al., 2008). If we look back, the history of celiac disease can be separated into many ages, each driven by diagnostic advancement and deeper knowledge of disease pathogenesis. These advances are paralleled by the recognition of new clinical patterns linked with CD and by an incessant redefinition of the pervasiveness of the disease in population. Due to its exclusive pathogenesis, celiac disease is extensively examined as a model immuno-genetic disorder (Mamone et al., 2011). Celiac disease is believed to have a genetic component because there is a strong association of the disease with the presence of specific HLA class II antigens, predominantly HLA DQ2 and (to a lesser extent) DQ8 (Louka and Sollid, 2003). It is believed that the proteins implicated in the disease, the prolamins, bind to the DQ2 or DQ8 molecule, giving rise to T-cell activation and triggering a sequence of events leading to full-blown disease. It was found by Sjostrom et al. (1998) that T-cell reactivity is enhanced by the action of tissue transglutaminase, which deamidates specific glutamine residues of gliadin and glutenin peptides.

In the beginning, CD was believed as a chronic indigestion, even if the causal food was not identified. Later, the disease was confirmed to depend on intolerance to wheat gliadin that leads to typical mucosal changes in the gut and to a malabsorption syndrome. These facts directed to cure the disease with a gluten-free diet. After the recognition of antibodies to gluten in the serum of patients and the recognition of gluten-specific lymphocytes in the mucosa, CD was depicted as an autoimmune disorder that usually presents as enteropathy in genetically susceptible individuals like a chronic "gluten infection" (Zhernakova et al., 2010; Tommasini et al., 2011). It is distinguished by polygenic predisposition, autoimmune nature, principally asymptomatic, or atypical clinical course (Pavlović et al., 2010). CD4(+) T cells have a vital function in CD, identifying and binding complexes bearing gluten peptides that have endured digestion and are deamidated by tissue transglutaminase (TG2) thus supporting disease progression (Lindfors et al., 2010; Huan et al., 2011). The intestinal mucosa of susceptible individuals is crossed by undigested gluten that direct to a marked inflammatory response (Bas et al., 2009). One of the most serious side effects is osteopenia, while increased risk of malignant diseases (James and Scott, 2001; Pengiran Tengah et al., 2002; Vestergaard, 2003). As there are indications that a gluten-free diet protects celiac patients against the development of these complications, the importance of compliance to such a diet is stressed. As there is no cure, a lifelong compliance to a gluten-free diet is the only way to alleviate symptoms. The innate immune system consists of a variety of immune responses that constitute the first line of defense against the invasion of foreign substances, e.g., pathogens. Its response to challenge is ahead of the induction of the adaptive immune response, is not antigen-specific and is without memory. Activation at inappropriate sites or to an excessive degree can exacerbate tissue damage in several diseases, and a possible role in the first stages of celiac disease has been suggested (Maiuri et al., 2003).

Typical celiac disease, distinguished by mild to harsh gastrointestinal symptoms, is less widespread than nonclassic celiac disease, illustrated by absence of gastrointestinal symptoms (Polanco, 2008; Snyder et al., 2008; Cabrera-Chávez and de-Barca, 2009; Silva et al., 2010). Celiac disease consequences from composite interactions between the innate immune system, an adaptive T and B cell response and the mucosal barrier where inflammation is eventually manifested (Heap and Van-Heel, 2009; Mothes et al, 2009; De Vincenzi et al., 2010).

Good devotion to gluten-free diet is compulsory to sustain the optimal bone health (Mora, 2008). A key mechanism of the disease is immune-mediated T-lymphocyte activation in the gastrointestinal mucosa following gluten ingestion. Inflammation

of the intestinal mucosa and atrophy of the villi occur, and can result in the inadequate absorption of nutrients (Fasano and Catassi, 2001). Briefly, mechanism of causing allergy at bowel level includes:

- ➢ Glutaminase (an intestinal enzyme) deficiency
- ➢ Increased permeability of the bowel to macromolecules, including the allergen
- ➢ The production of antibodies to the relevant prolamin, or a fragment of it
- ➢ Increased production of inflammatory mediators

The onset of noticeable symptoms of CD seems to be dependent on the following: exposure to wheat, as when an infant is weaned (introduction of solids); predisposition through family history; and some kind of "trigger" mechanism (Fasano and Catassi, 2001; Palosuo et al., 2001). The clinical manifestations of the disease vary markedly with the age of the affected person, the duration and severity of the disease and the presence of extra-intestinal pathologic conditions. The symptoms f CD include diarrhea, bloating, weight loss, anemia, chronic fatigue, bone pain, and muscle cramps. Symptoms vary with respect to age from young to elder children (Fasano and Catassi, 2001). Corn, rice, and other cereal grains such as sorghum, millet, teff, ragi, and Job's tears as well as buckwheat, quinoa, and amaranth can safely be ingested by a person with CD. Spelt and kamut however, should be avoided in CD (Thompson, 2000).

Baker's Asthma

Baker's asthma is an allergy caused by inhalation of cereal flour and is most common disease among workers with occupational exposure to cereal flour. Almost 4–25% of bakery workers are affected by prolonged exposure to wheat products. IgE-mediated reactions to wheat have been demonstrated for baker's asthma as early as the beginning of the 20th century (Houba, 1998). The insoluble gluten proteins are mainly responsible for these allergenic responses (Palosuo, 2003; Wiszniewska et al., 2011). Contact with or inhalation of wheat flour proteins is one of the causes of baker's asthma (an occupational allergy), but allergens other than the wheat itself may also be reasons. Symptoms of this disease include rhinitis, skin itching/rash, ocular symptoms (including tearing, itching and conjunctival injection), respiratory symptoms (including coughing, wheezing, and shortness of breath and sputum production), and "grain fever" (Matsumura et al., 1994).

Hypersensitivity reactions have been noted in case of wheat flour, both by inhalation and ingestion (Baldo et al., 1980; Merget et al., 2011). Most prominent allergens for baker's asthma have been related to the salt-soluble fraction of wheat. Gomez et al. (1990) identified and characterized several 12–16 kDa salt-soluble proteins, members of the α-amylase/trypsin inhibitor family, as major allergens associated with baker's asthma. In bakers' asthma, water-soluble proteins, i.e., members of the α-amylase inhibitor family, acyl-CoA oxidase, fructose-bisphosphtase aldolase (Weiss et al., 1997) and peroxidase (Sanchez-Monge et al., 1997) have been identified as important wheat allergens.

Wheat-Dependent Exercise-Induced Reactions

Wheat-dependent exercise-induced anaphylaxis is a separate form of wheat-allergy, which is induced by physical exercise after ingestion of wheat. Exercise within 3 hours of wheat consumption can induce an adverse reaction in susceptible individuals. In some cases, this can also occur when wheat is consumed directly after exercise. Typical symptoms experienced include asthma, urticaria, angioedema, dyspnoea, syncope, and anaphylaxis (Palosuo et al., 2001).

In a previous study, Ioachim et al. (2002) demonstrated that the circulating levels of gliadin, which is recognized as an allergen for a variety of wheat allergies, were correlated with the clinical symptoms in patients with WDEIA. Interestingly, increased serum gliadin levels induced by exercise and aspirin were also observed in healthy subjects. It is also hypothesized that aspirin facilitates the absorption of intact gliadin due to an increase in gastrointestinal permeability (Jones and Jones, 2000; Tsunoda et al., 2003). The typical symptom is generalized urticaria associated with shock or hypotension. Although the mechanism of physical exercise-induction in the anaphylaxis is indistinguishable, an immediate-type hypersensitivity to water/salt-insoluble fraction of wheat proteins (gluten) has been considered to underlie in this disease.

Atopic Dermatitis

AD is a relapsing inflammatory skin disease characterized by eczematous skin lesions and intense pruritus (Patriarca et al., 2007). In AD, pruritus is often resistant to H1-antihistamine treatment. Therefore other mediators, including neuropeptides, neurotransmitters, proteinases, arachidonic derivates, and cytokines, have been suggested for a pathophysiologic role of pruritus in AD (Meglio et al., 2004).

Children with atopic disorders tend to have a higher prevalence of food allergy; about 35% of children with moderate to severe AD have IgE mediated food allergy and about 6–8% of asthmatic children have food-induced wheezing (Novembre et al., 1998) but 80% of them outgrow their food allergy. Later, Ellman et al. (2002) found that children with AD for a period of 10 years did not manifest reactions to an increasing variety of foods.

At the start of present decade, Wantanabe et al. (2000) reported the safety and usefulness of hypoallergenic wheat product in patient with AD having wheat allergy (Yamamoto et al., 2004).

CONCLUSION

Wheat is consumed all over the world, considering as a staple food in many parts of the world. However, many people are intolerant to wheat proteins especially gluten protein. IgE-mediated wheat allergy is developed in the absence of OT. As a result of these reactions, different symptoms of allergy take place. Consequently, these symptoms result in different diseases like AD, CD, and baker's asthma. Baker's asthma is due to prolonged exposure of workers to the baking plant. Though, these diseases can be controlled by following different remedies. The preventive measures to avoid wheat allergy include consumption of fruits and vegetables and gluten free products. Additionally, avoid fried foods, sauces and all baked goods. Considering the nutshell of this review, various proteins present in wheat causes allergenic reaction in the community. So, the people who are intolerant to wheat should avoid the proteins mentioned in this paper. Though, further research is required to overcome the allergenic reactions caused by wheat as it is used as a staple food in many parts of the world and people cannot completely remove it from their diet.

REFERENCES

Ajala, A. R., Cruz, A. G., Faria, J. A. F., Walter, E. H. M., Granato, D. and Sant-Ana, A. S. (2010). Food allergens: Knowledge and practices of food handlers in restaurants. *Food Control*. **21**:1318–1321.

Akagawa, M., Handoyo, T., Ishii, T., Kumazawa, S., Morita, N. and Suyama, K. (2007). Proteomic analysis of wheat flour allergens. *J. Agric. Food Chem.* **55**:6863–6870.

Akiyama, M., Titeux, M., Sakai, K., McMillan, J. R., Tonasso, L., Calvas, P., Jossic, F., Hovnanian, A. and Shimizu, H. (2007). DNA-based prenatal diagnosis of harlequin ichthyosis and characterization of ABCA12 mutation consequences. *J. Investigat. Dermatol.* **127**:568–573.

Alderman, D. J. (2000). Summary final report: effects of exposure to high and low temperatures on the survival of the crayfish plague fungus A. astaci in vitro and in vivo. Australian Quarantine and Inspection Service, Canberra, Australia.

Alderman, Haddad, Lawrence, James, Harold, Appleton, Simon, Song, Lina, Yohannes, Yisehac (2002). Reducing child undernutrition, FCND Briefs 137, International Food Policy Research Institute (IFPRI).

Andera, A. E., Mannetje, A. T., Douwes, J., Cheng, S., McLean, D., Ellison-Loschmann, L. and Pearce, N. (2009). The New Zealand workforce survey II: Occupational risk factors for asthma. *Oxford J.* **54**(2):154–164.

Anna, N. W. and Antonella, M. (2009). Food protein-induced enterocolitis syndrome. *Curr. Opinion Allergy Clin. Immunol.* **9**(4):371–377.

Ann Dermatol Venereol. 2010 Apr; **137**(4):281–4.

Armentia, A., Sanchez-Monge, R., Gomez, L., Barber, D. and Salcedo, G. (1993). *In vivo* allergenic activities of eleven purified members of a major allergen family from wheat and barley flour. *Clin. Exp. Allergy.* **23**(5):410–5

Atchison, J., Head, L. and Gates, A. (2010). Wheat as food, wheat as industrial substance; comparative geographies of transformation and mobility. *Geoforum*. **41**:236–246.

Bachmann, M. F. and Kopf, M. (2002). Balancing protective immunity and immunopathology. *Curr Opin Immunol.* Aug; **14**(4):413–419.

Baldo, B. A., Krilis, S. and Wrigley, C. W. (1980). Hypersensitivity to inhaled flour allergens. *Allergy.* **35**:45–56.

Barber, D., Sánchez Monge, R., Gómez, L., Carpizo, J., Armentia, A., López, Otín C., Juan F. and Salcedo, G. (1989). A barley flourinhibitor of insect alpha amylase isa major allergen associated with bakers asthma disease. *FEBS Lett.* **248**:119–122.

Bas, A., Forsberg, G., Sjöberg, V., Hammarström, S., Hernell, O. and Hammarström, M. L. (2009). Aberrant extrathymic T cell receptor gene rearrangement in the small intestinal mucosa: A risk factor for coeliac disease? *Gut.* **58**(2):189–195.

Battais, F., Courcouxb, P., ves Popineaua, Y., Moneret-Vautrinc, K. D. A. and Denery-Papini, S. (2005). Food allergy to wheat: Differences in immunoglobulin E-binding proteins as a function of age or symptoms. *J. Cereal. Sci.* **42**:109–117.

Benngtsson, B. A., Eden, S., Lonn, L., Kvist, H., Stockland, A., Linstetd, G., Bosaeus, I., Tolli, J., Stosjrom, L. and Isaksson, O. G. (2001). Treatment of adult with growth hormone deficiency with recombinant humans. *J Clin Endocrinol. Metab.* **76**:309–317.

Biagini, R. E., MacKenzie, B. A. Sammons, D. L., Smith, J. P., Striley, C. A., Robertson, S. K. and Snawder, J. E. (2004). Evaluation of the prevalence of anti- wheat anti-flour dust, and antiamylase specific IgE antibodies in US blood donors. *Ann. Allergy Asthma Immunol.* **92**:649–653.

Bittner, C., Grassau, B., Frenzel, K. and Baur, X. (2010). Identification of wheat gliadins as an allergen family related to baker's asthma. *J. Allergy Clin. Immunol.* **121**(3).

Blands, J., Diamant, B., Kallós, P., Kallós-Deffner, L. and Lowenstein, H. (1976). Flour allergy in bakers. I. Identification of allergenic fractions in flour and comparison of diagnostic methods. *Int. Arch. Allergy Appl. Immunol.* **52**(1–4):392–406.

Bock, K. (1986). Syntactic persistence in language production. *J.Cognitive Psy.* **18**(3):355–387.

Bouchez-Mahiout, I., Snégaroff, J., Tylichova, M., Pecquet, C., Branlard, G. and Laurière, M. (2010). Low molecular weight glutenins in wheat-dependant, exercise-induced anaphylaxis: Allergenicity and antigenic relationships with Omega 5-Gliadins. *Int. Arch. Allergy Immunol.* **153**:35–45.

Brant, A. (2007). Baker's asthma. *Curr. Opin. Allergy Clin. Immunol.* **7**:152–155.

Branum, A. and Lukacs, S., (2008). Food Allergy Among U.S. Children: TrendS in Prevalence and Hospitalizations. NCHS Data Brief, No. 10. National Center for Health Statistics, Hyattsville, MD.

Bucka, J., Hattersleya, S. and Kimber, I. (2010). Food allergy – science and policy needs – The UK Food Standards Agency. *Res. Programme. Toxicol.* **278**:319–325.

Cabrera-Chávez, F. and de-Barca, A. M. (2009). Bovine milk intolerance in celiac disease is related to IgA reactivity to alpha- and beta-caseins. *Nutrition.* **25**(6):715–716.

Case, S. (2005). The gluten free diet: How to provide effective education and resources. *Gastroenterol.* **128**(4):128–134.

Castellanos-Rubio, A., Santin, I., Irastorza, I., CastaÒo, L., Vitoria, J. C., Bilbao, J. R. (2009). TH17 (and TH1) signatures of intestinal biopsies of CDpatients in response to gliadin. *Autoimmunity.* **42**:69–73.

Catassi and Fasano, (2008). C. Catassi and A. Fasano, Celiac disease. In: Arendt, E. K. and Dal Bello, F. eds., Gluten-Free Cereal Products and Beverages, Academic Press, London.

Čelakovská, J., Vaněčková, J., Ettlerová, K., Ettler, K. and Bukač, J. (2010). The role of atopy patch test in diagnosis of food allergy in atopic eczema/dermatitis syndrom in patients over 14 years of age. *Acta. Medica.* **53**(2):101–108.

Cho, H. N., Hong, S., Lee, S. H. and Yum, H. Y. 2011. Nutritional status according to sensitized food allergens in children with atopic dermatitis. *Allergy Asthma Immunol. Res.* **3**(1):53–7.

Ciclitira, P. J., Ellis, H. J., Lundin, K. E. A. (2005). Gluten free diet- what is toxic? *Best Practice Res. Clin. Gastroenterol.* **19**(3):359–371.

Codex Alimentarius Commission 2007. Report of the 29th session of the Codex Committee on Nutrition and Foods for Special Dietary uses. Draft revised Codex Standard for Foods for Special Dietary Use for Persons Intolerant to Gluten. Codex Alimentarius Alinorm 08/31/26, para. 64 and Appendix III, Rome, Italy, pp. 50–51.

Codex Alimentarius Commission 2008. Report of the 31st session of the Codex Committee on Nutrition and Foods for Special Dietary uses. Revised Codex Standard for Foods for Special Dietary Use for Persons Intolerant to Gluten. Codex Alimentarius Alinorm 08/31/REP, Appendix VII, Geneva, Switzerland, p. 107.

Constantin, C., Quirce, S., Grote, M., Touraev, A., Swoboda, I., Stoecklinger, A., Mari, A., Thalhamer, J., Heberle-Bors, E. and Valenta, R. (2008). Molecular and immunological characterization of a wheat serine proteinase inhibitor as a novel allergen in baker's asthma. *J. Immunol.* **180**:7451–7460.

Constantin, C., Quirce, S., Poorafshar, M., Touraev, A., Niggemann, B., Mari, A., Ebner, C., Akerstrçm, H., Heberle-Bors, E., Nystrand, M.m and Valenta, R. (2009). Micro-arrayed wheat seed and grass pollen allergens for component-resolved diagnosis. *Allergy.* **64**:1030–1037.

Cosnes, J., Cellier, C., Viola, S., Colombel, J. F., Michaud, L., Sarles, J., Hugot, J. P., Ginies, J. L., Dabadie, A., Mouterde, O., Allez, M., Nion–Larmurier, I. and The Groupe D'Etude et de Recherche Sur la Maladie Coeliaque. (2008). Incidence of augtoimmune disease in cieliac disease: Protective effect of the gluten free diet. *Clin. Gastroent. Hepatol.* **6**(7):753–758.

Crespo J. F. and Rodriguez J. (2003). Food allergy in adulthood. **58**(2):98–113.

Cross, A. H. and Golumbek, P. T. (2003). Neurologic manifestations of celiac disease Proven, or just a gut feeling? *Neurol.* **60**:1566–1568.

Dalal, I., Binson, I., Reifen, R., Amitai, Z., Shohat, T., Rahmani, S., Levine, A., Ballin, A. and Somekh, E. (2002). Food allergy is a matter of geography after all: sesame as a major cause of severe IgE-mediated food allergic reactions among infants and young children in Israel. *Allergy* **57**: 362–365.

De-Benedetto, A., Agnihothri, R., McGirt, L. Y., Bankova, L. G. and Beck, L. A. (2009). Atopic dermatitis: A disease caused by innate immune defects. *J. Invest. Dermatol.* **129**:14–30.

Denery-Papini, S., Lauriére, M., Branlard, G., Morisset, M., Pecquet, C., Choudat, D., Merlino, M., Pineau, F., Popineau, Y., Boulenc, E., Bouchez-Mahiout, I., Bodinier, M. and Moneret-Vautrin, D. A. (2007). Influence of the allelic variants encoded at the Gli-B1 locus, responsible for a major allergen of wheat, on IgE reactivity for patients suffering from food allergy to wheat. *J. Agric Food Chem.* **55**(3):799–805.

De-Vincenzi, M., Vincentini, O., Di-Nardo, G., Boirivant, M., Gazza, L. and Pogna, N. (2010). Two prolamin peptides from durum wheat preclude celiac disease-specific T cell activation by gluten proteins. *Eur. J. Nutr.* **49**(4):251–5.

De Vries, E. J., van der Meer, J. R., van Neerven, A. R., de Vos, W. M. and Zehnder, A. J. (1991). Cloning and characterization of plasmid-encoded genes for the degradation of 1,2-dichloro-, 1,4-dichloro-, and 1,2,4-trichlorobenzene of Pseudomonas sp. strain P5. *J Bacteriol.* **173**(1):6–15.

Dewar, D. H., Amato, M., Ellis, J., Pollock, E. L., Gonzalez-Cinca, N., Wieser, H. and Ciclitira, P. J. (2006). The toxicity of high molecular weight glutenin subunits of wheat to patients with coeliac disease. *Europ. J. Gastroenterol. Hepatol.* **18**:483–491.

Dickerson, F., Stallings, C., Origoni, A., Vaughan, C., Khushalani, S., Leister, F., Yang, S., Krivogorsky, B., Alaedini, A. and Yolke, R. (2010). Markers of gluten sensitivity and celiac disease in recent-onset psychosis andMulti-episode schizophrenia. *Biol. Psychiatry.* **68**:100–104.

Dieterich, W., Esslinger, B., Trapp, D., Hahn, E., Huff, T., Seilmeier, W., Wieser, H. and Schuppan, D. (2006). Cross linking to tissue transglutaminase and collagen favours gliadin toxicity in coeliac disease. *Gut.* **55** (4):478–484.

Dong, P., Reed, S. A., Yi, S. A., Kalmykov, S., Shvets, G. and Downer, M. C. (2010). Formation of optical bullets in laser-driven plasma bubble accelerators. *Phys. Rev. Lett.* **104**(13):134801.

Donovan, G. R. and Baldo, B. A. (1990). Crossreactivity of IgE antibodies from sera of subjects allergic to both ryegrass pollen and wheat endosperm proteins: Evidence for common allergenic determinants. *Clin. Exp. Allergy.* **20**(5):501–9.

Droste, J., Myny, K., Van Sprundel, M., Kusters, E., Bulat, P., Braeckman, L., Vermeire, P,. and Vanhoorne, M. (2003). Allergic sensitization, symptoms, and lung function among bakery workers as compared with a nonexposed work population. *J. Occup. Environ. Med.* **45**:648–655.

Dykewicz, M. S. and Hamilos, D. L. (2010). Rhinitis and sinusitis. *J. Allergy Clin. Immunol.* **125**(2):103–115.

Elder, J. H. (2008). "The gluten-free, casein-free diet in autism: An overview with clinical implications". *Nutr. Clin. Pract.* **23**(6):583–538.

Epub 2010 Feb 18. [Contact urticaria induced by hydrolyzed wheat proteins in cosmetics]. Olaiwan A, Pecquet C, Mathelier-Fusade P, Francès C.

Esch, R. E. (2004). Grass pollen allergens. *Clin. Allergy Immunol.* **18**:185–205.

FAO. (1995). Food allergles. Report of the technical consultation of the food and agriculture organization of the United Nations. Rome. November 13–14.

Fernandez-Jimenez, N., Castellanos-Rubio, A., Plaza-Izurieta, L., Gutierrez, G., Castano, L., Vitoria, J. C. and Bilbao, J. R. (2010). Analysis of β-defensin and Toll-like receptor gene copy number variation in celiac disease. *Human Immunol.* **71**:833–83.

Gao, L., Wang, A., Li, X., Dong, K., Wang, K., Appels, R., Ma, W. and Yan, Y. (2009). Wheat quality related differential expressions of albumins and globulins revealed by two-dimensional difference gel electrophoresis (2-D DIGE). *J. Proteomics.* **73**(2):279–296.

Gómez-Muñoz, A., Hamza, E. H. and Brindley, D. N. (1992). Effects of sphingosine, albumin and unsaturated fatty acids on the activation and translocation of phosphatidate phosphohydrolases in rat hepatocytes. *Biochim. Biophys. Acta.* **1127**(1):49–56.

Grant, E. C. (1979). "Food allergies and migraine". *Lancet* **1**(8123):966–969.

Guandalini, S. and Newland, C. (2011). Differentiating food allergies from food intolerances. *Curr Gastroenterol Rep.* **13**(5): 426–434.

Hadjivassiliou, M., Grünewald, R. A., Kandler, R. H., Chattopadhyay, A. K., Jarratt, J. A., Sanders, D. S., Sharrack, B., Wharton, S. B. and Davies-Jones, G. A. B. (2006). Neuropathy associated with gluten sensitivity. *J. Neurol. Neurosurg. Psychiatry.* **77**:1262–1266.

Hadjivassiliou, M., Rao, D. G., Wharton, S. B., Sanders, D. S., Grünewald, R. A. and Davies-Jones, A. G. B. (2010). Sensory ganglionopathy due to gluten sensitivity. *Neurol.* **75**:1003–1008.

Hansen, I., Klimek, L., Mosges, R. and Hormann, K. (2004). Mediators of inflammation in the early and the late phase of allergic rhinitis. *Curr. Opin. Allergy Clin. Immunol.* **4**(3):159–63.

Heap, G. A. and Van-Heel, D. A. (2009). Genetics and pathogenesis of coeliac disease. *Semin Immunol.* **21**(6):346–54.

Heffler, E., Nebiolo, F., Asero, R., Guida, G., Badiu, I., Pizzimenti, S., Marchese, C., Amato, S., Mistrello, G., Canaletti, F. and Rolla, G. (2011). Clinical manifestations, co-sensitizations, and immunoblotting profiles of buckwheat-allergic patients. *Allergy.* **66**(2):264–70.

Helm, R. and Burks, A. (2000). Mechanisms of food allergy. *Curr. Opin. Immunol.* **12**:647–653.

Heratizadeh, A., Wichmann, K. and Werfel, T. (2011). Food allergy and atopic dermatitis: How are they connected? *Curr. Allergy Asthma. Rep.* **11**(4):284–91.

Holtmeier, W. and Caspary, W. F. (2006). Celiac disease. *Orphanet. J. Rare. Dis.* **1**:3.

Huan, J., Meza-Romero, R., Mooney, J. L., Vandenbark, A. A., Offner, H., Burrows, G. G. (2011). Single-chain recombinant HLA-DQ2.5/peptide molecules block α2-gliadin-specific pathogenic CD4 +T-cell proliferation and attenuate production of inflammatory cytokines: A potential therapy for celiac disease. *Mucosal. Immunol.* **4**(1):112–20.

Hugh, A. and Sampson, M. D. Role of immediate food hypersensitivity in the pathogenesis of atopic dermatitis. Durham, N. C., USA. *Journal of Allergy and Clinical Immunology* **71**:473–480.

Hvatum, M., Kanerud, L., Hällgren, R. and Brandtzaeg, P. (2006). The gut-joint axis: Cross reactive food antibodies in rheumatoid arthritis. *Gut.* **55**(9):1240–7.

Ikezawa, H., Yamanegi, M., Taguchi, R., Miyashita, T. and Ohyabu, T. (1994). Effect of hypoallergenic wheat (HAW-A1) on atopic dermatitis (AD) with wheat allergy, and its antigenic analysis using sera from patients with AD. Jun; **43**(6):679–688.

Imai, T. and Y. Likura. (2003). The national survey of immediate type of food allergy. *Arerugi*. **52**:1006–1013.

Isolauri, E., Kalliomaki, M., Rautava, S., Salminen, S. and Laitinen, K. (2009). Obesity: Extending the hygiene hypothesis. *Nestle Nutr. Workshop Ser.* **64**:75–89.

Jabri, B. and Sollid, L. M. (2009). Tissue-mediated control of immunopathology in celiac disease. *Nat. Rev. Immunol.* **9**:858–70.

James, C., Morris, S., Keith, R., and Taylor, A. (2005). Impact on child mortality of removing user fees: simulation model. *British Medical Journal*. **331**: 747–749.

Jankowiak, C., Ludwig, D. (2008). Frequent causes of diarrhea: Celiac disease and lactose intolerance. *Med. Klin. (Munich).* **103**(6):413–22.

Joneja, J. M. V. (1998). Dietary Management of Food Allergies and Intolerances: A Comprehensive Guide. Second edition. Hall Publications, Vancouver, B.C.

Joneja, V. J. (1998). Dietary Management of Food Allergies & Intolerances: A Comprehensive Guide.

Jones, S. M., Magnolfi, C. F., Cooke, S. K. and Sampson, H. A. (1995). Immunologic cross-reactivity among cereal grains and grasses in children with food hypersensitivity. *J. Allergy Clin. Immunol.* **96**:341–51.

Karatay, S., Erdem, T., Kiziltunc, A., Mugnaini, L., Caffarelli, C., Cavagni, G., Giovane, A. and Vierucci, A. (2006). General or personal diet: The individualized model for diet challenges in patients with rheumatoid arthritis. *Rheumatol. Int.* **26**(6):556–60.

Kasarda, D. D., Autran, J., Lew, E. J. L., Nimmo, C. C. and Shewry, P. R. (1983). N-terminal amino acid sequences of u-gliadins and u-secalins. Implications for the evolution of prolamin genes. *Biochimica Biophysica Acta.* **747**:138–150.

Keet, C. A. and Wood, R. A. (2009). Risk factors for peanut allergy. *J. Allergy Clin. Immunol.* **24**(2):387.

Kusaba, M., Miyahara, K., Iida, S., Fukuoka, H., Takano, T., Sassa, H., Nishimura, M. and Nishio, T. (2003). Low glutelin content1: A dominant mutation that suppresses the glutelin multigene family via RNA silencing in rice. *Plant Cell.* **15**:1455–1467.

Lack, G. (2008). Epidemiologic risks for food allergy. *J. Allergy Clin. Immunol.* **121**:1331–1336.

Langeland, T. and Nyrud, M., (1982). Contact urticaria to wheat bran bath: A case report. *Acta Derm. Venereol.* **62** (1):82–3.

Laurière, M., Pecquet, C., Bouchez-Mahiout, I., Snégaroff, J., Bayrou, O., Raison-Peyron, N. and Vigan, M. (2006). Hydrolysed wheat proteins present in cosmetics can induce immediate hypersensitivities. *Contact Derm.* **54**(5):283–9.

Lehto, M., Airaksinen, L., Puustinen, A., Tillander, S., Hannula, S., Nyman, T., Toskala, E., Alenius, H. and Lauerma, A. (2010). Thaumatin-like protein and baker's respiratory allergy. *Ann. Allergy Asthma. Immunol.* **104**(2):139–146.

Leon, F. (2011). Flow cytometry of intestinal intraepithelial lymphocytes in celiac disease. *J. Immunol Methods.* **363**:177–187.

Lindfors, K., Mäki, M. and Kaukinen, K. (2010). Transglutaminase 2-targeted autoantibodies in celiac disease: Pathogenetic players in addition to diagnostic tools? *Autoimmun. Rev.* **9**(11):744–749.

Loussert, C., Popineau, Y. and Mangavel, C. (2008). Protein bodies ontogeny and localization of prolamin components in the developing endosperm of wheat caryopses. *J. Cereal. Sci.* **47**:445–456.

Maiuri, L., Ciacci, C., Ricciardelli, I., Vacca, L., Raia, V., Auricchio, S., Picard, J., Osman, M., Quaratino, S. and Londei, M. (2003). Association between innate response to gliadin and activation of pathogenic T cells in coeliac disease. *Lancet.* **362**:30–37.

Majithia, V. and Geraci, S. A. (2007). Rheumatoid arthritis: Diagnosis and management. *Am. J. Med.* **120**(11):936–939.

Mamone, G., Picariello, G., Addeo, F. and Ferranti, P. (2011). Proteomic analysis in allergy and intolerance to wheat products. *Exp. Rev. Proteom.* **8**(1):95–115.

Mangiavillano, B., Masci, E., Parma, B., Barera, G., Viaggi, P., Albarello, L., Tronconi, G. M., Mariani, A., Testoni, S., Santoro, T. and Testoni, P. A. (2010). Bulb biopsies for the diagnosis of celiac disease in pediatric patients. *Gastrointest. Endos.* **72**(3):564–568.

Matsuo, H., Morimoto, K., Akaki, T., Kaneko, S., Kusatake, K., Kuroda, T., Niihara, H., Hide, M. and Morita, E. (2005). Exercise and aspirin increase levels of circulating gliadin peptides in patients with wheat-dependent exercise-induced anaphylaxis. *Clin. Exp. Allergy.* **35**(4):461–466.

Matsuo, H., Morita, E., Tatham, A. S., Morimoto, K., Horikawa, T., Osuna, H., Ikezawa, Z., Kaneko, S., Kohno, K. and Dekio, S. (2004). "Identification of the IgE-binding epitope in omega-5 gliadin, a major allergen in wheat-dependent exercise-induced anaphylaxis. *J. Biol. Chem.* **279**(13):12135–12140.

May, J. R. and Smith, P. H. (2008). Allergic rhinitis. In: Dipiro, J. T., Talbert, R. L., Yee, G. C., et al. eds. Pharmacotherapy: A Pathophysiologic Approach. 7th ed. The McGraw-Hill Companies, Inc, New York, NY, pp. 1565–1575.

Merget, R., Sander, I., van-Kampen, V., Beckmann, U., Heinze, E., Raulf-Heimsoth, M. and Bruening, T. (2011). Allergic asthma after flour inhalation in subjects without occupational exposure to flours: An experimental pilot study. *Int. Arch. Occup. Environ. Health* **84**(7):753–60.

Metz-Favre, C., Linhart, B., Focke-Tejkl, M., Purohit, A.,de Blay, F., Valenta, F. and Pauli, G. (2007). Skin test diagnosis of grass pollen allergy with a recombinant hybrid molecule. *J. Allergy Clin. Immunol.* **120**(2): 315–321.

Mittag, D., Niggemann, B., Sander, I., Reese, I., Fiedler, E. M., Worm, M., Vieths, S. and Reese, G. (2004). "Immunoglobulin E-reactivity of wheat-allergic subjects (baker's asthma, food allergy, wheat-dependent, exercise-induced anaphylaxis) to wheat protein fractions with different solubility and digestibility. *Mol. Nutr. Food Res.* **48** (5):380–389.

Miyakawa, T., Tsuji, M. (1988) The association of tatter leaf virus with bud-union crease of trees on trifoliate orange rootstock. In: Proceedings of the 10th Conference of the International Organization of Citrus Virologists (Ed. by Timmer, L. W.; Garnse y, S. M.; Navarro, L.), pp. 360–364. IOCV, Department of Plant Pathology, University of California, Riverside, USA.

Moodie, S. J., Norman, P. J., King, A. L., Fraser, J. S., Curtis, D., Ellis, H. J., Vaughan, R. W. and Ciclitira, P. J. (2002). Analysis of candidate genes on chromosome 19 in coeliac disease: An association study of the KIR and LILR gene clusters. *Eur. J. Immunogenet.* **29**:287–91

Mora, S. (2008). Celiac disease in children: Impact on bone health. *Rev. Endocr. Metab. Disord.* **9**(2):123–130.

Morita, E., Kunie, K. and Matsuo, H. (2007). Food-dependent exercise-induced anaphylaxis. *J. Dermatol. Sci.* **47**(2):109–117.

Mothes, T., Uhlig, H. H. and Richter, T. (2009). Recent aspects of antibody determination for the diagnosis of coeliac disease. *Dtsch. Med. Wochenschr.* **134**(30):1525–8.

Mulitz, R. M., Pratt, D. S. and Schocket, A. L. (1979). Exercise-induced anaphylactic reaction to shellfish. *J. Allergy. Clin. Immunol.* **63**:433–434.

Niggemann, B., Reibel, S., Roehr, C. C., Felger, D., Ziegert, M., Sommerfeld, C. and Wahn, U. (2001). Predictors of positive food challenge outcome in non-IgE-mediated reactions to food in children with atopic dermatitis. *J. Allergy Clin. Immunol.* **108**:1053–1058.

Novembre, E., Cianferoni, A., Bernardini, R., Mugnaini, L., Caffarelli, C., Cavagni, G., Giovane, A. and Vierucci, A. (1998). Anaphylaxis in children: Clinical and allergologic features. *Pediatrics.* **101**(4).

Oita, S., Hayashi, T. and Ohnishi-Kameyama, M. (2009). Degradation of epitope peptides of wheat gliadin and glutenin for atopic dermatitis by crude proteases from germinated wheat seeds. *Food Sci. Technol. Res.* **15**:639–644.

Pacharn, P., Jirapongsananuruk, O., Daengsuwan, T., Vichyanond P. and Visitsunthorn, N. (2009). Wheat-dependent, exercise-induced anaphylaxis in Thai children: A report of 5 Cases. *Asian Pacific. J. Allergy Immunol.* **27**:115–120.

Paganelli, G., Riva, P., Deleide, G., Clivio, A., Chiolerio, F., Scassellati, G. A., Malcovati, M. and Siccardi, A. G. (1988). In vivo labelling of biotinylated monoclonal antibodies by radioactive avidin: a strategy to increase tumour radiolocalisation. *Int J Cancer.* **2**:121–125.

Palosuo, K., Alenius, H., Varjonen, E., Koivuluhta, M., Mikkola, J., Keskinen, H., Kalkkinen, N. and Reunala, T. (1999). A novel wheat gliadin as a cause of exercise-induced anaphylaxis. *J Allergy Clin Immunol*. **103**: 912–917.

Palosuo, K., Vergonen, E., Kikki, O. M., Klemola, T., Kalkinnen, L., Alenius, H. and Reunala, T. (2001). Wheat (0.5 gliadin is a major allergen in children with immediate allergy to ingest wheat. *J. Allergy Clin. Immunol.* **108**(4): 634–638

Palacin, L., Prada, C. D., Syafiie, S. and Tadeo, F. (2008). Library for dynamic simulation of reverse osmosis plants, Proc. of 20th European Modeling and Simulation Symposium. Sep. 17–19, Briatico, Italy, 2008.

Palacin, A., Quirce, S., Sánchez-Monge, R., Fernández-Nieto, M., Varela, J., Sastre, J. and Salcedo, G. (2008). Allergy to kiwi in patients with baker's asthma identification of potential cross-reactive allergens. *Ann. Allergy Asthma Immunol.* **101**:200–205.

Pascual, J. and Leno, C. (2005). A woman with daily headaches. *The Journal of Headache and Pain: Official Journal of the Italian Society for the Study of Headaches.* **6**(2):91–92.

Pastorello, E. A., Farioli, L., Conti, A., Pravettoni, V., Bonomi, S., Iametti, S., Fortunato, D., Scibilia, J., Bindslev-Jensen, C., Ballmer-Weber, B., Robino, A. M. and Ortolani, C. (2007). Wheat IgE-mediated food allergy in European patients: Alpha-amylase inhibitors, lipid transfer proteins and low-molecular-weight glutenins. Allergenic molecules recognized by double-blind, placebo-controlled food challenge. *Int. Arch. Allergy Immunol.* **144**(1):10–22.

Paula, R. A. and George, D. T. (2010). Pathophysiology, diagnosis and management of exercise-induced anaphylaxis. *Curr. Opinion Allergy Clin. Immunol.* **10**(4):312–317.

Pavlović, M., Radlović, N., Leković, Z., Berenji, K., Stojsić, Z., Radlović, V. (2010). Coeliac disease as the cause of resistant sideropenic anaemia in children with Down's syndrome: Case report. *Srp. Arh. Celok. Lek.* **138**(1–2):91–4.

Pérez-Pimiento, A. J., Rodríguez-Cabreros, M. I., Lombardero, M., Prieto, L., Reaño, M. and Iglesias, A. (2007). Late-Onset Food Hypersensitivity to Wheat Flour. *J. Investig Allergol. Clin. Immunol.* **17**(3):202–206.

Pfeil, S.A., Weaver, M., Abdul-Karim, F. and Yang, P. (1990). Colonic Lipomas: Outcome of Endoscopic Removal. *Gastrointestinal Endoscopy*. **36**:435–438.

Pizzuti, D., Senzolo, M., Buda, A., Chiarelli, S., Giacomelli, L., Mazzon, E., Curioni, A., Faggian, D. and De-Lazzari, F. (2011). In vitro model for IgE mediated food allergy. *Scand. J. Gastroenterol.* **46**(2):177–187.

Polanco, I. (2008). Celiac disease. *J. Pediatr. Gastro. Nutr.* **47**(1):3–6.

Pomeranz, Y. (1988). Composition and Functionallity of wheat flour components. In: Pomeranz, Y., ed. Wheat chemistry and technology. 3rd Association of Cereal Chemists, pp. 219–370.

Rabivane, J. P., Jouzel, D., Raynaud, N. I., Barkov, J.-M., Barnola, I., Basile, M., Bender, J., Chappellaz, M., Davis, G., Delayque, M., Delmotte, V. M., Kotlyakov, M., Legrand, V. Y., Lipenkov, C., Lorius, L., Pépin, C., Ritz, E., Saltzman and Stievenard, M. (1999). Climate and atmospheric history of the past 420,000 years from the Vostok ice core, Antarctica. *Nature* **399**:429–436.

Ramesh, S. (2008). Food allergy overview in children. *Clin. Rev. Allergy Immunol.* **34**(2):217–230.

Rodrigo, L., Rodrigo, (2006). Celiac disease. *World J. Gastroenterol.* **12**(41):6585–6593.

Rona, R., Keil, T., Summers, C., Gislason, D., Zuidmeer, L., Sodergren, E., Sigurdardottir, S., Lindner, T., Goldhahn, K., Dahlstrom, J., McBridge, D. and Madsen, C. (2007). The prevalence of food allergy: A meta-analysis. *J. Allergy Clin. Immunol.* **120**:638–646.

Rose, C., Armbruster, F. P., Ruppert, J., Igl, B. W., Zillikens, D. and Shimanovich, I. (2009). Autoantibodies against epidermal transglutaminase are a sensitive diagnostic marker in patients with dermatitis herpetiformis on a normal or gluten free diet. *J. Am. Acad. Dermatol.* **61**(1):39–43.

Sampson, H. A. (2001). Utility of food-specific IgE concentrations in predicting symptomatic food allergy. *J Allergy Clin Immunol*. **107**:891–896.

Sampson, H. A. (2004). Update on food allergy. Department of Pediatrics and Immunobiology, The Mount Sinai School of Medicine, One Gustave L. Levy Place, New York. *J Allergy Clin Immunol.* May; **113**(5):805–819.

Sampson, M. A., Munoz-Furlong, A. and Sicherer, S. H., (2006). Risk-taking and coping strategies of adolescents and young adults with food allergy. *J. Allergy Clin. Immunol.* **117**:1440–1445.

Santin, I., Castellanos-Rubio, A., Perez deNanclares, G., Vitoria, J. C., CastaÒo, L. and Bilbao, J. R. (2007). Association of KIR2DL5B gene with celiac disease supports the susceptibility locus on 19q13.4. *Genes Immun.* **8**:171–176.

Sander, J. D., Cade, L., Khayter, C., Reyon, D., Peterson, R. T., Joung, J. K. and Yeh, J. R. (2011). Targeted gene disruption in somatic zebrafish cells using engineered TALENs. *J. Nat. Biotechnol.* **29**(8):697–698.

Sandiford, P., Cassel, J., Montegro, M. and Sanchez, G. (1995). Theimpact of women's literacy on child health and its interaction with access to health services. *Population Studies* **49**, 5–17.

Santin, I., de Nanclares, G. P., Calvo, B., Gaafar, A., CastaÒo, L., GEPV-N Group, Bilbao, J. R. Killer cell immunoglobulin-like receptor (KIR) genes in the Basque population: Association study of KIR gene contents with type 1 diabetes mellitus. *Hum Immunol*. **67**:118–24.

Scibilia, J., Pastorello, E. A., Zisa, G., Ottolenghi, A., Ballmer-Weber, B., Pravettoni, V., Scovena, E., Robino, A. and Ortolani, C. (2008). Maize food allergy: A double-blind placebo-controlled study. *Clin. Exper. Allergy.* **38**:1943–1949.

Scibilia, J., Pastorello, E. A., Zisa, G., Ottolenghi, A., Bindslev-Jensen, C., Pravettoni, V., Scovena, E., Robino, A. and Ortolani, C. (2006). Wheat allergy: A double-blind, placebo-controlled study in adults. *J. Allergy Clin. Immunol.* **117**(2):433–439.

Shang, A., Huwiler-Müntener, K., Nartey, L., Jüni, P., Dörig, S., Sterne, J. A., Pewsner, D. and Egger, M. (2005). Are the clinical effects of homoeopathy placebo effects? Comparative study of placebo-controlled trials of homoeopathy and allopathy. *Lancet.* **366**(9487):726–732.

Shewry, P. R., (1995). Plant storage proteins. *Biol. Rev. Camb. Philos. Soc.* **70**:375–426.

Shewry, P. R. and Halford, N. G. (2002). Cereal grain storage proteins: Structures,properties and role in grain utilization. *J. Exper. Botany.* **53**:947–958.

Shewry, P. R., Tatham, A. S., Forde, J., Kreis, M. and Miflin, B. J. (1986). The classification and nomenclature of wheat gluten proteins: A reassessment. *J. Cereal. Sci.* **4**:97–106.

Shewry, R. P., Tatham, S. A., Paul, L. (1999). Biotechnology of Wheat Quality. *Journal of the Science of Food and Agriculture*. **73**(4):397–406.

Sicherer, S. H., Morrow, E. H. and Sampson, H. A. (2000). Dose-response in double-blind, placebo-controlled oral food challenges in children with atopic dermatitis. *J. Allergy Clin. Immunol.* **105**:582–586.

Sicherer, S. H., Sampson, H. A., 2010. Food allergy. *Allergy Clin. Immunol.* **125**, S116–S125

Sih, T. and Mion, O. (2010). Allergic rhinitis in the child and associated comorbidities. *Pediatr. Allergy Immunol.* **21**(1):107–113.

Silva, T. S. and Furlanetto, T. W. (2010). Diagnosis of celiac disease in adults. *Rev. Assoc. Med. Bras.* **56**(1):122–6.

Singh, J., Blundell, M., Tanner, G. and John, H. S. (2001). Albumin and globulin proteins of wheat flour: Immunological and *N*-terminal sequence characterisation. *J. Cereal. Sci.* **34**:85–103

Smith, T. A. (2004). Preventing baker's asthma: An alternative strategy. *Occup. Med.* **54**:21–27.

Snyder, C. L., Young, D. O., Green, P. H. R. and Taylor, A. K. (2008). Celiac Disease. Gene Reviews, University of Washington, USA.

Sotkovsky, P., Sklenar, J., Halada, P., Cinova, J., Setinova, I., Kainarova, A., Golias, J., Pavlaskova, K., Honzova, S. and Tuckova, L. (2011). A new approach to the isolation and characterization of wheat flour allergens. *Clin. Exp. Allergy* **41**(7):1031–43.

Sutton, R., Hill, D. J., Baldo, B. A., Wrigley, C. W. (1982). Immunoglobulin E antibodies to ingested cereal flour components: Studies with sera from subjects with asthma and eczema. *Clin Allergy*. **12**(1):63–74.

Tanaka, M., Nagano, T., Yano, H., Matsuda, T., Ikeda, T. M., Haruma, K. and Kato, Y. (2011). Impact of ω-5 gliadin on wheat-dependent exercise-induced anaphylaxis in mice. *Biosci. Biotechnol. Biochem.* **75**(2):313–7.

Taylor, P. E., Flagan, R. C., Valenta, R. and Glovsky, M. M. (2002). Release of allergens as respirable aerosols: A link between grass pollen and asthma. *J. Allergy Clin. Immunol.* **109**:51–56.

Tommasini, A., Not, T. and Ventura, A. (2011). Ages of celiac disease: From changing environment to improved diagnostics. *World J. Gastro.* **2817**(32):3665–71.

Tordesillas, L., Sirvent, S., Díaz-Perales, A., Villalba, M., Cuesta-Herranz, J., Rodríguez, R. and Salcedo, G. (2011). Plant Lipid Transfer Protein Allergens: No Cross-Reactivity between Those from Foods and Olive and Parietaria Pollen. *Int. Arch. Allergy Immunol.* **56**(3):291–296.

Troncone, G., Mazzarella, A. and Leone. (1998). Gliadin Activates Mucosal Cell-Mediated Immunity In In Vitro Cultured Rectal Mucosa from Coeliac Patients and a Subset of Their Siblings; **43**:484–489.

Valero Santiago, A., Amat Par, P., Sanosa Valls, J., Sierra Martínez, P., Malet Casajuana, A. and García Calderón, P. A. (1988). Hypersensitivity to wheat flour in bakers. *Allergologia et immunopathologia.* **16**(5):309–14.

Valet, R. S. and Fahrenholz, J. M. (2009). Allergic rhinitis: Update on diagnosis. *Consultant*. **49**:610–613

Van-der-Slik, A. R., Koeleman, B. P., Verduijn, W., Bruining, G. J., Roep, B. O., Giphart, M. J. (2003). KIR in type 1 diabetes: Disparate distribution of activating and inhibitory natural killer cell receptors in patients versus HLA-matched control subjects. *Diabetes.* **52**:2639–42.

Van-Eckert, R., Bond, J., Rawson, P., Klein, C., Stern, C. and Jordan, T. W. (2010). Reactivity of gluten detecting monoclonal antibodies to a gliadin reference material. *J. Cereal. Sci.* **51**(2):198–204.

Varjonen, E., Vainio, E. and Kalimo, K. (2000). Antigliadin IgE: Indicator of wheat allergy in atopic dermatitis. *Allergy.* **55**:386–391.

Vercelli, G., Bard, C., Laugier, C., Milési-Bellier, C., Troccaz, J. and Triggs, B. (1995). Achieving dextrous grasping by integrating planning and vision-based sensing. *The International Journal of Robotics Research* **14**(5):445.

Walsh, B. J. and Howden, M. E. (1989). A method for the detection of IgE binding sequences of allergens based on a modification of epitope mapping. *J Immunol Methods.* **26**:121(2):275–280.

Walsh, B. J., Wrigley, C. W., Musk, A. W. and Baldo, B. A. (1985). A comparison of the binding of IgE in the sera of patients with bakers' asthma to soluble and insoluble wheat-grain proteins. *J. Allergy Clin. Immunol.* **76**(1): 23–28.

Wang, W., Han, J., Wu, Y., Yuan, F., Chen, Y. and Ge, Y. 2011. Simultaneous detection of eight food allergens using optical thin-film biosensor chips. *J. Agric. Food Chem.* **59**(13):6889–6894.

Watanabe, M. (1993). Hypoallergenic rice as a physiologically functional food. *Trends Food Sci Technol.* **4**(5):125–128.

Wieser, H. (2007). Chemistry of gluten proteins. *Food Microbiol.* **24**(2): 115–119.

Wiszniewska, M., Nowakowska-Świrta, E., Pałczyński, C. and Walusiak-Skorupa, J. 2011. Diagnosing of bakers' respiratory allergy: Is specific inhalation challenge test essential? *Allergy Asthma Proc.* **32**(2):111–118.

Wong, G. K. Y., Huissoon, A. P., Goddard, S., Collins, D. M. and Krishna, M. T. (2010). Wheat dependent exercise induced anaphylaxis: Is this an appropriate terminology? *J. Clin. Pathol.* **63**:814–817.

Yacoub, S., Kotit, S. and Yacoub, M. H. (2011). Disease appearance and evolution against a background of climate change and reduced resources., Royal Society of London. Philosophical Transactions A. *Mathematical, Phy. Eng. Sci.* **369**:1719–1729.

Yamamoto, M., Haruna, T., Yasui, K., Takahashi, H., Iduhara, M., Takaki, S., Deguchi, M. and Arimura, A. (2007). A novel atopic dermatitis model induced by topical application with dermatophagoides farinae extract in NC/Nga mice. *Allergol. International.* **56**:139–148.

Yazicioglu, M., Oner, N., Celtik, C., Okutan, O. and Pala, O. (2004). Sensitization to common allergens, especially pollens, among children with respiratory allergy in the Trakya region of Turkey. *Asian Pac. J. Allergy Immunol.* **22**(4):183–90.

Young, E., Stoneham, M. D., Petruckevitch, A., Barton, J. and Rona, R. (1994). A population study of food intolerance. *Lancet.* **343**:1127–1130.

Zeiger, R. S., Heller, S., Mellon, M. H., Forsythe, A. B., O'Connor, R. D., Hamburger, R. N. and Schatz, M. (1989). Effect of combined maternal and infant food-allergen avoidance on development of atopy in early infancy: A randomized study. *J. Allergy Clin. Immunol.* **84**(1):72–89.

Zuidmeer, L., Goldhahn, K., Rona, R. J., Gislason, D., Madsen, C., Summers, C., Sodergren, E., Dahlstrom, J., Lindner, T., Sigurdardottir, S. T., McBride, D. and Keil, T. (2008). The prevalence of plant food allergies: A systematic review. *JACI*, **121**:1210–1218. Academic Medical Center, Department of Experimental Immunology, Laboratory of Allergy, Amsterdam, Netherlands.