بسم الله الرحمن الرحيم

MONA MAGHRABY

شبكة المعلومات الجامعية

التوثيق الالكتروني والميكروفيلم

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جامعة عين شمس

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قسم

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Functional properties of some gluten- free products for People with celiac disease

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INTRODUCTION

The growing public awareness of nutrition and health care substantiates the potential of phytochemicals such as polyphenols and dietary fiber on their health beneficial properties. Hence, there is in need to identify newer sources of neutraceuticals and other natural and nutritional materials with the desirable functional characteristics **(Devi *et al.*, 2014)**.

Celiac disease (CD) is a permanent intolerance to gluten. Those who suffer from celiac disease manifest anomalies of the intestinal mucosa with partial or total atrophy of the *Villi* following the consumption of food containing gluten. Therefore, this pathology (damage too mucosa of the small intestine) is often correlated with a malabsorption of several important nutrients, including iron, folic acid, calcium, and vitamins thus adversely affecting all systems of the body **(Mariotti *et al.*, 2011)**. CD relates specifically to the composition of the storage proteins present in many common cereals such as wheat, rye and barley, which are harmful for the sensitive consumers. It is characterized by a strong immune response to certain amino acid sequences found in the prolamin fractions of wheat. At the present time, the cornerstone treatment for CD remains the total lifelong avoidance of gluten ingestion, which means that celiac individuals must follow a gluten-free (GF) diet **(Karla., *et al.*, 2017; Fasano *et al.*, 2003).**

People suffering from celiac disease- gluten intolerance- cannot enjoy the structural and functional properties that gluten provides in many food products. Due to increasing number of people having intolerance for gluten, a need is raised for the production of breads without the gluten. A huge number of recipes are available to produce gluten-free breads. Industries, scientist, and also patients themselves are designing their own gluten-free recipes **(Van Riemsdijk *et al.*, 2011)**. Generally, those recipes contain many different ingredients such as gluten free cereals (**Demirkesen *et al.*, 2010)**

The gluten-free (GF) diet remains until now the only treatment for CD. GF diet includes benefits such as the recovery of the *Villi* of the small intestine

and reduced risk of malignant complications **(Seraphin and Mobarhan, 2002)**, However there are growing concerns over the nutritional adequacy of the GF dietary pattern because it is often characterized consumption of energy, proteins, fat, and a reduced intake of complex carbohydrates and dietary fiber **(Thompson *et al.*, 2005)**

Gluten is the structure-forming complex in wheat, responsible for the viscoelastic properties needed to produce good quality baked products. Interactions of gliadins and glutenins through covalent and non-covalent bonds to form gluten complexes result in viscoelastic dough that has the ability to withstand stresses applied during mixing and to retain gas during fermentation and baking, producing a light baked product. Unfortunately, this complex can be harmful for people suffering from CD or from other allergic reactions or intolerances to gluten consumption. CD, in particular, is a chronic malabsorption disorder of the small intestine caused by exposure to gluten in the genetically predisposed individual **(Laurin *et al.*, (2002)**.

The replacement of gluten in bakery products is a major technological challenge, as it is the essential structure-building protein; its removal impairs dough's capacity to properly develop during kneading, leavening and baking. The absence of gluten often results in a liquid batter rather than dough and can result in breads and other post-baking quality defects **(Gallagher *et al.*, 2004)**. Thus, substances that imitate the viscoelastic properties of gluten, in order to provide structure and retain gas, are always required. Recently, there has been an increasing interest in GF product, whose formulations mainly involve the incorporation of starches of different origin, dairy proteins, other non-gluten proteins, gum, hydrocolloids (it comprise a number of water-soluble polysaccharides with varied chemical structures providing a range of functional properties such as thickeners, stabilisers or gelling agents that make them suitable for different food applications) **(Rosell *et al.*, 2010)**, and their combinations, into a GF flour base that could simulate the viscoelastic properties of gluten and could result in maintaining structure mouthfeel, acceptability and shelf-life of the finished products. However, currently,

many GF products available on the market are of low technological and nutritional quality. GF products are frequently produced with the addition of various proteins to a starchy base, to increase their nutritional value. The incorporation of dairy proteins has long been established in baking industry, cereal-based foods since they increase the protein content and complement the nutritional value of the final product. Thus, the selection of the proteins used in a gluten-free formulation is a critical issue. **(Mariotti *et al.*, 2009).** Pseudo cereals such as corn, quinoa and millet can also be useful for the above purpose.

Corn is considered as one of the principle crops in Egypt and its production is increasing steadily; however, the majority of the crop is directed beneficial to introduce new manufactured corn products to the Egyptian food market such as Tortillas. In the last decade the volatility of corn prices, consequence of a continuous increase in biofuels production as well as oil price rise and speculation **(Ajanovic, 2010)**, has caused the increase in the production. The future of this crop is bright because it is environmentally more flexible than other cereals and shows better tolerance to diseases, drought, and pests than its parental species costs of nixtamalized corn flour **(Darvey *et al.*, 2000)**.

Quinoa *(Chenopodium quinoa Willd.)* has gained popularity worldwide largely due to the attractive nutritional profile. Starch is the main component of quinoa grain and makes up to 70% of the dry matter. The starch plays a crucial role in functional properties of quinoa and related food products **(Zhu and Li, 2018).** The flours obtained from quinoa seeds, can be used for elaborated bread or biscuits. Nowadays, in the market, different products with a 20% content of quinoa are commercialy available: backed products, infant foods, gluten free products, **(Pellegrini and Agostoni, 2015; Wang and Zhu, 2016).** Additionally, the gluten-free nature of quinoa seeds makes to this pseudocereal a valuable dietary source of digestible protein for people with gluten sensitivity and coeliac disease **(Tang *et al.*, 2015a).**

Millets are one of the cereals asides the major wheat, rice, and maize. Millets are major food sources for millions of people, especially those who live in

hot, dry areas of the world and underdeveloped countries because of their ability to grow under adverse weather conditions like limited rainfall. **(Adekunle, 2012)**. It is the major source of energy, protein and still part of the major diet in most African countries because it has many nutritious, health benefits and medical functions, and it use in the food industry. **(Amadou *et al.*, 2011a).** Millets are classified with maize, sorghum, and Coix (Job's tears) in the grass sub-family *Panicoideae* **(Yang *et al.*, 2012).** Millet is gluten-free, therefore an excellent option for people suffering from celiac diseases often irritated by the gluten content of wheat and other more common cereal grains. It is also useful for people who are suffering from atherosclerosis and diabetic heart disease **(Gélinas *et al.*, 2008).**

This wide range applicability is due to is versatility as food ingredient, represents an interesting field of research due to the high content of different macromolecules and phytochemicals that these seed showed **(Gordillo-Bastidas *et al.*, 2016).** This pseudocereal contains high biological value proteins and bioavailable essential amino acids, unsaturated lipids, dietary fiber, complex carbohydrates and other beneficial bioactive compounds such as polyphenolic compounds because of their beneficial health properties to consumers **(Wu, 2015; Fischer *et al.*, 2017).** These substances have already shown different in vitro biological potentials **(Gawlik-Dziki *et al.*, 2013)** and in vivo activities against several diseases and metabolic conditions **(Graf *et al.*, 2015; Gordillo-Bastidas *et al.*, 2016).**

The main aim of this study was to produce and evaluate functional properties of some experimental GF products containing different levels of quinoa and millet as a novel pseudo-cereal for CD patient.

2. REVIEW OF LITERATURE

2.1. Celiac disease

Celiac disease (CD) is more than just an “allergy” or “sensitivity” to wheat and gluten. It is a lifelong, permanent intolerance to the gliadin fraction of wheat protein and its related alcohol-soluble proteins (prolamins) found in rye and barley. In patients with the genetic susceptibility to CD, ingesting these proteins leads to an autoimmune enteropathy that will self-perpetuate as long as these foods remain in the diet. The good news is that, unlike most autoimmune conditions, removal of the environmental trigger (gluten) from the diet of biopsy-proven celiac results in complete symptomatic and histologic resolution of the disease in the majority of patients **(Lee *et al*., 2003)**. Differentiating CD from wheat allergy, gluten sensitivity, and other autoimmune gastrointestinal Gluten intolerance (GI) diseases (such as Crohn’s disease) can be challenging. Likewise, CD can present at any age with “classic” GI features, such as diarrhea and weight loss, or outside the GI tract with anemia, rashes, infertility, osteoporosis, joint pain, short stature, delayed puberty, and even malignancy. It is common that patients experience chronic ill health and nutritional deficiencies prior to the correct diagnosis being made. These patients commonly incur high healthcare costs because of the multiple subspecialists and tests performed on them prior to the confirmation of CD **(Hankey and Holmes, 1994)**.

CD is not a food allergy. It is an autoimmune disorder in which the small intestine is hypersensitive to gluten. The digestive tract contains tiny hair like projections called *villi*, where food is absorbed. These *villi* are destroyed in people with unmanaged CD. When the *villi* are not functioning properly, nutrient deficiencies will result because carbohydrates, fats, proteins, vitamins, and minerals, and even water in some instances, cannot be absorbed. In the athlete, the mal absorption also leads to decreased exercise performance **(Wessling-Resnick, 2000)**.

Vojdani *et al.*, (2020) indicated that environmental factors such as infections, chemicals, and diet play a major role in autoimmune diseases; however, relatively little attention has been given to food components as the most prevalent modifiers of these afflictions. The primary factor controlling food-related immune reactions is the oral tolerance mechanism. The failure of oral tolerance triggers immune reactivity against dietary antigens, which may initiate or exacerbate autoimmune disease when the food antigen shares homology with human tissue antigens. Because the conformational fit between food antigens and a host's self-determinants has been determined for only a few food proteins, we examined evidence related to the reaction of affinity-purified disease-specific antibody with different food antigens. We also studied the reaction of monoclonal or polyclonal tissue-specific antibodies with various food antigens and the reaction of food specific antibodies with human tissue antigens. Examining the assembled information, we postulated that chemical modification of food proteins by different toxicants in food may result in immune reaction against modified food proteins that cross-react with tissue antigens, resulting in autoimmune reactivity. Because we are what our microbiome eats, food can change the gut commensals, and toxins can breach the gut barrier, penetrating into different organs where they can initiate autoimmune response. Conversely, there are also foods and supplements that help maintain oral tolerance and microbiome homeostasis. Understanding the potential link between specific food consumption and autoimmunity in humans may lay the foundation for further research about the proper diet in the prevention of autoimmune diseases.

2.1.1. Diseases Associated with Celiac Disease

There are several conditions associated with an elevated risk of CD like first- and second- degree family members of biopsy-proven CD patients are at increased risk of the disease with a prevalence estimated at 10 % and 2.6–5.5 % **(Dube *et al.*, 2005)**, respectively. Type 1 diabetics have a clustered

prevalence of CD estimated at 2–5 % in adults and 8 % in children **(Not *et al.*, 2001)** and patients with autoimmune thyroid disease have a pooled prevalence of 3 % these and other disorders that warrant screening include autoimmune adrenal disease **(Myhre *et al.*, 2003 ;Biagi *et al.*, 2006)** autoimmune connective tissue disorders such as Sjögren syndrome **(Szodoray *et al.*, 2004)**, juvenile rheumatoid arthritis **(Neuhausen *et al.*, 2008)**, and systemic lupus erythematosus **(Ludvigsson *et al.*, 2012)** autoimmune dermatological disorders including psoriasis **(Ludvigsson *et al.*, 2011)** and alopecia areata **(Collin and Reunala, 2003)** autoimmune hepatobiliary disorders comprising autoimmune hepatitis, primary biliary cirrhosis, and primary sclerosing cholangitis; **(Rubio-Tapia and Murray, 2007)** IgA deficiency **(Chow *et al.*, 2012)** IgA nephropathy **(Collin *et al.*, 2002)** Down syndrome **(Nisihara *et al.*, 2005)** and Turner syndrome **(Bonamico *et al.*, 2002)**.

The decision to screen all cases of irritable bowel syndrome (IBS) has recently been challenged by a large American study that found that despite a common finding of celiac disease antibodies in non constipated IBS sufferers (7.3%), the prevalence of histological celiac disease was almost identical to that of healthy controls (0.41 vs. 0.44%, P>0.99) .Two smaller studies have reported similar histological rates of 2 **(Korkut *et al.*, 2010)** and 0.4% in all subtypes of IBS, but despite reporting the lowest prevalence, **(El-Salhy *et al.*, 2011)** recommend routine screening of celiac disease in all IBS cases.

For some people, eating GF is a choice. But for a growing number of people, eating GF is necessary. People for whom a GF diet is beneficial and even life-saving are those with CD, gluten intolerance (GI), and wheat allergy (WA). Although these types of sensitivities to gluten are different in their origins, they are treated the same way: a GF diet **(Margaret and Nanna, 2013)**

2.1.2. General diagnosis of Celiac Disease

Once considered a rare disease, the prevalence of CD has increased dramatically during the last 100 years. Today, it is thought to affect 1% of the

population **(Fasano *et al.*, 2003)**. This disease is under diagnosed, and this estimate is thought to be grossly underestimated. Because this disease is genetically based, first-degree relatives will have an increased risk of also being diagnosed with CD, as high as 1 in 22 **(Hadjivassiliou *et al.*, 2010).**
However, false-negatives are an issue. A combination of blood tests (i.e., testing for antibodies and tissue damage), genetic markers, and history is ideal. A tissue biopsy of the small intestine is the ultimate standard for CD diagnosis. Because the only treatment available for CD is a strict GF diet, a person may want to try a GF diet even if his or her test is negative. People who test negative at first may test positive years later. When undergoing testing, individuals who have been following a GF diet will yield negative results on blood tests and biopsies because the body will have had a chance to heal. For accurate testing for CD, the patient needs to eat gluten for several weeks before the test **(Margaret and Nanna, 2013).**

2.1.3. Testing for Celiac Disease

Clinicians should consider celiac disease when a patient has multiple or vague symptoms that don't seem to fit a clear diagnosis of another illness. The presence of any of the following should prompt testing: a first-or second-degree relative with celiac disease, selective IgA deficiency, connective tissue disorders such as rheumatoid arthritis or lupus, Down syndrome, autoimmune endocrinopathies such as type 1 diabetes or Graves' disease, epilepsy, dermatitis, and chronicfatigue **(Nelsen, 2002; Michael, 2003).** Once gluten is removed from the diet, antibody levels decrease. In a longitudinal study of 20 patients, **Midhagen *et al.*, 2004)** found that antibody titers fell sharply within one month after introduction of a gluten-free diet. So, it's important for clinicians to teach patients that they should continue to ingest gluten until all testing is completed.
Routine screening for celiac disease is not currently practiced in the United States. Some researchers support screening, especially for people in high-risk categories, such as those with first- or second-degree relatives who have

celiac disease and those who have another autoimmune disease **(Shamir *et al*., 2006; Ch'ng *et al*., 2007).**

Children under the age of three years with any of the above or with failure to thrive and persistent diarrhea should also be evaluated for celiac disease **(University of Chicago Celiac Disease Center, 2012)**. Testing for celiac disease currently includes serologic testing for auto-antibodies, including antigliadin, deaminated gliadin peptide, and antiendomysium antibodies **(Anderson, 2008).** Although the antigliadin antibodies test does not have good sensitivity, test panels include it to determine whether a person is IgA deficient. Combination testing identifies patients who are candidates for a jejunal biopsy, which remains the gold standard for diagnosis **(NDDIC, 2009)**.

2.1.4. Management of Celiac Disease

CD is an immune-mediated enteropathic disease, triggered by gluten and related prolamins in cereals viz. wheat, rye, barley **(Bakshi *et al*., 2012; Saturni *et al*., 2012)**. Gluten intolerance is a major health issue in the Western world. It causes chronic inflammation of the intestinal mucosa and atrophy of intestinal villi. Nutritional intervention is considered the only effective treatment for it **(Arendt *et al*., 2011)**. Lifelong exclusion of gluten-rich food is required by the patients. On the other hand, gluten protein network is vital for the texture and the overall quality of the food products, especially bakery. So, the gluten-free products show low baking performances and are poor in nutritional quality. In this regard, the pseudocereal quinoa seeds hold great promise, as they are gluten-free and have high levels of protein, fat, fiber and minerals. Several products were formulated from quinoa, rice and corn flours and starches for celiac patients. Among the foods prepared, scones and pancakes were accepted for their quality proteins, good textural characteristics and nutritional content **(Del Castillo *et al*., 2009a)**. Cookies were prepared from defatted hazel nut and quinoa flour for enhancing nutritional food supply to celiac population. The

ingredient and process parameters were optimized by Taguchi methodology. The optimum conditions turn out to be hazel nut flour 24.3 %; quinoa flour7.1 %; ammonium bicarbonate 0.6 % and 22 min baking time. The shelf life study expressed as conjugated dienes was 3.6 % after 45 days of storage at 30 °C, proving its stability to rancidity. The products were approved by all, the acceptance level ranging from liking very much to liking **(Del Castillo *et al.*, 2009b).** Quinoa-based diet was recommended for celiac patients considering its high nutrition density and absence of gluten **(Hager *et al.*, 2012)**.

2.1.5. Treatment of Celiac Disease

The mainstay of treatment of CD and DH is a GFD. The term gluten should be used to indicate not only wheat-based proteins (gliadins), but it also includes those from barley (hordeins) and rye (secalins), and cereal hybrids such as triticale**.** Originally oats were also avoided in the GFD. Earlier research indicates that oats uncontaminated by gluten are probably safe for patients with CD **(Janatuinen *et al.*, 2000).** This is important because oats contain soluble fibre, are able to lower blood glucose and attenuate insulin response **(Sadiq *et al.*,2008)**.

The appearance of symptoms related to introducing oats might be due to cross contamination. Also, a small percentage of patients with CD may be sensitive to oats **(Comino, *et al.*, 2011)** and develop symptoms or even mucosal damage **(Arentz-Hansen *et al.*, 2004).** Patients with CD should be educated to avoid cereals and food containing gluten (breakfast cereals, flours, pasta, cakes, biscuits, sauces etc) derived from wheat, barley or rye and food made from gluten-contaminated oats, and encouraged to eat naturally occurring gluten-free foods and alternative sources of starch (corn, rice, potatoes etc). Levels of susceptibility to gluten contamination of food vary among patients with CD. Although it has also been suggested that the acceptable threshold for gluten content in gluten-free products can from the clinical point of view be set at 100 ppm (¼ mg/kg**), (Case, 2005).**

Codex Alimentarius Commission of the WHO issued new guidelines for gluten content of processed food in 2008 and a law from the European Commission (EC41/2009), effective since January2012, stipulated that foods labelled as 'gluten free' should contain ≤20 parts per million of gluten, and that this gluten content is safe for the coeliac population. The 20ppm threshold for gluten-free food is also accepted by the US Food and Drug Administration, effective since August 2013. Newly diagnosed patients should be referred to a dietitian to discuss dietary management. **(Nelson, *et al.*, 2007).** It is important that they are educated not only to avoid gluten but also to have a sufficient intake of nutrients, vitamins, fibre and calcium present in their gluten free diet (GFD) **(Wild *et al.*, 2010)**. Recent data also indicate that a strict GFD might be of help in reaching ideal body weight, whether an individual is underweight or obese at diagnosis. Data suggest that adherence to the GFD is better achieved when the patient is well educated and supported by carers and families. However, there is a wide variation in provision of dietary consultation services for patients diagnosed with CD in the world **(Ukkola *et al.*, 2012)**.

2.2. Proteins in Food Allergy

2.2.1. Wheat Allergy

Wheat allergy (WA) differs from food allergy (FA), Gluten intolerance (GI) and CD. People who have a WA have a systemic response to wheat similarly to how people with nut allergies may react. Symptoms of WAs are similar to symptoms of other allergies, namely, hives, swelling, and possibly stomach pain **(Wessling-Resnick, 2000)**.

Prevalence of wheat allergy ranges from 0.5 **(Zuidmeer *et al*., 2008)** to 9 % **(Matricardi *et al*., 2008)** and may be age dependent. There is controversy as to whether sensitization to wheat decreases over time **(Ostblom *et al*., 2008)**. Amongst food allergies, wheat is identified by the Food and Drug Administration as one of the eight most common allergens, along with milk, eggs, fish, shellfish, tree nuts, peanuts, and soybeans. Together, these foods