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Medical nutrition therapy: use of sourdough lactic acid bacteria as a cell factory for delivering functional biomolecules and food ingredients in gluten free bread

Elke K Arendt^{1,2*}, Alice Moroni^{1,2}, Emanuele Zannini^{1,2}

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Abstract

Celiac disease (CD) is an immune-mediated disease, triggered in genetically susceptible individuals by ingesting gluten from wheat, rye, barley, and other closely related cereal grains. Currently, the estimated prevalence of CD is around 1 % of the population in the western world and medical nutritional therapy (MNT) is the only accepted treatment for celiac disease. To date, the replacement of gluten in bread presents a significant technological challenge for the cereal scientist due to the low baking performance of gluten free products (GF). The increasing demand by the consumer for high quality gluten-free (GF) bread, clean labels and natural products is rising. Sourdough has been used since ancient times for the production of rye and wheat bread, its universal usage can be attributed to the improved quality, nutritional properties and shelf life of sourdough based breads. Consequently, the exploitation of sourdough for the production of GF breads appears tempting. This review will highlight how sourdough LAB can be an efficient cell factory for delivering functional biomolecules and food ingredients to enhance the quality of gluten free bread.

Celiac disease

Celiac disease (CD) is the most common food-induced enteropathy in humans caused by intolerance to wheat gluten and similar proteins originating from barley and rye in genetically susceptible individuals [1]. Previously regarded as a rare disorder, it is now accepted that CD is a major health problem affecting around 1 % of the population in the western world [2,3]. CD has manifested itself in the form of a broad spectrum of clinical symptoms [4-7] (Table 1), which are associated with a large variety of changes in the mucosa of the small intestine [8,9]. The celiac enteropathy is an end-stage lesion that depends on both genetic and environmental factors for expression [6] (Figure 1). To the present day, medical nutrition therapy (MNT) with supportive

nutritional care (particularly in relation to iron, calcium and vitamin deficiencies) [10,11] is the only accepted treatment for CD. The current treatment is therefore a strict gluten-free (GF) diet for life.

Gluten is a heterogeneous mixture of wheat storage proteins consisting of gliadins and glutenins. Similar proteins are also present in barley (hordeins) and rye (secalins) and their effect on the health of celiac patient are very well documented. Based on their size, electrophoresis mobility and differential N-terminal sequence, gluten is divided into gliadins which are classified as α , β , γ , and ω -gliadins in addition to the high and low -molecular weight glutenins [12]. Gliadins, also called prolamins due to their high content of the amino acids proline and glutamine, are described as the main triggering factor in CD (Table 2) [13]. Dietary gluten represents a common component of the human diet, not only in wheat bread but also in a wide range of other foods. Due to its visco-elastic properties, gluten plays

* Correspondence: e.arendt@ucc.ie

¹School of Food and Nutritional Sciences, University College Cork, Western Road, Cork, Ireland

Full list of author information is available at the end of the article

Table 1 Clinical manifestations and related signs of celiac disease¹

Gastrointestinal Symptoms	Extraintestinal symptoms
Chronic diarrhoea	Infertility or fetal loss
Recurrent pancreatitis	Anaemia
Abdominal distension	Loss of appetite
Abdominal pain	Short stature
Duodenal obstruction	Osteomalacia/osteoporosis
Vomiting	Fatigue
Constipation	Dementia
Flautolerance	Weakness (myopathy, neuropathy)
Muscle wasting	Vitamin deficiency
Steatorrhea	Type 1 diabetes
Weight loss	Hypo/hyperthyroidism
Anorexia	Alopecia areata
Bulky, sticky and pale stools	Depression
Failure to thrive	Behavioral changes
	Late-onset puberty
	Epilepsy
	Dermatitis herpetiformis
	Arthritis
	Aphthous stomatis
	Dental enamel hypoplasia
	Cerebellar ataxia
	Myelopathy
	Esophageal reflux

¹Source : Feighery (1999); Murray (1999); Fasano and Catassi (2001); Tack et al., 2010).

a key role in determining the unique baking quality of wheat by being responsible for the water absorption capacity, cohesiveness, viscosity, and elasticity of dough [14].

Gluten-free diet and bread

Total life-long avoidance of gluten ingestion remains the cornerstone treatment for CD. Compliance with a strict gluten-free diet is not easy, because (i) harmful gluten may contaminate food during processing steps, (ii) it is socially limiting, (iii) gluten-free products are generally not widely available and more expensive, are less palatable than conventional wheat bread [15] and (iv) may lead to nutritional deficiencies. Moreover, a marketing review found that most of the gluten-free products were of low quality, exhibiting poor mouth-feel and very often having off-flavours [16]. For these reasons, the replacement of the gluten in gluten-free cereal products is a challenging task for the cereal technologist and bakers.

In the past decades, there has been a significant increasing interest in research on the development of gluten-free bakery products, involving various approaches. These include the use of: (i) gluten-free

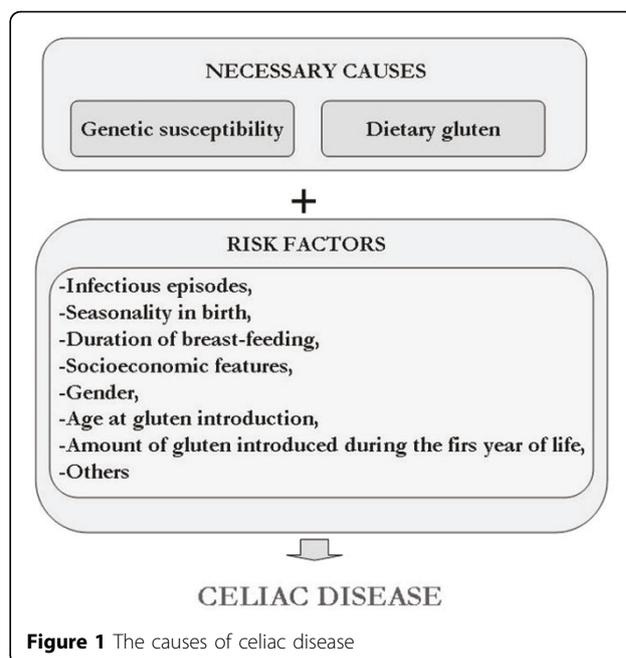


Figure 1 The causes of celiac disease

flours such as, rice, sorghum, oats, buckwheat, amaranth, quinoa, teff, corn (Table 3), (ii) starches, (iii) dairy products [17], (iv) protein supplementation i.e. egg proteins [18], (v) gums and hydrocolloids [19] (vi), dietary fibres [17,20], (vii) the use of functional ingredients, and (viii) alternative technologies such as, enzymatic processing [21,22] and high hydrostatic pressure processing [23]. All these strategies have been shown to improve, to different extents, gluten free cereal products with a final product quality similar to their gluten-containing counterparts. Despite the appealing results obtained so far, the inclusion of these ingredients/additives in bread formulations to improve the quality of GF bread presents several disadvantages. First of all, the GF product prices are excessive and most of the ingredients/additives used represent high-cost components with the average price of GF bread on the market being significantly higher than that of conventional bread (<http://www.glutenfree.com/baked-goods/breads/category357>) [24]. Additionally, some of these ingredients, e.g. dairy powders, and in particular those with the high lactose content, are not suitable for coeliacs since a large number of celiac patients are also lactose intolerant, particularly at the early stages of the disease. Furthermore, some additives do not meet the consumers' requirements for natural products. Thus, there is an impelling call for researchers to find alternative technologies for the production of good quality GF bread. In the next paragraphs we address how sourdough lactic acid bacteria can act as "cell factories" for the production of functional biomolecules and food ingredients able to

Table 2 Immunogenic gliadin peptides

Amino acid sequences	Position	Immunogenicity
VRVPVQLQPQNPSQQQPQ	α-gliadin: 1–19	+
QNPSQQQPQEQVPLVQQQ	α-gliadin: 11–28	+
QVPLVQQQFFGQQQPFPPQ	α-gliadin: 21–40	+
PGQQQFPFPQQPYQPQPF	α-gliadin: 31–49	+
FPGQQQFPFPQQPYQPQPF	α-gliadin: 30–49	+
QPYQPQPFPSQQPYLQL	α-gliadin: 41–58	+
PQPFPSQQPYLQLQPFQ	α-gliadin: 46–63	+
PQPQLPYQPQLPY	α-gliadin: 62–75/(a)	+ /+++
QLQPFQQLPY	α-gliadin: 57–68 (a)	+ /+++
QLQPFQ	α-gliadin: 57–63 (a)	+++
LQLQPFQQLPYQPQLPYQPQLPYQPQPF	α-gliadin: 57–89/(a)	+ /+++
QLQPFQQLPY	α-gliadin: 58–69/(a)	+ /+++
PQPQLPYQPQLPY	α-gliadin: 63–76/(a)	+ /+++
PFRPQQPYQPQ	α-gliadin: 93–106 (a)	+
LIFCMDWLQ	α-gliadin: 123–132	+
QQPLQQYPLGGSFRPSQQNPQAQ	α-gliadin: 198–222	+
QYPLGGSFRPSQQNPQA	α-gliadin: 203–220/(a)	+ /+
PSGQGSFQPS	α-gliadin: 205–214	-
PSGQGSFQPSQQ	α-gliadin: 205–216/(a)	+ /+++
SGQGSFQPSQQN	α-gliadin: 206–217/(a)	+ /+++
QGSFQPSQQN	α-gliadin: 208–217/(a)	- /+++
LQPQQFPFPQQPYQPQ	γ-gliadin: 60–79	+
FPQQPQQPYQPQ	γ-gliadin: 66–78	+
FSQPQQFPQ	γ-gliadin: 102–113/(a)	- /+
OQPQQSFPEQQ	γ-gliadin: 134–153/(a)	+ /+++
VQGQGIIPQQPAQL	γ-gliadin: 222–236/(a)	+ /+
QQQPPFSSQQQSPFSSQQQ	glutenin: 40–59/(a)	- /+
QQPPFSSQQQLPQ	glutenin: 46–60/(a)	- /+
SGQGQRPGWLQPGQGQQGYPTSPQSGQGQLGQ	glutenin: 707–742/(a)	+ /+
PGQGQQGYPTSPQSGQ	glutenin: 719–736	+
GYPTSPQSGQGQLGQ	glutenin: 725–742	+
GYPTSPQSG	glutenin: 725–735	+
QGYPTSPQSS	glutenin: 724–734/(a)	- +
QQGYPTSPQSG	glutenin: 723–735	+
GQQGYPTSPQSG	glutenin: 722–735	+
GQQGYPTSPQSS	glutenin: 722–734	+

(a): deamidated

Source (Ciccocioppo et al., 2005)

counteract the problems associated with the production of high quality GF breads.

GF sourdough fermenting microorganisms

Sourdough is a mixture of flour and water which is fermented with lactic acid bacteria (LAB) and yeasts; these microorganisms determine its characteristics in terms of acid production, aroma and leavening properties [25].

Ecological studies on GF sourdoughs indicate that GF materials harbour novel and competitive LAB and yeasts strains which are not commonly isolated in traditional sourdoughs and could serve as suitable candidates for

starter dough development [26-30]. These studies revealed that *Lactobacillus fermentum*, *L. plantarum*, and also *L. paralimentarius* are frequently isolated in GF sourdoughs produced from rice, maize, buckwheat, teff and amaranth. Furthermore, species such as *L. gallinarum*, *L. graminis*, *L. sakei* and *Pediococcus pentosaceus*, which are not commonly associated with conventional sourdoughs, were part of the dominant microbiota of the various GF sourdoughs [24]. Since these particular strains are adapted to the various GF-systems, they can be applied as promising cell factory for the delivery of functional biomolecules and food ingredients in gluten free bread.

Table 3 Grain storage proteins

Storage protein not allowed for CD patient	Storage protein allowed CD patient
Wheat (<i>Triticum</i> spp. Including spelt, emmer, farro, einkorn, kamut, dickel, durum)	Amaranth ^a
Rye (<i>Secale</i>)	Buckwheat ^a
Triticale (a <i>Triticum x Secale</i> cross)	Corn
Barley (<i>Hordein</i>)	Millet
Oat *	Quinoa ^a
	Rice
	Sorghum ^a
	Soy ^a
	Legumes ^a
	Teff

^aThese sources contain higher levels of fiber, protein, calcium and iron.

* Most oats have been grown, stored, transported or processed with the gluten-containing grains and are therefore contaminated with gluten.

Exopolysaccharides (EPS) producing LAB as hydrocolloid replacer in GF system

The addition of hydrocolloids such as xanthan gum, guar gum and hydroxypropylmethylcellulose (HPMC) is essential in gluten-free baking to obtain acceptable product quality in terms of volume, texture, and shelf life [31]. Many lactic acid bacteria (LAB) can produce a wide variety of long-chain sugar polymers called exopolysaccharides (EPS), which are varied in their chemical composition, structure and physical properties [32]. These polysaccharides are synthesised extracellularly from sucrose by glycansucrases, or intracellularly by glycosyltransferases from sugar nucleotide precursors.

LAB isolated from various cereal based sources frequently produce oligo- and homopolysaccharides from sucrose, which can improve the technological as well as the nutritional properties of gluten-free breads acting as prebiotics and hydrocolloids, respectively.

Recently, the applicability of the EPS-producing strains *L. reuteri* LTH5448 and *Weissella cibaria* 10M was investigated in GF sourdoughs [33]. Both strains were shown to be suitable as sourdough fermentation starters for quinoa and sorghum, and during the fermentation were able to produce levan (fructo-oligosaccharides - FOS) and dextran (gluco-oligosaccharides - GOS), respectively. GF breads containing sourdough fermented by *W. cibaria* were softer than the ones containing no EPS. Moreover, GOS produced by *W. cibaria* were not digested by baker's yeast and they were still present in the final bread. Thus, the consumption of 300 g of sorghum GF bread prepared with *W. cibaria* 10M would allow for a significant intake of prebiotic GOS [33]. Recently, Galle et al. [34] screened EPS-forming *Weissella* strains for their potential use as starter strains in sorghum and wheat sourdoughs. Independent of which strain is used, higher amounts of EPS were formed in

sorghum sourdough than in wheat, due to the higher concentration of glucose in the GF flour. In particular, the strains *Weissella kimchii* and *W. cibaria* MG1 produced dextrans in concentrations high enough to be used as potential replacers of non-bacterial hydrocolloids, such as guar gum and HPMC in gluten-free sourdough bread. All together, these studies indicate that EPS-producing LAB in sourdough could play a promising role for the production of GF products with improved quality characteristics and reduced additive content. However, more research is needed to identify the most suitable EPS for the replacement of hydrocolloids in gluten-free cereal products.

Production of peptidase for gluten detoxification

During endoluminal digestion, gliadins of wheat, rye and barley release a family of peptides rich in Pro and Gln, which are responsible for the inappropriate T cell-mediated immune response associated with celiac disease [35] (Table 2). Recently, sourdough LAB have been considered as cell factories for the production of enzymes able to decrease the toxicity of wheat and rye flours over a long fermentation period (12-24 h). Di Cagno et al. [36] showed that four sourdough LAB strains - *Lactobacillus alimentarius* 15M, *L. brevis* 14G, *L. sanfranciscensis* 7A and *L. hilgardii* 51B were selected based on their enzyme substrate specificity and ability to hydrolyse the 33-mer peptide (corresponding to a fragment of 57-89 of α 2-gliadin that represents the most potent inducer of gut-derived human T cell lines in patients with celiac disease) [37]. The above mentioned strains were then used for the production of a sourdough containing wheat. Breads were produced by mixing the selected wheat sourdough with untreated GF flours. The final products showed acceptable quality and induced no alterations in the baseline values of celiac patients during in vivo acute challenge test [36]. The same pool of LAB showed also to be effective in reducing the toxicity of rye flour [38] and, when used in association with *L. sanfranciscensis* and fungal protease, produced non-toxic wheat sourdough bread of acceptable quality [39]. Additionally, VSL#3 probiotic preparation (VSL Pharmaceuticals, Gaithersburg, MD), containing *Streptococcus thermophilus*, *Lb. plantarum*, *Lb. acidophilus*, *Lactobacillus casei*, *Lactobacillus delbrueckii* spp. *bulgaricus*, *Bifidobacterium breve*, *Bifidobacterium longum* and *Bifidobacterium infantis* was also tested successfully by the same authors [40].

However, even if this approach is not directly applicable to the industrial production of gluten-free bread, the results collected so far strongly indicate that selected LAB can be used to degrade any potential contaminant present in gluten-free flours and, at the same time, improve the nutritional properties of GF-breads [41,42].

Beyond the gluten detoxifying activity, sourdough-induced proteolysis was also found to be a key event for delaying staling of GF breads [43,44]. Improved textural properties have been reported for sourdough-based sorghum bread [45]. Nonetheless, more investigations are needed in order to understand which GF flours would be positively influenced by sourdough treatment, which fermentation conditions should be applied and which degree of enzymolysis is required in order to enhance their baking performances.

Production of antifungal compounds

When conventional wheat bread is compared with GF bread currently on the market, it becomes apparent that the majority of the GF products have a very long shelf life. This increase in shelf life is achieved by using modified atmosphere packaging (MPA) and/or the addition of chemical preservatives [46]. The majority of GF products are based on hydrocolloids, which are essential for structure formation in these products. Hydrocolloids are able to bind a high amount of water which leads to a much higher water activity (*aw*) in GF breads than in their wheat containing counterparts. This increase in *aw* leads to a significant reduction in shelf life which can mainly be attributed to mould growth. For this reason the use of MPA and/or chemical preservatives are necessary. The interest in the concept of food biopreservation, which is the control of one organism by another, has increased in recent years. LAB with antifungal activity, preventing growth of bread spoilage fungi, are a promising alternative to chemical preservation [47-50].

To date, only one study has investigated into the use of sourdough to extend the shelf life of GF bread. In this study, Moore et al. [44] used the antifungal strain *L. plantarum* FST 1.7 [48] to produce GF sourdough from a mixture of brown rice, corn starch, buckwheat, and soya flours. Results showed that fermenting 20% of the GF flours with *L. plantarum* FST 1.7 could retard the onset of staling in respect to chemically acidified GF control breads. Furthermore, the sourdough retained its inhibitory activity in the bread, where the growth of *Fusarium culmorum* was retarded by up to 3 days when compared to the control bread. This study clearly indicates that the production of GF sourdough with antifungal properties can be regarded as a valuable alternative to the use of chemical additives for retarding staling and prolonging shelf life of GF breads. However, further research is needed to identify the optimal sourdough starter and fermentation conditions for achieving GF bread of improved shelf life and quality.

LAB with antimycotoxigenic activity

Different cereals (rice, maize, millet, sorghum) and pseudocereals (amaranth, buckwheat and teff) are widely

utilized, with other functional ingredients, in the formulation of gluten-free products, especially for the production of gluten-free bread [45,51-54]. All these alternative grains are mainly produced in tropical and sub tropical regions, where climate and poor storage conditions are conducive to fungal growth and mycotoxin production [55]. Mycotoxin (e. g. Trichothecene, Zearalenone, Fumonisin, Ochratoxin, Aflatoxin, Deoxynivalenon) contamination in maize, rice, sorghum, millet, buckwheat, teff, have been widely reported [53,55-58]. The occurrence of mycotoxins in gluten-free grains is regarded as a major economical problem [59] and is also potentially dangerous particularly for people suffering of CD. LAB, and in particular the species belonging to the genera *Lactobacillus*, have long been known to possess antimycotoxigenic activity against the most harmful mycotoxins like Zearalenone, Fumonisin, Ochratoxin, Aflatoxin and Deoxynivalenon.

El-Nezami et al.[60] report, that two food-grade *Lactobacillus rhamnosus* GG and *L. rhamnosus* LC705 were able to reduce the contamination of zearalenone (ZEN) and its derivatives α' -zearalenol (α' -ZOL) by up to 55% (w/w) using binding sites on the bacteria surface. When the two toxins were tested in combinations, binding of individual toxins was compromised indicating the possibility of the two toxins sharing similar surface binding sites. Similarly, *L. rhamnosus* strains GG and LC705 are also shown to effectively bind aflatoxin B1 [60]. Additionally, many other strains of LAB, such as *L. acidophilus* VM20 [61], *L. acidophilus* CH-5, *L. plantarum* BS, *L. brevis* and *L. sanfranciscensis* [62] have been reported to bind ochratoxin A (OTA) in a strain specific manner causing its decrease by up to 95%. This allows reduction in the absorption of these toxins from the intestine and hence reducing their estrogenic effects in humans.

Thus, even though further studies in gluten-free bread systems are required, the potential antimycotoxigenic activity of LAB places them in a promising position for developing a new approach for detoxification of mycotoxins in GF products.

Phytase producing LAB

Phytic acid is the major storage form of phosphorous in grains and it binds minerals such as Ca, Fe, K, Mg, Mn and Zn, and therefore making them insoluble and thus unavailable for adsorption in the intestinal tract of humans [63]. Phytic acid is therefore considered an anti-nutritional factor, especially for celiac patients who suffer from micronutrient deficiencies. GF flours/ingredients show a wide range of phytate contents, examples are: 0.12% rice, 0.25% pearl millet, 0.47% amaranth, 0.70% teff, 0.77% lupin, 0.92% corn, 1.13% oats, 1.18% quinoa, 1.33% soybean [64]. In wheat grain the

level of phytate is around 1.2%. Since phytate is mainly found in the aleurone layer, the content of phytate in a specific flour is very much depends on the milling regime applied. During bread-making, phytic acid can be degraded by phytases whose activity is influenced by temperature, pH, fermentation time and by the presence of certain additives [65]. Studies conducted on whole wheat show that the moderate decrease in pH caused by sourdough fermentation is sufficient to significantly reduce the phytate content of bread produced from whole wheat flour. Recent studies also showed that phytate can be synthesized by microorganisms, e.g LAB [66] and yeast [67].

De Angelis et al., [66] reported a reduction in phytic acid content of about 64-74% in a wheat dough fermented with *L. sanfranciscensis* CB1 compared to a control sourdough. To date, no work has been published on phytase activity in GF sourdough breads. Yet, phytase activity has been investigated during fermentation of some GF crops. In particular, fermentation of sorghum and pearl millet was shown to induce a decrease in the phytic acid content and two phytase-positive strains, i.e., *L. plantarum* and *L. fermentum*, were isolated from fermenting pearl millet [68].

Generation of aroma compounds using LAB

The addition of sourdough to bread product can strongly influence the flavour profile of the bread. This flavour modification is dependent on the raw material, type of starter cultures, fermentation and baking condition applied [69]. Among these factors, LAB and yeast play a pivotal role in the generation of volatile metabolites in the final cereal products. The fermentation of GF flours by LAB has been shown to induce the production of flavour compounds. One example is the fermentation of sorghum for the production of *towga* where different flavouring compounds were generated during the fermentation. The flavour changes were attributed to the production of alcohol and diacetyl [70]. Diacetyl was produced in high concentration when the fermentation was carried out with *L. plantarum* and *Pediococcus pentosaceus* and alcohols were produced in significant amount if *Issatchenkia orientalis* was used in combination with *L. brevis* or *L. plantarum*. The *L. plantarum* /yeasts co-fermentation also induced the production of aldehydes. Finally, Edema and Sanni [29] showed that maize flours fermented with mixed cultures containing *L. plantarum* lead to an increased diacetyl content when compared to a control. Thus, even if further studies are required, sourdough technology might be a promising tool to produce flavour enhancing compounds which will improve the poor sensorial quality of GF breads.

Production of bioactive compounds

Sourdough fermentation is well recognized as a useful aid rendering cereal products palatable. Moreover, the sourdough process represents an important tool in increasing the extractability of bioactive compounds from various raw materials or in releasing functional biomolecules which are part of the LAB/yeast metabolism. However, beyond the potential of sourdough fermentation, the type of raw material (cereal, pseudocereals, and legumes) used is seen of key importance for the optimal delivery of bioactive compounds for human nutrition.

To date, only one research study has investigated the use of LAB to ferment GF flours for the production of functional bread enriched with bioactive compounds. In this study Coda et al., [71] used *L. plantarum* C48 and *Lactococcus lactis* subsp. *lactis* PU1, selected for the capacity to synthesizing GABA (γ -Aminobutyric acid), through sourdough fermentation of common wheat, durum wheat, rye, spelt, oat, buckwheat, rice, amaranth, millet, chickpea, soy and quinoa flours. γ -Aminobutyric acid (GABA), acts as the chief inhibitory neurotransmitter of the central nervous system [72]. Other physiological functions of GABA are induction of anti-hypertensive, prevention of diabetes, diuretic and tranquiliser effects [73]. The highest biosynthesis of GABA was detected when buckwheat (643 ± 13 mg/Kg) and quinoa (415 ± 10 mg/Kg) were fermented with *Lb. plantarum* C48. *Lc. lactis* subsp. *lactis* PU1 revealed the best results when amaranth (816 ± 11 mg/Kg) and chickpea (1031 ± 9 mg/Kg) were used as substrates. A blend of selected flours was also fermented with two GABA-producing strains; the best performance was found when *Lb. plantarum* C48 was applied with a GABA production equal to 989 ± 10 mg/kg. On the contrary, when common wheat and durum wheat flours were used as a substrate, *Lc. lactis* subsp. *lactis* PU1 showed the worse performance producing 70 ± 15 mg/Kg and 84 ± 26 mg/Kg of GABA respectively.

In conclusion, the use of a blend of buckwheat, amaranth, chickpea and quinoa flours subjected to sourdough fermentation by selected GABA-producing strains represent a promising potential tool for enhancing the nutritional quality of GF-bread.

Conclusions

Many factors have contributed to the increased prevalence of celiac disease, which has emerged as the most common food intolerance worldwide that can be diagnosed at all ages. Even though, in the past decade, an impressive effort has been made to development potential therapeutic solutions for CD [74], the only currently available and safe treatment for CD consists of the

dietary exclusion of grains containing gluten and the supportive nutritional care in case of mineral and vitamins deficiencies in celiac patients [10]. Gluten is an essential structure-building protein, contributing to the appearance, crumb structure, and consumer acceptability of many baked products. Therefore, the biggest challenge for food scientists and bakers in the area of GF products is probably the production of high quality GF bread. Sourdough fermentation positively influences all aspects of bread quality such as texture, aroma, nutritional properties and shelf life. Recently, sourdough has been successfully applied for the improvement of the quality of GF bread due to the complex metabolic activity of the sourdough lactic acid bacteria. The examples presented in this review demonstrate that LAB might be considered as “burgeoning” cell factories for the delivering of functional biomolecules and food ingredients for the production of high quality GF cereal products.

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Author details

¹School of Food and Nutritional Sciences, University College Cork, Western Road, Cork, Ireland. ²National Food Biotechnology Centre, University College Cork, Cork, Ireland.

Authors' contributions

EKA received the invitation, critically revised and commented the manuscript. AM contributed to the content of the review article. EZ designed and drafted the manuscript.

Competing interests

The authors declare that they have no competing interest.

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