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**Role of oats in celiac disease**

Comino I *et al*. Oats in celiac disease

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**Abstract**

A gluten-free diet is currently the only effective means of treating individuals with celiac disease. Such a diet enables celiac patients to control their symptoms and avoid various complications associated with this condition. However, while the quality of gluten-free foods has significantly improved during recent decades, maintenance of a gluten-free diet does not necessarily ensure adequate nutritional intake. Because oats are an important source of proteins, lipids, vitamins, minerals, and fibre, their inclusion in a gluten-free diet might improve the nutritional status of a celiac patient. Although oats are included in the list of gluten-free ingredients specified in European regulations, their safety when consumed by celiac patients remains debatable. The results of some studies have indicated that pure oats are safe for consumption by individuals with celiac disease; however, the possibility that any batch of oats may be contaminated with other types of cereal grains continues to be a problem. Batches of oats usually contain many different genetic varieties characterized by proteins with different amino acid sequences and are capable of producing different degrees of immune reactions associated with toxic effects. As a result, several studies have shown that the immunogenicity of oats varies depending on the cultivar consumed. Thus, it is essential to thoroughly study the variety of oats used in a food ingredient before including it in a gluten-free diet.

**Key words:** Oats; Celiac disease; Gluten-free diet

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**Core tip:** Symptoms of celiac disease are triggered by an abnormal reaction to gluten, and the only treatment for celiac disease is the patient’s adherence to a strict gluten-free diet. While inclusion of oats in a gluten-free diet might improve its overall nutritional value, their use in such diets remains controversial. This review summarizes recent advances made in understanding the nutritional properties of oats and their role in celiac disease.

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**INTRODUCTION**

Celiac disease (CD) is a lifelong autoimmune disease characterized by an aberrant inflammatory response to dietary gluten in genetically susceptible individuals. CD is one of the most common chronic digestive disorders, and afflicts about 1% of the population in Western countries; moreover, recent studies suggest that its prevalence is increasing[1,2]. Certain individuals show a strong and complex genetic predisposition to this disease. Although 95% of celiac patients are *HLA-DQ2* or -*DQ8* positive, the presence of these alleles is not strongly predictive for the disease[3,4]. In recent years, the clinical spectrum of CD patients has been expanded to include asymptomatic individuals, as well as individuals with minimal symptoms (the most difficult to detect) and extra-intestinal symptoms[5-7]. However, regardless of its symptomatic presentation, virtually all cases of active CD occur after the susceptible individual has received dietary exposure to the common environmental antigen, gluten. In patients with CD, the ingestion of gluten proteins contained in wheat, barley, and rye results in characteristic inflammation, villous atrophy, and crypt hyperplasia in the upper small intestine[5].

During the early 1980s, the spectrum of gluten-related disorders was relatively simple: CD and dermatitis herpetiformis (CD of the skin). While a gluten-free diet (GFD) is still recommended for all patients with CD, the area of CD research is changing rapidly, and wheat allergies, gluten ataxia, and nonceliac gluten sensitivity have recently been added as new gluten-related topics for study[8]. The only treatment for these disorders remains adherence to a GFD; however, many patients experience persistent CD-related symptoms despite their best efforts to avoid dietary gluten. A GFD is expensive and difficult to maintain because many products made from gluten-containing grains are Western dietary staples. Moreover, the contents of a GFD do not always ensure that an individual receives adequate nutrition[9,10]. In fact, medical problems related to inadequate nutrition have been described in CD patients following their long-term treatment with a strict GFD. Such observations might possibly be explained by the composition and nutritional quality of commercially available gluten-free products. While individuals on a GFD need to replace wheat, barley, rye, and their derivatives with foods derived from naturally gluten-free cereal grains (*e.g.*, rice, corn, buckwheat, sorghum, *etc*.), it can be more difficult to obtain the recommended amounts of fibre, iron, and calcium when adhering to such a diet, and thus good dietary and meal planning are required[11]. Oats contain both soluble and insoluble dietary fibre, B-complex vitamins, iron, and proteins[12,13], and have recently been considered for inclusion in a GFD. However, while oats might improve the nutritional value of a GFD, their safety for consumption by celiac patients has been the subject of controversy.

**NUTRITIONAL AND PHARMACOLOGICAL PROPERTIES OF OATS**

***Composition***

Oat grain is characterized by its good taste and dietetic properties, as well as an ability to stimulate metabolic changes in the bodies of humans and animals. Furthermore, oat grain is a rich source of proteins with favourable amino acid contents and high nutritional value, and as other beneficial ingredients including dietary fibre, antioxidants, vitamins, phenolic compounds, minerals, and essential unsaturated fatty acids[14-16]. When compared with other cereal grains, oat grain contains larger amounts of total protein and crude fat, and a small amount of crude fibre. The major nutritional components of oats are shown in Table 1.

***Health benefits***

Several studies have described oats as a functional food with the ability to lower blood cholesterol and sugar levels, reduce hypertension, help control childhood asthma, reduce body weight, and also provide immunomodulatory, antioxidant, and antiatherogenic effects[14,17-19] (Table 2). Oats also contain significant amounts of vitamins, minerals, fibre, and phytochemicals that regulate intestinal transit times and increase the production of butyrate and/or other faecal short chain fatty acids produced by gut microflora. As a result, the long-term dietary intake of oats or oat bran might benefit patients suffering from inflammatory bowel disease, ulcerative colitis, colorectal adenoma or cancer. However, further studies are required to accurately assess the benefits provided by increased oat consumption when treating bowel disorders[20].

Additionally, due to the well-established effect of oats on the risk for coronary heart disease, in 1997 the United States Food and Drug Administration (FDA) approved the heart-health benefit claim shown on the label of many foods containing soluble fibre derived from oats. Moreover, in 2010, a European Food Safety Authority (EFSA) panel concluded that current scientific evidence supports the following two-part statement: “Oat -glucan has been shown to lower/reduce blood cholesterol. Blood cholesterol lowering may reduce the risk of coronary heart disease.”

**oats and celiac disease**

***Oat avenins***

As the prolamin components of oat seeds, the avenins are known to exist as both monomers and disulfide-linked aggregates[21]. Similar to other cereal prolamins, the avenin polypeptides in oats tend to be rich in proline and glutamine, and the protein regions enriched in these two amino acids are associated with elicitation of CD. However, when compared to prolamins in other cereal grains, oat prolamins show the following differences in their molecular size, percentage, and amino acid content: (1) prolamins account for 10%-20% of the total protein in oats, compared to 40%-50% of the total protein in wheat[22,23]; (2) among the accepted prolamins, those found in maize, sorghum, and rice generally have the lowest contents of proline and glutamine (25%-30%), while prolamines in the Triticeae tribe (wheat, barley, and rye) can have proline plus glutamine contents that exceed 70% of their total amino acids. In contrast, proline and glutamine generally comprise 35%-50% of amino acids found in the prolamins of oats[24]; (3) in contrast to the single longer repetitive domain found in Triticeae prolamins, oat avenins contain two shorter domains with high contents of proline and glutamine[24]; and (4) the disulfide pattern in oat prolamins is different from those reported in wheat -gliadins[25] and low molecular weight (LMW)-glutenins[26]. In particular, the tandem cysteines at positions 145–146 in oat prolamins form a disulfide bond. This is in contrast to wheat proteins, where the two tandem cysteines are bonded to more distant cysteines within the prolamin[24].

Despite these reported differences, the avenins have not been well studied. As a result, the complete avenin genes described in current genetic databases represent only a few genotypes, and the variability displayed by avenin genes in oats is not well represented[21].

***Clinical studies***

The inclusion of oats in gluten-free foods is controversial, as previous studies have shown contradictory results regarding their toxicity. Janatuinen *et al*[27] conducted the first controlled study on the toxic effects of oats in CD patients, and since that time several other similar investigations have been conducted. Some researchers have claimed that celiac patients can consume oats and show no signs of intestinal inflammation[12,28-31]. In a study conducted by Størsrud *et al*[32,33], a small number of adult celiac subjects consumed pure oats (93 g/d) for 2 years with no reported adverse effects. The same researchers also conducted a study in which a group of celiac children ingested a median of 43 g (up to 81 g/d) of oats daily for 2 years[34] with no adverse effects. Moreover, a randomized double-blind study conducted with newly diagnosed CD children showed that consumption of an oat-containing GFD for 1 year did not interfere with their clinical, serological or small bowel mucosal recovery. However, despite those results, 26% of the children in the oat-containing GFD group withdrew from that studyfor unknown reasons[34,35].

While the previously mentioned studies appear to support the safety of oat consumption by celiac patients, the results of other studies suggest that regular consumption of certain types of oats may be impossible for such patients, due to their toxic effects. Those studies revealed that oats can trigger an immune reaction in celiac patients[28,36-38] that results in activation of mucosal T-cells, subsequent gut inflammation, and eventual villous atrophy[37]. In those patients, the immune response against avenins may have been triggered by a mechanism similar to that which triggers a response to gluten contained in wheat, rye, or barley. Lundin *et al*[36] studied 19 celiac patients who consumed 50 grams of oats/day for 12 weeks, and found that one patient was oat sensitive. CD patients have circulating anti-avenin antibodies[39,40], and a recent study revealed that dietary oats can alter the mRNA immune status of intestinal mucosa cells; suggesting T-cell activation and the presence of leaky tight-junctions[41]. Such findings indicate the need to distinguish between groups of celiac patients based on their sensitivity to different cereal grains, and also to identify the source of immunogenicity in avenin peptides.

***Gluten contamination of commercial oat products***

The phrase "pure oats" is used to describe oats that after being analysed using current test methods, appear to be uncontaminated with gluten from other closely related cereal grains, such as wheat, barley, and rye. However, differences in the methods used to test oat products and report their purity have hindered completion of any comprehensive safety assessment. When studying literature reports, the study design or protocol did not always clearly describe the specifications used for defining “pure and uncontaminated” oats. While the most recent reports usually indicate whether the oats used in a particular study were tested for purity, many studies fail to indicate the lower limit of detection for their testing techniques or the cut-off values used when reporting that oat samples were free of gluten from other cereal grains.

According to the Codex Standard for food for special dietary use by persons intolerant to gluten, CODEX STAN118-1979 (revised 2008, http://www.foedevarestyrelsen.dk/SiteCollectionDocuments/25\_PDF\_word\_filer%20til%20download/07kontor/Maerkning/Codex%20standard%20for%20gluten.pdf), oats can be tolerated by most but not all people who are intolerant to gluten. Therefore, whether oats that are not contaminated with wheat, rye or barley and are contained in foods covered by this standard can be considered safe for consumption by celiac patients may eventually be determined at the national level. Moreover, according to Commission Regulation (EC) No 41/2009 (http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2009:016:0003:0005:EN:PDF), which addresses the composition and labelling of foodstuffs suitable for people intolerant to gluten, the risk that oats may become contaminated with wheat, rye or barley during grain harvesting, transport, storage or processing remains a major concern. Therefore, the risk that oat-containing products might be contaminated with exogenous gluten should be taken into consideration when creating their labels.

Some studies have utilized the R5 ELISA method to determine the level of contamination in wheat, barley, rye, or oat products[42-44]. Koerner *et al*[43] used this method to confirm that the commercial oat supply in Canada is heavily contaminated with gluten from other grains. For example, about 88% of the tested oat samples (*n* = 133) showed a gluten level > 20 mg/kg. However, the problem with using this method is that the R5 antibody can react with certain types of pure oat seed[45]; hence, a test result suggesting "suspected contamination" from exogenous toxic cereal grains may not be real, but due the R5 antibody reacting with certain amino acid sequences in the native oat proteins.

***Diversity in potential immunogenicity depends on oat cultivars***

Differences in the type of oat grain, oat purity, study design, as well as the specifications for gluten-free products in different countries, are some reasons why the current studies have not clearly established whether or not oats can be safely consumed by all celiac patients. These apparent contradictions might be explained by the fact that the oat varieties used in the diverse studies were different in regards to their prolamin genes, protein amino acid sequences, and the immunoreactivities of their toxic prolamins[46,47].

Our research group conducted a study using nine different varieties of oats obtained from various Australian and Spanish commercial sources, and demonstrated that oat immunogenicity varies depending on the cultivar used[45]. The oat grains were carefully inspected, controlled to maintain purity, and shown to be free of contamination. An analysis of DNA amplification products confirmed that the oat samples were not contaminated with wheat, barley, rye, or any mixture of these grains. The toxicity of each oat variety was evaluated using a moAb G12 immunoassay. The antibody used in the assay was obtained from the α-2 gliadin 33-mer peptide, which is one of the most toxic peptides for CD patients. The nine varieties of oats were classified into three groups (high reactivity, intermediate activity, and no reactivity) based on their moAb G12 reactivity. We found that reactivity with the anti-33-mer moAb shown by the different oat varieties was correlated with T-cell proliferation and interferon gamma production by blood T-cells isolated from CD patients. These results suggest that a moAb G12-based immunotechnique may be a pragmatic method for evaluating the potential immunotoxicity of commercial cereals and grains[45,48].

Subsequent studies confirmed a direct correlation between the immunogenicity of the different varieties of oats and the presence of specific peptides with higher/lower potential immunotoxicity. This finding may explain why certain varieties of oats produce toxic effects when consumed by celiac patients, while others produce no adverse effects[21,49]. Moreover, oat peptides obtained from toxic cultivars have showed to differentially stimulate bona fide circulating dendritic cells obtained from celiac patients.

While inclusion of oats in a GFD might be beneficial due to their nutritional and health benefits, the source of the oats used and the cultivar selected are important factors to be considered. These factors must also be taken into account when developing food safety regulations, labelling oat-containing products as gluten-free, and designing clinical trials to study the effect of oats in celiac patients.

**CONCLUSION**

In summary, oats possess a variety of pharmacological activities and may exert antioxidant, anti-inflammatory, antidiabetic, and anticholesterolaemic effects. These properties have led to their wider use in human food. Inclusion of oats in a gluten-free diet might be valuable due to their nutritional and health benefits, and several countries currently permit oats to be included as an ingredient in such diets. However, it is extremely important to remember that *in vitro* studies have shown that the immunogenicity of oats varies depending on the cultivar used. Future clinical studies should be directed to the development of clinical trials with varieties previously identified as safe by reliable *in vitro* methods, such as moAb G12-based immunotechniques.

**REFERENCES**

1 **Jabri B**, Sollid LM. Mechanisms of disease: immunopathogenesis of celiac disease. *Nat Clin Pract Gastroenterol Hepatol* 2006; **3**: 516-525 [PMID: 16951668 DOI: 10.1038/ncpgasthep0582]

2 **Ludvigsson JF**, Leffler DA, Bai JC, Biagi F, Fasano A, Green PH, Hadjivassiliou M, Kaukinen K, Kelly CP, Leonard JN, Lundin KE, Murray JA, Sanders DS, Walker MM, Zingone F, Ciacci C. The Oslo definitions for coeliac disease and related terms. *Gut* 2013; **62**: 43-52 [PMID: 22345659 DOI: 10.1136/gutjnl-2011-301346]

3 **Sollid LM**, Jabri B. Is celiac disease an autoimmune disorder? *Curr Opin Immunol* 2005; **17**: 595-600 [PMID: 16214317 DOI: 10.1016/j.coi.2005.09.015]

4 **Koning F**, Thomas R, Rossjohn J, Toes RE. Coeliac disease and rheumatoid arthritis: similar mechanisms, different antigens. *Nat Rev Rheumatol* 2015; **11**: 450-461 [PMID: 25986717]

5 **Robins G**, Howdle PD. Advances in celiac disease. *Curr Opin Gastroenterol* 2005; **21**: 152-161 [PMID: 15711206 DOI: 10.1097/01.mog.0000153312.05457.8d]

6 **Logan RF**, Tucker G, Rifkind EA, Heading RC, Ferguson A. Changes in clinical features of coeliac disease in adults in Edinburgh and the Lothians 1960-79. *Br Med J (Clin Res Ed)* 1983; **286**: 95-97 [PMID: 6401509 DOI: 10.1136/bmj.286.6359.95]

7 **Fasano A**, Catassi C. Current approaches to diagnosis and treatment of celiac disease: an evolving spectrum. *Gastroenterology* 2001; **120**: 636-651 [PMID: 11179241 DOI: 10.1053/gast.2001.22123]

8 **Mulder CJ**, van Wanrooij RL, Bakker SF, Wierdsma N, Bouma G. Gluten-free diet in gluten-related disorders. *Dig Dis* 2013; **31**: 57-62 [PMID: 23797124]

9 **Alvarez-Jubete L**, Arendt EK, Gallagher E. Nutritive value and chemical composition of pseudocereals as gluten-free ingredients. *Int J Food Sci Nutr* 2009; **60 Suppl 4**: 240-257 [PMID: 19462323 DOI: 10.1080/09637480902950597]

10 **Segura ME**, Rosell CM. Chemical composition and starch digestibility of different gluten-free breads. *Plant Foods Hum Nutr* 2011; **66**: 224-230 [PMID: 21769691 DOI: 10.1007/s11130-011-0244-2]

11 **Thompson T**, Dennis M, Higgins LA, Lee AR, Sharrett MK. Gluten-free diet survey: are Americans with coeliac disease consuming recommended amounts of fibre, iron, calcium and grain foods? *J Hum Nutr Diet* 2005; **18**: 163-169 [PMID: 15882378 DOI: 10.1111/j.1365-277X.2005.00607.x]

12 **Thompson T**. Oats and the gluten-free diet. *J Am Diet Assoc* 2003; **103**: 376-379 [PMID: 12616264 DOI: 10.1053/jada.2003.50044]

13 **Haboubi NY**, Taylor S, Jones S. Coeliac disease and oats: a systematic review. *Postgrad Med J* 2006; **82**: 672-678 [PMID: 17068278 DOI: 10.1136/pgmj.2006.045443]

14 **Singh R**, De S, Belkheir A. Avena sativa (Oat), a potential neutraceutical and therapeutic agent: an overview. *Crit Rev Food Sci Nutr* 2013; **53**: 126-144 [PMID: 23072529 DOI: 10.1080/10408398.2010.526725]

15 **Wani SA**, Shah TR, Bazaria B, Nayik GA, Gull A, Muzaffar K, Kumar P. Oats as a functional food: a review. *Univ J Pharm* 2014; **3**: 14-20

16 **Biel W**, Bobko K, Maciorowski R. Chemical composition and nutritive value of husked and naked oats grain. *J Cereal Sci* 2009; **49**: 413-418 [DOI: 10.1016/j.jcs.2009.01.009]

17 **Truswell AS**. Cereal grains and coronary heart disease. *Eur J Clin Nutr* 2002; **56**: 1-14 [PMID: 11840174 DOI: 10.1038/sj.ejcn.1601283]

18 **Brown L**, Rosner B, Willett WW, Sacks FM. Cholesterol-lowering effects of dietary fiber: a meta-analysis. *Am J Clin Nutr* 1999; **69**: 30-42 [PMID: 9925120]

19 **Kelly SA**, Summerbell CD, Brynes A, Whittaker V, Frost G. Wholegrain cereals for coronary heart disease. *Cochrane Database Syst Rev* 2007; **(2)**: CD005051 [PMID: 17443567 DOI: 10.1002/14651858.cd005051.pub2]

20 **Thies F**, Masson LF, Boffetta P, Kris-Etherton P. Oats and bowel disease: a systematic literature review. *Br J Nutr* 2014; **112** Suppl 2: S31-S43 [PMID: 25267242 DOI: 10.1017/S0007114514002293]

21 **Real A**, Comino I, de Lorenzo L, Merchán F, Gil-Humanes J, Giménez MJ, López-Casado MÁ, Torres MI, Cebolla Á, Sousa C, Barro F, Pistón F. Molecular and immunological characterization of gluten proteins isolated from oat cultivars that differ in toxicity for celiac disease. *PLoS One* 2012; **7**: e48365 [PMID: 23284616 DOI: 10.1371/journal.pone.0048365]

22 **Peterson DM**, Smith D. Changes in nitrogen and carbohydrate fractions in developing oat groats. *Crop Sci* 1976; **16**: 67-71 [DOI: 10.2135/cropsci1976.0011183X001600010017x]

23 **Frey KJ**. The relation between alcohol-soluble and total nitrogen contents of oats. *Cereal Chem* 1951; **28**: 506-509

24 **Anderson OD**. The spectrum of major seed storage genes and proteins in oats (Avena sativa). *PLoS One* 2014; **9**: e83569 [PMID: 25054628 DOI: 10.1371/journal.pone.0083569]

25 **Muller S**, Wieser H. The location of disulphide bonds in monomeric gamma-type gliadins. *J Cer Sci* 1997; 169–176

26 **Muller S**, Vensel WH, Kasarda DD, Köhler P, Wieser H. Disulphide Bonds of Adjacent Cysteine Residues in Low Molecular Weight Subunits of Wheat Glutenin. *J Cereal Sci* 1998; **27**: 109–116 [DOI: 10.1006/jcrs.1997.0158]

27 **Janatuinen EK**, Pikkarainen PH, Kemppainen TA, Kosma VM, Järvinen RM, Uusitupa MI, Julkunen RJ. A comparison of diets with and without oats in adults with celiac disease. *N Engl J Med* 1995; **333**: 1033-1037 [PMID: 7675045]

28 **Pulido OM**, Gillespie Z, Zarkadas M, Dubois S, Vavasour E, Rashid M, Switzer C, Godefroy SB. Introduction of oats in the diet of individuals with celiac disease: a systematic review. *Adv Food Nutr Res* 2009; **57**: 235-285 [PMID: 19595389 DOI: 10.1016/S1043-4526(09)57006-4]

29 **Fric P**, Gabrovska D, Nevoral J. Celiac disease, gluten-free diet, and oats. *Nutr Rev* 2011; **69**: 107-115 [PMID: 21294744 DOI: 10.1111/j.1753-4887.2010.00368.x]

30 **Kilmartin C**, Lynch S, Abuzakouk M, Wieser H, Feighery C. Avenin fails to induce a Th1 response in coeliac tissue following in vitro culture. *Gut* 2003; **52**: 47-52 [PMID: 12477758 DOI: 10.1136/gut.52.1.47]

31 **Kaukinen K**, Collin P, Huhtala H, Mäki M. Long-term consumption of oats in adult celiac disease patients. *Nutrients* 2013; **5**: 4380-4389 [PMID: 24201240 DOI: 10.3390/nu5114380]

32 **Størsrud S**, Hulthén LR, Lenner RA. Beneficial effects of oats in the gluten-free diet of adults with special reference to nutrient status, symptoms and subjective experiences. *Br J Nutr* 2003; **90**: 101-107 [PMID: 12844381 DOI: 10.1079/BJN2003872]

33 **Størsrud S**, Olsson M, Arvidsson Lenner R, Nilsson LA, Nilsson O, Kilander A. Adult coeliac patients do tolerate large amounts of oats. *Eur J Clin Nutr* 2003; **57**: 163-169 [PMID: 12548312 DOI: 10.1038/sj.ejcn.1601525]

34 **Holm K**, Mäki M, Vuolteenaho N, Mustalahti K, Ashorn M, Ruuska T, Kaukinen K. Oats in the treatment of childhood coeliac disease: a 2-year controlled trial and a long-term clinical follow-up study. *Aliment Pharmacol Ther* 2006; **23**: 1463-1472 [PMID: 16669961 DOI: 10.1111/j.1365-2036.2006.02908.x]

35 **Högberg L**, Laurin P, Fälth-Magnusson K, Grant C, Grodzinsky E, Jansson G, Ascher H, Browaldh L, Hammersjö JA, Lindberg E, Myrdal U, Stenhammar L. Oats to children with newly diagnosed coeliac disease: a randomised double blind study. *Gut* 2004; **53**: 649-654 [PMID: 15082581 DOI: 10.1136/gut.2003.026948]

36 **Lundin KE**, Nilsen EM, Scott HG, Løberg EM, Gjøen A, Bratlie J, Skar V, Mendez E, Løvik A, Kett K. Oats induced villous atrophy in coeliac disease. *Gut* 2003; **52**: 1649-1652 [PMID: 14570737 DOI: 10.1136/gut.52.11.1649]

37 **Arentz-Hansen H**, Fleckenstein B, Molberg Ø, Scott H, Koning F, Jung G, Roepstorff P, Lundin KE, Sollid LM. The molecular basis for oat intolerance in patients with celiac disease. *PLoS Med* 2004; **1**: e1 [PMID: 15526039 DOI: 10.1371/journal.pmed.0010001]

38 **Tuire I**, Marja-Leena L, Teea S, Katri H, Jukka P, Päivi S, Heini H, Markku M, Pekka C, Katri K. Persistent duodenal intraepithelial lymphocytosis despite a long-term strict gluten-free diet in celiac disease. *Am J Gastroenterol* 2012; **107**: 1563-1569 [PMID: 22825364 DOI: 10.1038/ajg.2012.220]

39 **Hollén E**, Holmgren Peterson K, Sundqvist T, Grodzinsky E, Högberg L, Laurin P, Stenhammar L, Fälth-Magnusson K, Magnusson KE. Coeliac children on a gluten-free diet with or without oats display equal anti-avenin antibody titres. *Scand J Gastroenterol* 2006; **41**: 42-47 [PMID: 16373275 DOI: 10.1080/00365520510023945]

40 **Guttormsen V**, Løvik A, Bye A, Bratlie J, Mørkrid L, Lundin KE. No induction of anti-avenin IgA by oats in adult, diet-treated coeliac disease. *Scand J Gastroenterol* 2008; **43**: 161-165 [PMID: 18224563 DOI: 10.1080/00365520701832822]

41 **Sjöberg V**, Hollén E, Pietz G, Magnusson KE, Fälth-Magnusson K, Sundström M, Holmgren Peterson K, Sandström O, Hernell O, Hammarström S, Högberg L, Hammarström ML. Noncontaminated dietary oats may hamper normalization of the intestinal immune status in childhood celiac disease. *Clin Transl Gastroenterol* 2014; **5**: e58 [PMID: 24964993 DOI: 10.1038/ctg.2014.9]

42 **Hernando A**, Valdes I, Méndez E. New strategy for the determination of gliadins in maize- or rice-based foods matrix-assisted laser desorption/ionization time-of-flight mass spectrometry: fractionation of gliadins from maize or rice prolamins by acidic treatment. *J Mass Spectrom* 2003; **38**: 862-871 [PMID: 12938107 DOI: 10.1002/jms.502]

43 **Koerner TB**, Cléroux C, Poirier C, Cantin I, Alimkulov A, Elamparo H. Gluten contamination in the Canadian commercial oat supply. *Food Addit Contam Part A Chem Anal Control Expo Risk Assess* 2011; **28**: 705-710 [PMID: 21623493 DOI: 10.1080/19440049.2011.579626]

44 **Thompson T**. Gluten contamination of commercial oat products in the United States. *N Engl J Med* 2004; **351**: 2021-2022 [PMID: 15525734 DOI: 10.1056/NEJM200411043511924]

45 **Comino I**, Real A, de Lorenzo L, Cornell H, López-Casado MÁ, Barro F, Lorite P, Torres MI, Cebolla A, Sousa C. Diversity in oat potential immunogenicity: basis for the selection of oat varieties with no toxicity in coeliac disease. *Gut* 2011; **60**: 915-922 [PMID: 21317420 DOI: 10.1136/gut.2010.225268]

46 **Silano M**, Di Benedetto R, Maialetti F, De Vincenzi A, Calcaterra R, Cornell HJ, De Vincenzi M. Avenins from different cultivars of oats elicit response by coeliac peripheral lymphocytes. *Scand J Gastroenterol* 2007; **42**: 1302-1305 [PMID: 17852883 DOI: 10.1080/00365520701420750]

47 **Silano M**, Pozo EP, Uberti F, Manferdelli S, Del Pinto T, Felli C, Budelli A, Vincentini O, Restani P. Diversity of oat varieties in eliciting the early inflammatory events in celiac disease. *Eur J Nutr* 2014; **53**: 1177-1186 [PMID: 24240659 DOI: 10.1007/s00394-013-0617-4]

48 **Comino I**, Moreno Mde L, Real A, Rodríguez-Herrera A, Barro F, Sousa C. The gluten-free diet: testing alternative cereals tolerated by celiac patients. *Nutrients* 2013; **5**: 4250-4268 [PMID: 24152755 DOI: 10.3390/nu5104250]

49 **Moreno ML**, Comino I, Sousa C. Alternative Grains as Potential Raw Material for Gluten-Free Food. Development in The Diet of Celiac and Gluten-Sensitive Patients. *Austin J Nutri Food Sci* 2014; **2**: 9

50 **Klose C**, Arendt EK. Proteins in oats; their synthesis and changes during germination: a review. *Crit Rev Food Sci Nutr* 2012; **52**: 629-639 [PMID: 22530714 DOI: 10.1080/10408398.2010.504902]

51 **Klose C**, Schehl B, Arendt EK. Fundamental study on protein changes taking place during malting of oats. *J Cereal Sci* 2009; **49**: 83-91 [DOI: 10.1016/j.jcs.2008.07.014]

52 **Sadiq Butt M**, Tahir-Nadeem M, Khan MK, Shabir R, Butt MS. Oat: unique among the cereals. *Eur J Nutr* 2008; **47**: 68-79 [PMID: 18301937 DOI: 10.1007/s00394-008-0698-7]

53 **Lyly M**, Salmenkallio-Marttila M, Suortti T, Autio K, Poutanen K, Lahteenmaki L. Influence of oat β-glucan preparations on the perception of mouth feel and rheological properties in beverage prototypes. *Cereal Chem* 2003; **80**: 536-541 [DOI: 10.1094/CCHEM.2003.80.5.536]

54 **Zhou MX**, Glennie Holmes M, Robards K, Helliwell S. Fatty acid composition of lipids of Australian oats. *J Cereal Sci* 1998; **28**: 311-319 [10.1016/S0733-5210(98)90011-X]

55 **Peterson DM**. Oat antioxidants. *J Cereal Sci* 2001; **33**: 115-129 [DOI: 10.1006/jcrs.2000.0349]

56 **Bao L**, Cai X, Xu M, Li Y. Effect of oat intake on glycaemic control and insulin sensitivity: a meta-analysis of randomised controlled trials. *Br J Nutr* 2014; **112**: 457-466 [PMID: 24787712 DOI: 10.1017/S0007114514000889]

57 **Battilana P**, Ornstein K, Minehira K, Schwarz JM, Acheson K, Schneiter P, Burri J, Jéquier E, Tappy L. Mechanisms of action of beta-glucan in postprandial glucose metabolism in healthy men. *Eur J Clin Nutr* 2001; **55**: 327-333 [PMID: 11378805 DOI: 10.1038/sj.ejcn.1601160]

58 **Beck EJ**, Tapsell LC, Batterham MJ, Tosh SM, Huang XF. Oat beta-glucan supplementation does not enhance the effectiveness of an energy-restricted diet in overweight women. *Br J Nutr* 2010; **103**: 1212-1222 [PMID: 19930764]

59 **Jacobs DR**, Andersen LF, Blomhoff R. Whole-grain consumption is associated with a reduced risk of noncardiovascular, noncancer death attributed to inflammatory diseases in the Iowa Women's Health Study. *Am J Clin Nutr* 2007; **85**: 1606-1614 [PMID: 17556700]

60 **Jacobs DR**, Meyer KA, Kushi LH, Folsom AR. Whole-grain intake may reduce the risk of ischemic heart disease death in postmenopausal women: the Iowa Women's Health Study. *Am J Clin Nutr* 1998; **68**: 248-257 [PMID: 9701180]

61 **Lener MR**, Gupta S, Scott RJ, Tootsi M, Kulp M, Tammesoo ML, Viitak A, Metspalu A, Serrano-Fernández P, Kładny J, Jaworska-Bieniek K, Durda K, Muszyńska M, Sukiennicki G, Jakubowska A, Lubiński J. Can selenium levels act as a marker of colorectal cancer risk? *BMC Cancer* 2013; **13**: 214 [PMID: 23627542 DOI: 10.1186/1471-2407-13-214]

62 **Pins JJ**, Geleva D, Keenan JM, Frazel C, O'Connor PJ, Cherney LM. Do whole-grain oat cereals reduce the need for antihypertensive medications and improve blood pressure control? *J Fam Pract* 2002; **51**: 353-359 [PMID: 11978259]

63 **Mantovani MS**, Bellini MF, Angeli JP, Oliveira RJ, Silva AF, Ribeiro LR. beta-Glucans in promoting health: prevention against mutation and cancer. *Mutat Res* 2008; **658**: 154-161 [PMID: 17827055 DOI: 10.1016/j.mrrev.2007.07.002]

64 **Liu L**, Zubik L, Collins FW, Marko M, Meydani M. The antiatherogenic potential of oat phenolic compounds. *Atherosclerosis* 2004; **175**: 39-49 [PMID: 15186945 DOI: 10.1016/j.atherosclerosis.2004.01.044]

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**Table 1 Main nutritional components of oats**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Components** | **Properties** | **References** |
| **Proteins** | Albumins, globulins, prolamins, and glutenins | Oats are distinct among cereals due to their higher protein concentration and distinct protein composition. The major storage proteins are globulins. | [50,51] |
| **Carbohydrates** |  β-glucan, glucose, fructose, pentosans, saccharose, kestose, neokestose, bifurcose, neobifurcose, acid galactoarabinoxylan, etc. | β-glucan is the most important component because it is a constituent of the dietary fibre obtained from oats. β-glucan has important functional and nutritional properties, and exhibits a high viscosity at relatively low concentrations. | [52,53] |
| **Lipids** | Oat lipids are highly unsaturated and contain several essential fatty acids | Oats, after corn, have the highest lipid content of any cereal. Oat lipids include very high levels of antioxidants. | [54,55] |
| **Antioxidants** | Vitamin E (tocols), phytic acid, phenolic compounds, avenanthramides, flavonoids, and sterols | Antioxidants may reduce serum cholesterol concentrations, and inhibit the growth of certain cancer cells.  | [55] |

**Table 2 Health benefits of oats**

|  |  |  |
| --- | --- | --- |
| **Effect** | **Findings** | **References** |
| Hypocholesterolemic  | An effect derived from β-glucan content, and demonstrated in normal and hypercholesterolemic subjects. The statistical significance of this cholesterol reduction has been variable, and remains controversial. | [15,18] |
| Hypoglycaemic  | Studies have suggested that oat consumption can significantly decrease insulin response, fasting blood glucose levels, and the incidence of postprandial hyperglycaemia. However, some studies have failed to identify a diet-related effect on glycaemic control or a person’s insulinemic response to oat-enriched products. | [56-58] |
| Prevention of cancer | Selenium, present in oats, is involved in DNA repair and associated with a reduced risk for cancer; especially colon cancer. Furthermore, it is found in foods with a high fibre content. | [59-61] |
| Reduction of hypertension | Soluble fibre-rich whole oats may be effective when consumed as dietary therapy for the prevention and adjunct treatment of hypertension. | [62] |
| Immunomodulatory | β-glucans act by stimulating the immune system and inhibiting the growth of various bacteria, viruses, fungi, and parasites. | [63] |
| Antioxidant  | Oats contain chemicals with potential antioxidant properties; *e.g.*, vitamin E (tocols), phytic acid, and phenolic compounds, etc. | [55] |
| Antiatherogenic  | *In vivo* studies of atherosclerosis showed that oat bran reduced plasma cholesterol levels. However, it was difficult to determine whether its antiatherogenic effect was a result of reduced plasma cholesterol alone, or if additional effects of other oat components contributed to the result. | [64] |
| Obesity control | Studies revealed that oats effectively reduced obesity, as well as indexes of serum lipid levels and liver function. These effects were observed when using β-glucan with the proper molecular weight.  | [14,52] |