

Celiac Disease, Beer and Brewing

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Abstract

Celiac disease, also called celiac sprue, is an auto-immune disease in which a reaction to a sequence of amino acids in prolamins, especially gliadin of wheat gluten, causes deformation of absorptive villae of the small intestine. As a result, nutrients are poorly absorbed. Children fail to thrive and, in the adult-onset form of the disease, intense intestinal distress is a characteristic, with severe weight loss, malaise, loss of calcium from bones, iron deficiency, dermatitis, loss of night vision and increased chance of diabetes and certain cancers. No body organ or system is unaffected by the condition. The disease affects about 1 percent of the population in the USA, but the disease is undoubtedly under-diagnosed. Though gluten occurs at its highest concentration in wheat-based products, which celiacs must assiduously avoid, other prolamins-containing grains, including barley (malt) and rye, must also be excluded. Although beers contain very small amounts of gluten fragments, all beers are banished from the diets of celiacs by the standard that they are not made from gluten-free raw materials. The FDA will define the term “gluten free” under a minor provision of the recently passed Federal Allergic Labeling and Consumer Protection Act, in which brewers should take an intense interest. Considerable progress has been made in identifying the specific protein fragment(s) of gluten that trigger the immune reaction, and physicians have begun to consider ways to alleviate the disease other than by strict and life-long dietary control. One potential method is to eliminate the offending protein fragments during food manufacture. This is clearly well suited to beer and brewing, because barley proteins are modified and/or eliminated during malting and brewing and manipulation of grain proteins is well understood by brewers as a central part of normal processing. This paper explores these possibilities. Eating “gluten free” is necessary for celiacs and becoming popular among food aficionados and faddists. The brewing industry has successfully harnessed the ultra-low carbohydrate dietary choice to certain beers; besides addressing the need of a significant population of celiacs, gluten-free beers could similarly prosper from a general “eat-gluten-free” movement.

Introduction

Brewers make beer from malted barley; therefore beer is excluded from the diet of celiacs, i.e. those who are “gluten-sensitive” because they suffer from celiac disease or celiac (coeliac) sprue. This exclusion assumes that beer has the potential to trigger the auto-immune response characteristic of the condition; however, there is no evidence to that effect. Barley does not contain the signature tenacious and elastic protein material (gliadin plus glutenin fraction) of wheat, the eponymous “gluten”, that gives dough its cohesiveness, but barley does contain prolamins, the proline-rich class of proteins to which gluten belongs. These are the hordein or storage proteins of barley. Some celiacs drink modest amounts of some beers without triggering overt symptoms of the disease and some beers do not register, and most barely register, on the scale of analysis currently used to measure gluten (personal communications). There is therefore good reason to examine the proscription of beer from the diet of celiacs.

Recent passage (July 2004) of the Federal Allergic Labeling and Consumer Protection Act (FALCPA) brings this issue to a head because, under a minor provision of the act, the FDA is required to write a definition of “gluten free” so that celiacs will be able to distinguish easily between safe and unsafe foods. As it stands at the moment in the USA and Canada, no beers or other beverages of any kind made with any amount of malted barley will meet the standard of gluten free, because the definition of “gluten free” typically used by physicians and clinical nutritionists (and therefore likely the FDA) is “made from gluten-free raw materials, only.” That is the food must contain no particle of any material derived from wheat, barley and/or rye. The European definition is different and more generous (5).

Celiac disease cannot be cured; the only treatment is a lifelong dedication to a gluten-free diet; this is not easy because many staples of the Western diet are based on wheat flour, such as bread, pasta, cookies and baked goods of all sorts. Of much greater difficulty for celiacs however, is “hidden” gluten used as an ingredient in otherwise innocuous products. FALCPA should aid celiacs to identify such unsafe foods. While the nature of the labeling requirement is unknown at the moment, passage of the Act affords an opportunity and issues a challenge to the brewing industry.

Four main ideas drive the presentation of this paper:

(1) Brewers serve their consuming public with an excellent natural product that a host of people enjoy; though the celiac market might not be a large one, about 1 percent of the population (3), brewers would surely not wish some 2-3 million potential consumers to be needlessly denied the pleasure of access to their product.

(2) Ordinary processes of beer manufacture completely eliminate native barley proteins from beer; some polypeptides survive the process. However, because prolamin-derived polypeptides (hordeins) cause haze problems in beers, brewers have a direct interest in removing them; processing to achieve a gluten-free status, therefore, is perfectly in line with brewers’ practices used to manufacture a haze-stable product. Celiacs and brewers have common cause.

(3) Eating “gluten free” is a choice currently offered in some restaurants (and such foods are available in some stores) and might very well become a much more significant part of dietary choice than it is today, perhaps even equivalent to the no-carbohydrate diets. Brewers might wish to seek approval of some beers as “gluten free” to serve not only celiacs but also consumers of the future who might wish to make this emerging dietary choice.

(4) Brewers should engage with the FDA in writing regulations that define “gluten free” with the goal of placing some beers in the marketplace that meet a true, safe and documentable gluten-free standard. In addition, brewers might wish to engage with the cereal science and medical communities as they seek to identify more exactly the offending molecules in wheat, barley and rye and develop ways to measure them. This is probably necessary if the definition of “gluten free” is to be other than “made without wheat, barley or rye.”

What is Celiac Disease?

Celiac disease is an auto-immune reaction of the body to certain proteins of the diet (or to fragments of them produced during normal digestion) especially the gliadin of wheat gluten and, presumably, the general class of proteins to which gluten belongs, the prolamins; these include barley hordein and rye secalin. A 33-unit peptide has been identified (9) as the offending polypeptide. A longstanding ELISA method, linked to wheat gliadin, is used to measure gluten in foods (1); beers are virtually gluten free as measured by this method.

Celiac disease is not an allergy. The offending polypeptide(s) set in motion a cascade of events that ultimately causes the small intestine to attack itself with destruction of the absorptive villae (10). Symptoms of the disease are idiosyncratic varying from (a) intense intestinal disturbances such as bloating, diarrhea and cramps and weight loss (sometimes severe), with fatigue, migraines, anemia, dermatitis, loss of bone mass, joint pains, loss of night vision, to (b) much less obvious “silent” forms of the disease. Reduction in the capacity of the small intestine to absorb nutrients causes an underlying malnutrition, and there is no organ or system of the body that is not potentially affected by this auto-immune reaction (7). The condition therefore also aggravates other conditions such as arthritis, thyroid and liver disease, circulatory conditions, diabetes and certain cancers. Celiac disease is not to be taken lightly. The conservative approach of clinicians and celiac patients in defining gluten-free foods as without any wheat, barley or rye is, therefore, understandable. Blood tests indicate the disease but the gold standard for diagnosis is microscopic examination of a sample of the lining of the small intestine taken by endoscope probe.

Until quite recently the disease was thought to be rare and an occasional cause of poor development in early childhood; the late onset form of the disease is now well documented. Celiac disease remains low on the radar screen of many physicians though it is increasingly recognized e.g. it was featured in TIME magazine (July 19, 2004 issue Vol.164, No.3) under the headline “Allergic to Wheat? Millions are without knowing it...” Also, celiac disease was the subject of an American Gastrointestinal Association Clinical Symposium at Digestive Disease Week, May 2004 in New Orleans, La. In June 2004 it was the subject of a National Institute of Health Consensus Development Conference, Bethesda, Md. The condition is commonly under-diagnosed, misdiagnosed, ignored or its existence denied and it can take many years for the correct diagnosis to be made (7). In fact it is the most common genetic disease of humankind and among the most common lifelong chronic illnesses.

Dietary Restriction and Treatment

Physicians and nutritionists in the USA take a conservative view of gluten-free foods that they approve for their celiac patients and urge their patients assiduously to avoid any wheat-, barley- or rye-containing products. Until quite recently whiskey, gin and vodka were excluded for celiacs because they are grain-based products. However, even the smallest fragment of a protein, an amino acid, (let alone a polypeptide of significant size) is non-volatile and cannot pass the distillation stage of spirits manufacture. Shown this logic, physicians have been persuaded by it; such beverages are now deemed safe (provided e.g. any caramel coloring agents or botanicals, or post-distillation processes are

gluten-free). Similarly, celiacs face a dilemma with the Catholic Church whose Code of Canon Law requires that only bread (and therefore wheat) may be used as host at the holiest moment of the Mass. Catholics who are celiacs are therefore denied the comfort of the Eucharist. Fortunately a new host has been developed that meets the requirements of the Church; it contains wheat starch (not wheat flour) and gluten at a level that is acceptable to clinical professionals (2). These two anecdotes illustrate that though clinical professionals in the USA (and therefore, likely, the FDA) take an extreme view of what comprises gluten-free food, their proscriptions and exclusions are not absolute and mindless but might be open to sensible well-supported argument and scientific debate. The Codex Alimentarius permits the “gluten free” label on foods containing no more than 200 ppm gluten (0.2 grams per kilo (or per liter?)) and is the European standard for “gluten free” (1,5,11).

Physicians have begun to consider treatments for celiac disease; most are drug-based approaches that interrupt the cascade of events leading to the auto-immune reaction (4). They are of no interest in the context of this paper. Another approach is to completely break down the offending polypeptides formed in normal digestion with an added enzyme. A proteolytic enzyme from *Flavobacterium meningosepticum* with prolyl endopeptidase activity appears promising in model and animal systems (4,7) though how the enzyme will be applied in practice remains obscure. However, this enzyme, or one like it, might have simple practical applications in brewing where use of exogenous enzymes is not unknown. Perhaps uniquely in the food industry, therefore, the raw materials of brewing, the process and/or the product could be modified to meet rigorous gluten-free standards.

Beer and the regulatory debate

The present “raw-materials” definition of gluten-free foods used by clinical professionals, if adopted by the FDA, will amount to a “zero tolerance” definition; this will permanently exclude any malt-based beer, or any other malt-based beverages, from the gluten-free approbation, regardless of how it might be made. This is not a good outcome for the brewing industry and their consumers, and the brewing industry should take a lively interest in this debate.

Two questions arise: Can brewers make a good argument for beers as being gluten-free? Or, in addition: Can brewers envisage reasonable processing practices that will make some beers (at least) gluten free? The answer to both questions is “Yes!”

The most obvious way to make a gluten-free beer is to start with gluten-free raw materials. This method is used to make many gluten-free foods especially baked products such as bread, pasta, cookies, cakes and pie-crusts, which celiacs must otherwise strictly avoid. While these are generally acceptable and edible foods, they fall well short of their true wheat-containing parent foods in flavor and texture. Though they are unmistakably ersatz versions of the real thing, there are no alternatives. In contrast, there are many safe ordinary alcoholic beverages for celiacs to enjoy, including ciders, wines and distilled beverages, and an ersatz beer is unlikely to appeal to many.

On the other hand, success in producing a gluten-free beer might well lie in the ordinary malt-based brewing process itself, because brewing is a process designed to remove

unwanted factors from the raw materials; brewers are already expert at removing proteins from brewing raw materials and controlling them in beer. Thus, removing or limiting the celiac-triggering protein(s) may already take place in ordinary processing (especially of light beers) or could be but a small additional step to ordinary processing.

Brewing practices for gluten-free beers

Here are 10 factors (6,8) that suggest that some beers might be (a) considered naturally gluten free or (b) poor carriers of polypeptides and hence of the celiac-triggering protein; hence (in either case) beer may be so dilute in practical use as to be the functional equivalent of gluten free:

- (1) Malting barleys used for brewing are low-protein barleys; they contain roughly one-third less protein than wheat for baking, and much less of the protein is in the prolamin fraction. Barley contains no true “gluten”.
- (2) Before use, barley is malted, and that results in the considerable destruction of proteins to the extent of 40 to 50 percent (the Kolbach Index). Also a good deal of proline is released and persists into beer; does this suggest strong prolyl endopeptidase activity? Proteins and peptides might also be modified by proteolysis during mashing.
- (3) During mashing much protein/polypeptide is precipitated by reaction with polyphenols, and is separated from the wort by lautering. Spent grain, as a result, has a high content of protein.
- (4) During mashing the malt fraction is significantly diluted (a) with 30-70 percent (depending on the product) rice or corn products that do not carry the offending proteins and (b) with water, so that ordinary wort contains no more than, say, 6 percent whole wheat malt solids (i.e. half the original gravity of a 12° Plato wort), most of it carbohydrate.
- (5) More protein is precipitated as a result of boiling the wort (hot-break) and cooling it to fermentation temperature (cold break) and these fractions are also usually removed from the process and product at this stage.
- (6) Prolonged exposure to the cool and reducing conditions of fermentation precipitates more protein that separates with the yeast.
- (7) Beer is finally aged and matured, by various means, one central purpose of which is to remove even more protein, especially prolamin, so that the beer is finally rendered chill-haze stable. Prolonged cold storage (minus 2° C) and settlement is one practice; another, or additional, practice is to treat beer with silica gel products that selectively adsorb prolamin (haze-forming) polypeptides that originate in the hordein fraction. The beer is then tightly filtered while cold.
- (8) Unlike bread, which might be eaten at every meal in considerable amount as a staple of the Western diet, grain is consumed in much lower amounts and with much less frequency when in the form of beer. Thus, a kilo (liter) of beer might deliver 0.5 gram of total protein yet a kilo of bread yields some 80-100 grams of protein (containing about 60

grams of gliadin) (1). It is worth noting that gluten from wheat is the second most common component of the Western diet (after starch/sugar) (4).

(9) If 40 percent or less of the total protein in a beer is generic gliadin/gluten (i.e. less than 200 ppm or mg/L gluten), which is a good bet, the product would meet the European standard for gluten free. Note also, the prolamins of wheat differ from those of barley and other cereals (8).

(10) Generally celiacs can tolerate some 10 mg per day of gluten (11). Thus, by rough calculation, a celiac could enjoy one or even two bottles of some beers each day, assuming the total protein content of it comprises no more than one-twentieth of the specific celiac-triggering polypeptide (also a good bet).

Modification of brewing practices

The extensive list (above) of protein-modifying and protein-removing processes that happen during ordinary beer-making confirms that brewers really do understand, as part of their ordinary work, the control of protein in their product and also suggests many ways to exploit the removal of proteins/polypeptides, and hence the protein fragments that injure celiacs. These include most obviously (6,8):

(1) Selection of suitable low-protein barley varieties for malting, most likely two-row varieties; even perhaps the development of more appropriate barleys including those with a more appropriate battery of proteolytic enzymes.

(2) Modification of malting to encourage and perhaps direct proteolysis. In fact, celiac disease suggests a specific reason and objective for focused research on barley/malt proteases and polypeptidases.

(3) Management of brewhouse processes to maximize protein degradation and/or precipitation, perhaps including the use of adsorbents. For gluten-free beers, brewers might choose higher levels of adjuncts and perhaps select different ones.

(4) Addition of enzymes with appropriate proteolytic/peptidolytic action in the brewhouse or in fermentation or finishing, in much the same way as e.g. amyloglucosidase is now used to promote wort fermentability or β -glucanase to lower viscosity. There is ample availability of commercial proteases; it appears that prolyl endopeptidase activity is particularly prized.

(5) Re-examination, selection and perhaps improvement of silica-gel adsorbents and their practical application to beer during finishing to remove even more protein/polypeptide materials. Perhaps simply *more* adsorbent will do the job for targeted beers. Such increased removal of non-hydrophobic haze-forming proteins might even promote foam.

Conclusion, research needs and regulation

Thus there are many reasons why beer might be considered naturally gluten free and might justify the risk some celiacs take in consuming some beers, especially light beers. Also, as discussed, many strategies suggest themselves by which beer might be rendered gluten free.

There is however one consideration, referred to earlier in this paper, that needs to be revisited here: all the arguments of why beer should be considered naturally gluten free or rendered gluten-free by process modification, depend absolutely and ultimately on one thing: brewers must be able to demonstrate without equivocation that they have succeeded in producing a gluten-free product. This can best be done if the nature of the offending peptide is known and reliable methods for measuring it are developed. (Currently an ELISA method linked to wheat gliadin is used (1); beers barely register on the scale of measures by this method). Therefore, the brewing industry might usefully join with the medical community in seeking a more exact definition of the peptide sequence that triggers the celiac reaction and help to develop methods to analyze it. Beyond such analysis is the potential for clinical trials to demonstrate directly whether or not beer can trigger the celiac auto-immune reaction.

Based on the discussion above, it is perfectly reasonable to assume that barley (as beer) is infinitely less potent for triggering celiac disease than wheat (as bread); unfortunately, such argument alone will unlikely carry sufficient weight with clinical professionals and the FDA. These communities will favor the conservative (though questionable, in the case of beer) zero tolerance (i.e. raw materials) definition of “gluten free.” It is imperative that brewers seek to avoid such a definition if the possibility of a gluten-free, celiac-safe beer is to be explored. Not only will generations of celiacs be grateful, but also the industry may well reap a reward in addressing a useful market and one that will likely grow, especially if “eating gluten-free” approaches the level that “eating carbohydrate-free” has done. The FDA definition of gluten free must be sufficiently open-ended, to permit the food industry to innovate appropriate products; brewers have a process and product that is ideally suited to such innovation.

Without input from the brewing industry to research and regulation, beers and other malt-based beverages will find themselves permanently regulated out of the gluten-free market.

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