



## Novel insights on the functional/nutritional features of the sourdough fermentation



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### ARTICLE INFO

#### Keywords:

Sourdough  
Lactic acid bacteria  
Fermentation  
Nutrition

### ABSTRACT

As one of the most traditional biotechnologies, sourdough fermentation has deep effects on rheology, sensory and shelf life attributes of baked goods. The most recent literature has also highlighted the effects of sourdough fermentations on several functional/nutritional features of baked goods. While some aspects such as the potential to lower glycemic index, increase mineral bioavailability and decrease the gluten content have been proven almost definitively, others potentialities are emerging, which deserve novel insights. This reviews reports the main evidence on the use of sourdough fermentation for salt reduction in baked goods, management of irritable bowel syndrome (IBS), synthesis/release of bioactive compounds, especially the metabolism of phenolic compounds, and exploitation of the potential of non-conventional flours (legumes and pseudo-cereals) and milling by-products (bran and germ). A brief description on the spiritual, cultural and functional/nutritional significance of leavened bread throughout centuries has also given.

### 1. Introduction

Lactic acid fermentation is the most traditional, natural, sustainable and effective tool for ensuring hygiene, rheology, sensory and shelf life features, and improving the functional/nutritional value of many animal and plant foods and beverages. As known since many centuries, this definition also fits in part for sourdough fermentation, which uses lactic acid bacteria in mixture with yeasts. Most of the scientific research on sourdough biotechnology was approximately begun in 1990. Initially, the focus was on the technological effects of sourdough on flavor, rheology and shelf life (e.g., delay of staling, spoilage prevention) and microbial interactions in such complex ecosystem. A number of reviews well described this state of the art (for review see Corsetti and Settanni, 2007; De Vuyst et al., 2017; Gänzle et al., 2008; Gobetti, 1998; Katina, 2005; Minervini et al., 2014). More recently, the scientific research has also moved towards the functional/nutritional features of sourdough fermentation (for review see De Vuyst et al., 2016; Gobetti et al., 2014; Zannini et al., 2012; Zhao et al., 2016). Some positive

effects have been almost definitively proven. The sourdough fermentation lowers the glycemic index (GI) of bread, reducing starch digestibility, mostly through the formation of organic acids and other complementary mechanisms. The averaged GI of whole wheat bread is ca. 71, and the glycemic load (GL) for a 30-g serving size is 9. The same indices for white wheat flour bread are, respectively, ca. 71 and 10. The GI of sourdough wheat bread is ca. 54, and its GL for a 30-g serving size is 8 (D'Alessandro and De Pergola, 2014). According to the Harvard Medical School recommendation, which ranks food with a GI  $\leq 55$  as low, between 56 and 69 as moderate and  $\geq 70$  as high GI foods, sourdough wheat bread is, therefore, recognized as a low GI food (D'Alessandro and De Pergola, 2014). Sourdough fermentation is undoubtedly efficient in reducing to less than half the phytate content of whole wheat bread. This is mainly due to the reduction in pH, which provides favorable conditions for cereal endogenous phytase activities (Gobetti et al., 2014). Phytic acid degradation allows an increase in mineral, free amino acid (FAA) and protein bioavailability. Proteolysis via cereal endogenous cereal protease or exogenous protease and

**Abbreviations:** ACE, Angiotensin I-converting enzyme; ANF, anti-nutritional factors; ATIs, amylase/trypsin inhibitors; BOA, 1,3-benzoxazol-2-one; BP, Bioactive peptides; Bx, Benzoxazinoids; CVD, cardiovascular disease; DF, dietary fibers; DIBOA, 2,4-dihydroxy-1,4-benzoxazin-3-one; DPPH, diphenyl-2-picryl-hydrazyl; FAA, free amino acids; FLAB, fructophilic lactic acid bacteria; FODMAPs, fermentable oligo-, di-, and monosaccharides and polyols; FRAP, ferric ion-reducing antioxidant power; GABA, glutamate into  $\gamma$ -amino butyric acid; GI, glycemic index; GL, glycemic load; HBOA, 2-hydroxy-1,4-benzoxazin-3-one; HPAA, N-2-hydroxyphenyl-acetamide; IBS, irritable bowel syndrome; RFOs, raffinose family oligosaccharides; WGA, wheat germ agglutinins

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<https://doi.org/10.1016/j.ijfoodmicro.2018.05.018>

Received 11 April 2018; Received in revised form 15 May 2018; Accepted 17 May 2018

Available online 18 May 2018

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peptidases from sourdough lactobacilli positively influences the allergy and intolerance responses of cereal sensitive individuals (Gobbetti et al., 2014). A prime example of this potential is the manufacture of baked goods with wheat flour, whose gluten has been fully hydrolyzed during sourdough fermentation, thus becoming safe for consumption by individuals with celiac disease (Gobbetti et al., 2014).

As supported by an abundant literature, other functional/nutritional aspects of the sourdough fermentation have emerged in recent years. The focus of research has been on the use of sourdough fermentation for salt reduction in baked goods, management of irritable bowel syndrome (IBS), synthesis/release of bioactive compounds and exploitation of the potential of non-conventional flours (legumes and pseudo-cereals) and milling by-products (bran and germ). This review reports novel insights on the above functional/nutritional features of sourdough fermentation, following a brief summary of the spiritual, cultural and functional/nutritional significance of leavened bread throughout centuries.

## 2. The cultural and nutritional significance of leavened bread

Leavened bread has always been a central element of the history. Its narration has reflected human spirituality and civilization, especially in the Mediterranean populations. Pronouncing bread, human brain activates a plurality of images, which refer not only to foods but also to spiritual events. Egypt is probably the motherland for sourdough bread (Guidotti, 2005). In the Egyptian dialect, bread and life are pronounced using the same Arabic term *aish*, which means life. The Catholic religion magnifies bread as the “food of eternal life”. This statement assumes a Eucharistic meaning that had and has no equal in history. Biblical and medieval traditions describe bread as an indispensable staple food. What we eat in a meal together with bread is defined as the *companatico*, which literally indicates a complementary food that accompanies the primary nourishment. The Bible reports: “you will obtain bread with the sweat of your forehead” (Gen 3:19). This symbolizes the way of redemption, which followed the disobedience of progenitors who had taken fruits from the forbidden tree. Consequently, the history never reported contraindication to bread consumption. Everyone may have bread under different social, cultural and religious contexts. Even the Benedictine rule, whose diet relies on rigorous ascetic rules, considers bread the primary nourishment for monks. During the punishment for more or less serious faults, the limitation to “bread and water” establishes the minimum but indispensable food supply. Bread is the symbol for eternal salvation in the Christian tradition. Gospel identifies bread with Christ himself. “I am the bread of life, whoever comes to me will never be hungry”, or “whoever eats this bread will live forever” (Jn 6, 35:58). According to Gospel by Luke, Jesus, during the Last Supper, took a loaf, gave thanks, broke it and gave it to apostles saying “this is my body, which is given for you; do this in memory of me” (Lk 22:19).

The history of art used bread for a multitude of representations. In the *Tacuina Sanitatis* (11th century) bread becomes the key element of many religious reproductions, also with nutritional meaning: “white bread improves human wellness but it had to be completely fermented”. To date, bread is among the fundamental foods for planet sustenance. UNESCO included bread within the list of the intangible heritage of humanity. Bread is a fundamental food of the “Mediterranean diet”, which could be considered the modern projection of the Benedictine “monastic diet”. The miracle of bread is summarized as follows: it greets every morning with its fragrant freshness and, at the same time, it evokes the Father in the Christian tradition “*panem nostrum cotidianum da nobishodie*” to have his blessing (Archetti, 2014).

## 3. Salt reduction

The elevated consumption of dietary sodium (ca. 10 g/day) is the leading cause of cardiovascular disease (CVD) and hypertension, with a link to risks of stroke, stomach cancer, kidney disease and bone demineralization (De Wardener and Macgregor, 2002). High blood pressure

is one of the major manageable factors used to monitor CVD (He and Macgregor, 2007). Therefore, controlling blood pressure through the reduction of sodium intake became a non-deferrable issue. The World Health Organization and EU have recommended cooperation with food industries to encourage a reduction in the sodium contentment in products, in order to effectively lower the consumer intake to < 2 g Na/day. Bread and other cereal-baked goods contribute ca. 30% to the daily intake of sodium in the Western diet. Salt reduction is challenging since sodium chloride impacts on flavor and other physical properties of baked goods. Bakeries have explored various technology options (for review see Silow et al., 2016). Overall, these concerned the systematic reduction in sodium levels, the enhancement of sodium chloride perception by taste contrast, and the addition of bittering agents to the recipe. Salt replacers such as potassium chloride, spices and taste enhancers, malt and barley, amino acids, monosodium glutamate and yeast products have also been investigated. Results were contradictory and none of these options is entirely effective or suitable salt replacement strategy.

The sourdough fermentation has beneficial effects either masking the decreased salt content or enriching bakery products with functional antihypertensive compounds. Because of the synthesis of flavoring FAA and amino acid derivatives during fermentation, the sourdough has compensative effects on salt reduction, which also depends on the species and strain of lactic acid bacteria. The addition of rye malt sourdough, fermented with glutamate-accumulating *Lactobacillus reuteri* strains, enabled a lowering of the salt content in bread from 1.5 to 1%, without affecting taste and other quality parameters (Zhao et al., 2015). Breads containing sourdough-fermented wheat germ tasted more salty when compared to conventional bread (Rizzello et al., 2010a). The higher saltiness was provided by the combined effect of acidification and proteolysis, and wheat germ chemical composition. The bread of Altamura has a very long tradition, being the first bread in Europe that had the status of Protected Denomination of Origin. Recently, a novel low-sodium sourdough-fermented recipe was set up for this bread and in vivo challenged through a 6-month randomized, controlled pilot trial on stage I-II hypertensive patients (Cosola et al., 2018). Compared to patients consuming the conventional bread or following a low-sodium (2300 mg Na/day) diet but consuming the conventional bread, those following the low-sodium diet and eating the novel low-sodium bread (280 mg Na/100 g) showed decreased urinary sodium, and systolic and diastolic blood pressure. The flow-mediated dilation also improved. Lactobacilli have the capacity of converting glutamate into  $\gamma$ -amino butyric acid (GABA) by glutamate decarboxylase, which represents a defense mechanism to counteract acidification. GABA has several well-characterized bioactive functions, including the induction of hypotension. Although further clinical studies are needed to strengthen the efficiency of sourdough breads enriched in GABA, sourdough bread or other baked goods are staple foods and their daily consumption easily favors the ingestion of physiological levels of GABA (10–12 mg/day) to decrease blood pressure in moderately hypertensive patients (Inoue et al., 2003). The sourdough fermentation of flours from protein rich pseudo-cereals (e.g., quinoa, amaranth, buckwheat) and chickpea (Coda et al., 2010) or buckwheat sprouts (Nakamura et al., 2013) was another possibility to enrich various baked goods with GABA. During sourdough fermentation, lactic acid bacteria may also synthesize Angiotensin I-converting enzyme (ACE) inhibitory and antioxidant peptides (Gobbetti et al., 2014). ACE inhibitory peptides hinder the vasoconstrictor effects of Angiotensin II and enhance the vasodilator activity of bradykinin. Both of these activities lower blood pressure. Targeting blood pressure reduction, the manufacture of sourdough breads combined the capacity to synthesize GABA and ACE inhibitory peptides.

The Gaussian distribution and the lack of a definable bimodal distribution of blood pressure suggest a regulation through complex group of genes, which interact with epigenetic and environmental factors (Pedro and Raj, 2015). Among these factors, the gastrointestinal tract is part of the overall regulation of sodium balance and blood pressure,

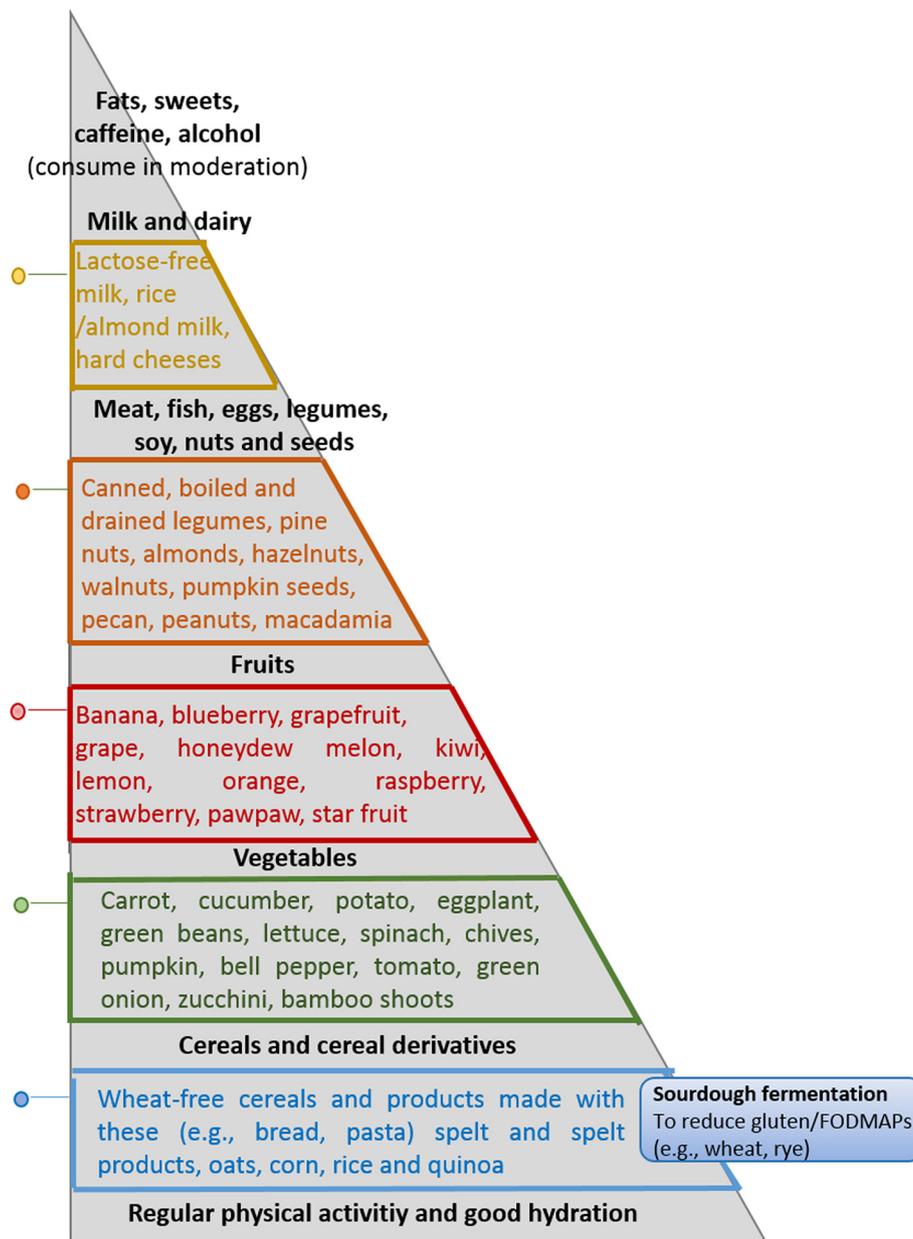


Fig. 1. Concept of low FODMAPs diet in the management of the Irritable Bowel Syndrome. Colored boxes indicate the recommended foods in the diet. (Adapted from Cozma-Petruț et al., 2017)

being the first organ exposed to ingested sodium. Consequently, the gut microbiota may have the capacity to modify the expression of hypertensive phenotypes. Fermented/metabolized products by gut microbiota influence blood pressure by regulating expenditure of energy, intestinal metabolism of catecholamine, gastrointestinal and renal ion transport, and, thus, salt sensitivity (Pedro and Raj, 2015). Adherence to a low-sodium diet, also including low-sodium sourdough bread, was effective not only in decreasing blood pressure and in improving flow-mediated dilation, but also in reducing the microbial dysbiosis associated with hypertension (Cosola et al., 2018). In general, the consumption of whole grain breads, particularly if fermented with sourdough, has the potential to guarantee gut microbiota homeostasis.

#### 4. Irritable bowel syndrome

Irritable bowel syndrome (IBS) is a common intestinal disorder causing abdominal pain, bloating, gas, diarrhea, constipation and altered gut microbiota. It has high global prevalence (11.2%) and

relevantly affects the quality of life. Dietary management is the pillar of IBS treatment. Healthcare professionals have proposed a novel and user-friendly IBS food pyramid (Cozma-Petruț et al., 2017). IBS-like complaints are often part of the non-celiac gluten or wheat sensitivity clinical picture. Conversely, recent evidence supports the hypothesis that, together with the ingestion of other specific foods, gluten, lipopolysaccharides, amylase/trypsin inhibitors (ATIs), wheat germ agglutinins (WGA) and fermentable oligo-, di-, and monosaccharides and polyols (FODMAPs) from cereals may trigger IBS symptoms (Catassi et al., 2017).

Although its role in IBS still needs clarification, a considerable proportion of IBS patients report symptoms in response to gluten, the major source of dietary protein. These patients improve under a gluten-free diet (Zannini and Arendt, 2017). As demonstrated previously (Gobbetti et al., 2014), the sourdough fermentation, under selective and specific conditions, renders free of gluten those flours (e.g., wheat, rye, barley), which are naturally rich in this protein network. Under another perspective, the peptic/tryptic-digests of a bread made with

wheat flour, having an intermediate content of gluten (ca. 70%) and still keeping rheology and sensory features almost similar to the full gluten counterpart, showed absence of toxicity towards K562 and T84 human cell lines (Gobetti et al., 2014). The protein digestibility of this bread as well as other nutritional indices improved. A randomized, crossover-controlled trial with IBS patients showed the safety of reduced-gluten wheat bread and pasta (Calasso et al., 2018). After 6 weeks of consumption, the Visual Analogue Scale for IBS and Hospital Anxiety and Depression Scale analyses showed a statistically ( $P < 0.05$ ) significant improvement in the overall IBS symptom severity. The chemical, rheology and sensory features of these bread and pasta approached those of the gluten-containing counterparts. An interference, also due to the low FODMP content of these food products, could not be excluded. The wheat flour, rendered gluten-free ( $< 10$  ppm of residual gluten) by sourdough fermentation, was the main ingredient for making pasta (Curiel et al., 2014). Compared to gluten containing pasta and pasta made with naturally gluten-free ingredients, the in vitro protein digestibility, essential FAA profile, biological value and nutritional index were higher, while maintaining suitable technological and cooking parameters. The conclusive proof for the overall higher digestibility of sourdough breads with respect to chemically leavened counterparts or to breads fermented with baker's yeast alone is the in vivo challenge. Such investigation is almost completed in the author's laboratory, while it has preliminarily shown that croissants made with sourdough promoted better postprandial gastrointestinal function in healthy adults and were more acceptable with respect to those prepared with baker's yeast (Polese et al., 2018).

FODMAPs have received increasing attention in the dietary management of IBS. Luminal distension caused by short-chain carbohydrates, which pass unabsorbed to the colon, increases water retention and gas production, thereby leading to bloating, pain and visceral hypersensitivity. Conversely, a dramatic reduction of FODMAPs in the diet removes their potentially positive prebiotic function, causing gut microbiota dysbiosis. Contemplating these two aspects, the low FODMAP diet is the most efficient therapy (de Roest et al., 2013), which do not exclude the main vegetable and fruit nutrients and prebiotics but focuses on the degradation of FODMAPs during food processing (Fig. 1). Usually, FODMAP diet consists of a two-stage strategy. The first stage relies on the elimination phase, where all foods naturally rich in FODMAPs are excluded from the diet. In the second stage, defined as challenged phase, individuals re-introduce selectively foods rich in FODMAPs to identify the type of sugar responsible for triggering IBS symptoms. Fructans are the main cereal FODMAPs, with contents varying from 1.5 to 3.7%. Other carbohydrates present in cereals include excess fructose (1.1–3.8%), sorbitol (traces), mannitol (traces to 1.6%) and raffinose (1.4–3.8%) (Biesiekierski et al., 2011). Although the levels of these FODMAPs are not particularly high, the consumption of baked goods and, especially, bread occurs at any one meal in Western diet. Prolonged sourdough fermentation during bread making should allow diminishing FODMAP levels by up to 90% (Ziegler et al., 2016). Substantially, the processing method is more important than selection of cereal varieties with low-FODMAP contents. Compared to baker's yeast bread, sourdough wheat bread without baking improvers and using a long-time ( $> 12$  h) fermentation lowered ATIs and, especially, FODMAPs (Laatikainen et al., 2017). A randomized double-blind controlled 7-day challenge showed significantly more feelings of tiredness, joint symptoms and decreased alertness when the participants ate the sourdough bread (Laatikainen et al., 2017). Even in the presence of most fructans degraded, the accumulation of fructose is still unsafe for IBS patients. A novel biotechnological process, based on a consortium of fructophilic lactic acid bacteria (FLAB) strains and targeted commercial enzymes, degraded wheat FODMAPs during sourdough fermentation (Di Cagno et al., 2018). Endo-inulinases (EC 3.2.1.7), exo-inulinases (EC 3.2.1.80) and invertases (EC 3.2.1.26) were selected based on their complementary capacities to fully hydrolyze wheat fructans having different linkages [ $\beta$ -(1/2),  $\beta$ -(6/2), and both  $\beta$ -(1/2)

and  $\beta$ -(6/2)] and range of polymerization. *Lactobacillus kunkeii* B231, PLA21 and PF16 completely metabolized fructose, the main products of this hydrolysis, during sourdough fermentation (4 h at 30 °C). FLAB belong to a special group of lactic acid bacteria that prefer fructose instead of glucose as a carbon source. These strains are mainly isolated from fructose-rich niches (e.g., fruits, flowers-based fermented foods, gastrointestinal tract of honeybees) (Endo et al., 2009). Sourdough yeasts also have the capacity to degrade fructans. Bread making using *Saccharomyces cerevisiae* invertase allowed the degradation of ca. 80% fructans. Inulinase-secreting *Kluyveromyces marxianus* strains decreased the level of fructan by ca. 90% (Struyf et al., 2017). As shown using in vitro batch cultures, breads manufactured according to various times of sourdough fermentation favored a different assembly of the colonic microbiota in healthy subjects and IBS donors (Costabile et al., 2014). Long-time fermented sourdough bread (up to 6 h) caused a significant decrease of  $\gamma$ -Proteobacteria and most Gemmatimonadetes species and, more in general, favored a low cumulative gas emission. Sourdough fermented breads were less likely to induce IBS symptoms with respect to breads made with baker's yeast or using the Chorleywood process.

## 5. Bioactive compounds

According to tradition, cultural heritage and recent scientific evidence, only cereal foods with low GI and rich in fiber, as those subjected to sourdough fermentation, found place at the base of the Mediterranean diet pyramid (Fig. 2). Other functional features strengthen this recommendation and placement. Cereals per se contain classes of phytochemicals. These phytochemicals roughly divide into flavonoids (relatively scarce) and non-flavonoid phenolics, which mainly include alkylresorcinols, lignans, phenolic acids (the most abundant) and tocots. Others are benzoxazinoids, betaines, folates, phytate and sterols. Most of these chemicals have inherent functional features, mainly antioxidant activity, but processing conditions (e.g., milling, malting/germination, fermentation) influence markedly their levels and bioavailability (Hassani et al., 2016).

Cereal germination and malting not only produce fermentable extracts for brewing and distilling industries, but also allow the natural and sustainable increase of health-promoting ingredients. For millennia, soaking in water and germination preceded grain consumption. Flours from germinated cereals have better nutritional features than those from non-germinated grains. The concentration of folate (vitamin B9) in germinated wheat and rye grains was higher than that of non-germinated grains (Hefni and Witthöft, 2012). The same regarded the content of vitamin B2 (riboflavin) in germinated red and white sorghum (Ochanda et al., 2010). Beers have different contents of thiamin (vitamin B1) and riboflavin since the use of raw matrices and malting conditions, including the activity of fermenting microbiota (Hucker et al., 2011). Steeping at low temperature prior germination enhance the accumulation of GABA during germination of waxy barley grain hulls (Chung et al., 2009). Lactic acid fermentation of buckwheat sprouts allowed the release of new BP with significant blood pressure-lowering effects in hypertensive rats and with increased levels of GABA and tyrosine (Koyama et al., 2013). Sourdough fermentation of mixtures of wheat, rye, spelt, oat, buckwheat, rice, amaranth, millet, chickpea, soy and quinoa flours by *Lb. plantarum* and *Lactococcus lactis* made functional a bread enriched in GABA (Coda et al., 2010). The fermentation with *Lactobacillus sakei* enriched of GABA rice bran extracts (Kook et al., 2010). Germination triggers  $\alpha$ - and  $\beta$ -amylases, proteases and di-phenol-oxidases in grains, which break down starch, fibers, and proteins, and increase the content of functional compounds. Anti-nutritional factors (ANF) (e.g., enzyme inhibitors, hemagglutinins, anti-vitamins) also decrease or disappear during germination (Singh and Sharma, 2017). Grain germination shapes and assembles the flour autochthonous microbiota, which, in turn, influences the preparation and/or use of sourdough. Germinated sprout varieties harbored low abundances of *Pseudomonadaceae*, and elevated numbers of *Bacillaceae*,

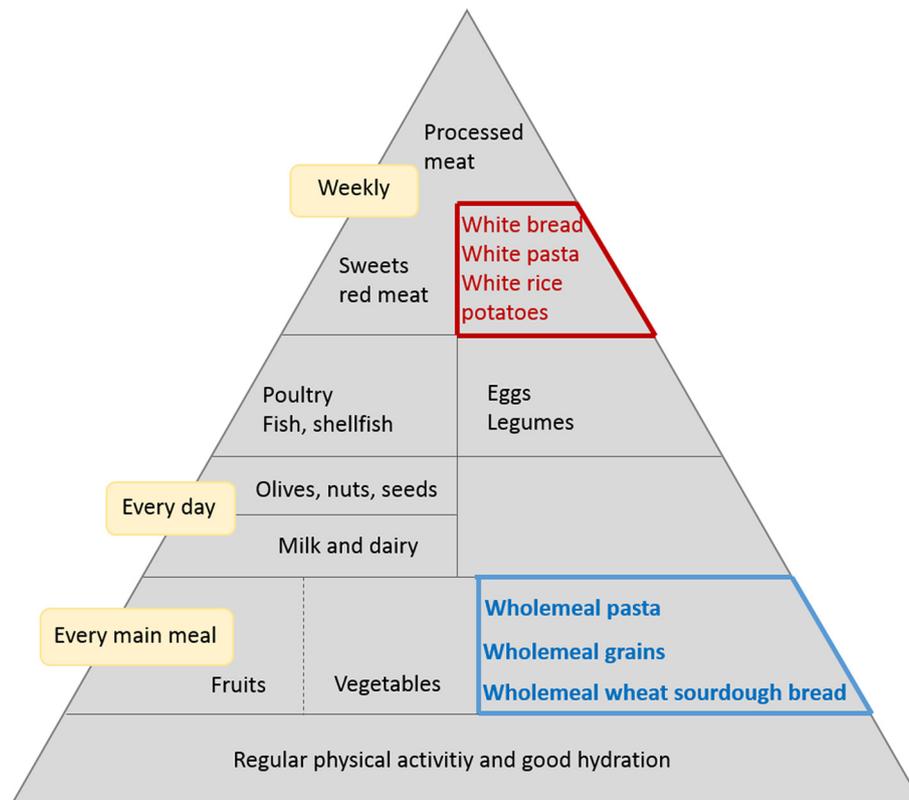


Fig. 2. Example of Mediterranean diet pyramid. (Adapted from D'Alessandro and De Pergola, 2014)

*Sphingomonadaceae*, *Phyllobacteriaceae* and *Lactobacillaceae* (Landry et al., 2018).

Among processing conditions, the sourdough fermentation has the most pronounced impact on the levels and bioavailability of phytochemicals. The antioxidant potential of wheat bran-flour mixture and rye flour was higher than that found in conventional products, when subjected to sourdough fermentation (Rizzello et al., 2012a). The antioxidant potential of sourdough rye breads was higher than that of white wheat breads. Sourdough fermentation increased the levels of extractable phenolic compounds (Liukkonen et al., 2003). The levels of lignans and alkylresorcinols, and, in particular, those of folates and free phenolic acids increased, respectively, up to seven- and ten-times during sourdough fermentation of germinated rye (Katina et al., 2007). Sourdough fermentation increased the levels of folates in rye bread because of the presence of sourdough folate producing yeasts. The high level of carotenoids in einkorn maintained during exposure to atmospheric oxygen because the favorable environmental modification induced by sourdough fermentation. Einkorn sourdough breads evidenced marked anti-inflammatory activity (Antognoni et al., 2017). The mechanisms for explaining these effects are diverse (Fig. 3). The complex metabolic pathways involve several secondary cereal metabolites according to the metabolic labyrinth model undertaken by bacteria during plant fermentation (for review see Filannino et al., 2018). The physiological significance of the metabolism of phenolic compounds in lactic acid bacteria has explained as an efficient mechanism to detoxify such compounds. Overall, phenolic acids account for almost one-third of the dietary phenols. Either they are present in soluble form within the cytoplasm or they covalently bonded to plant cell wall. Specific glycosyl hydrolases of *Lactobacillus plantarum* and *Lactobacillus rhamnosus* disintegrated the plant cell wall matrix, leading to the release of bound phenolic compounds, which favored the de-polymerization of high molecular weight phenolics (Filannino et al., 2018). Usually, the increase of extractable phenolic compounds is responsible for the

enhancement of the antioxidant capacity. Long-time sourdough fermentation of several cereals (e.g., buckwheat, barley, wheat, rye) increased the total content and extractability of phenolics, and antioxidant activities as measured bydiphenyl-2-picryl-hydrazyl (DPPH) radical scavenging activity, ferric ion-reducing antioxidant power (FRAP), and lipid peroxidation inhibition ability (Đorđević et al., 2010). Enzymes of *Lb. plantarum* and *Lactobacillus casei* released flavonoids and isoflavone aglycones from corresponding glycosides. The aglycones metabolism by lactic acid bacteria liberated ferulic and *p*-coumaric acid, which were first decarboxylated into 4-vinylguaiacol and 4-vinylphenol, and then reduced into 4-ethylguaiacol and 4-ethylphenol, respectively (Filannino et al., 2018). *Lactobacillus fermentum* decarboxylated caffeic acid into 4-vinylcatechol or reduced it into dihydro-caffeic acid (Svensson et al., 2010). Although endogenous cereal enzymes may have a potential role in the hydrolysis of phenolic acid esters and flavonoid glycosides, other specific esterase, glucosidase, phenolic acid decarboxylase, and phenolic acid reductase activities by lactobacilli had the capability to convert phenolic compounds during sorghum sourdough fermentation (Gänzle et al., 2014; Gänzle, 2014). The use of decarboxylase-positive lactobacilli explained the formation of the pyrano-3-deoxyanthocyanidins during sorghum fermentation by bacterial decarboxylation of hydroxycinnamic acids (Bai et al., 2014). Benzoxazinoids (Bx) are present in cereal grains as stable hexose or dihexose conjugates, the main compounds being 2,4-dihydroxy-1,4-benzoxazin-3-one (DIBOA) and 2-hydroxy-1,4-benzoxazin-3-one (HBOA) (Tanwir et al., 2013). Bx and their metabolites are molecules with potential human health benefits showing an increasing and recent interest (Dihm et al., 2017). The sourdough process favored the hydrolysis of DIBOA into a single hexose conjugate and degraded it even into 1,3-benzoxazol-2-one (BOA). The N-2-hydroxyphenyl-acetamide (HPAA) was a metabolite of benzoxazinoids in sourdough rye bread. HPAA may derive from both BOA and HBOA, and the sourdough microbiota has the capacity of a similar conversion (Hanhineva et al.,

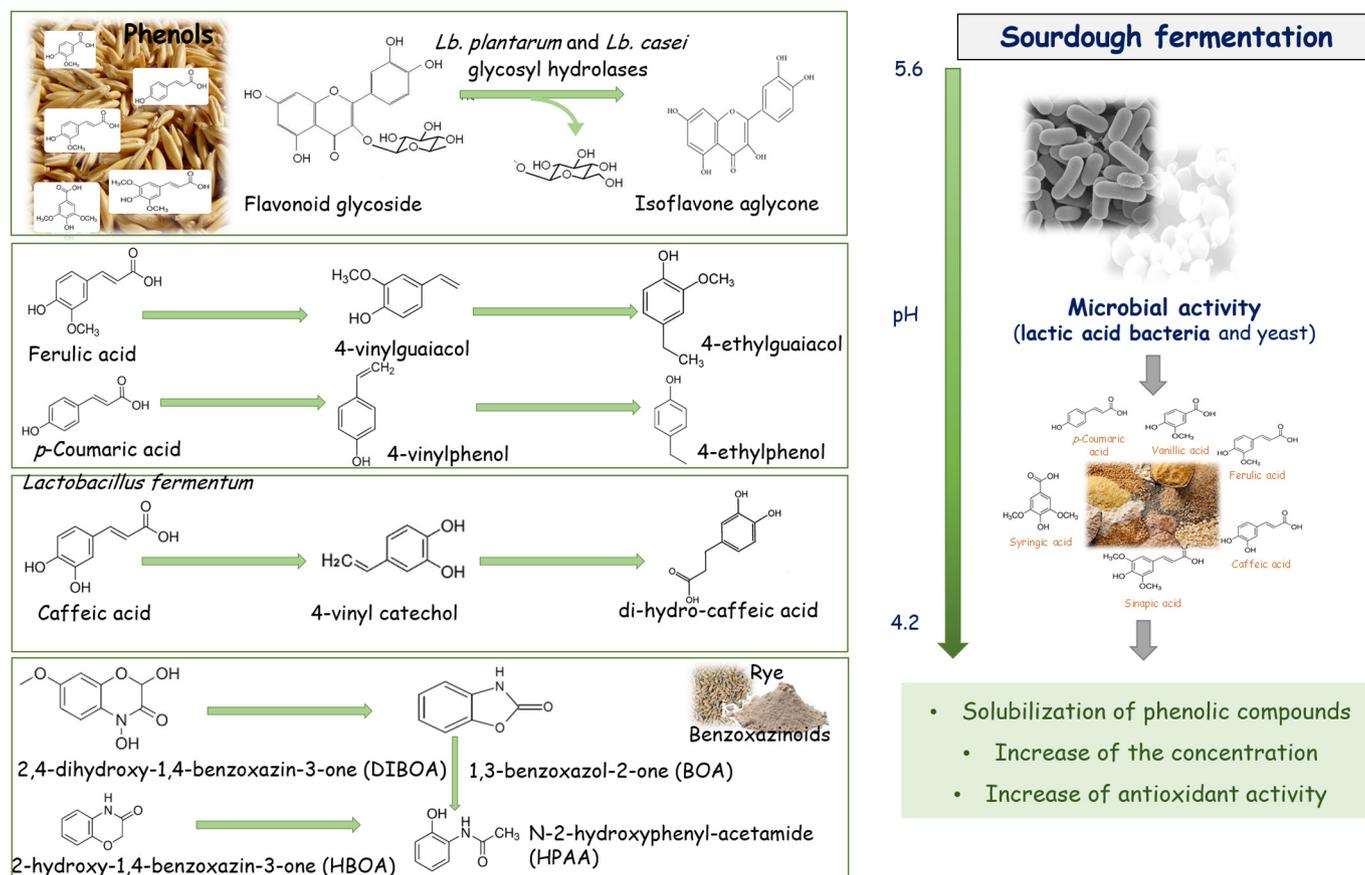


Fig. 3. Examples of phenolic compounds metabolism by lactic acid bacteria during sourdough fermentation.

2014). The de-conjugation of Bx occurring during sourdough fermentation continued in the colon by microbial enzymes, which release the aglycone of HBOA and promote its potential further degradation into unknown metabolites. The antioxidant activity by sourdough lactic acid bacteria relies also on other complementary physiological mechanisms. A number of lactobacilli reinforce their inherent cellular antioxidant defense through the secretion of antioxidant enzymes like superoxide dismutase. Lactobacilli promote the synthesis of glutathione, the main non-enzymatic antioxidant and free-radical scavenger. Exopolysaccharides are other biomolecules synthesized by lactic acid bacteria, which also share antioxidant activity (Laurent-Babot and Guyot, 2017).

Bioactive peptides (BP) are amino-acid chains natively encrypted in protein sequences that, once liberated, exhibit several functionalities in humans. The proteolysis occurs during digestion or food processing, being, in this latter case, fermentation and microbial enzyme activity as the primary tools of releasing such. Cereals (e.g., wheat, barley, corn, rice) and pseudo-cereals (e.g., buckwheat, amaranth) are important sources of BP with anticancer, anti-inflammatory, antioxidant, and cardiovascular protective features (Malaguti et al., 2014). Fermentation of whole meal wheat, soybean, barley, amaranth and rye flours with sourdough lactic acid bacteria, previously selected for their proteolytic activity, successfully increased the concentration of the anticancer peptide lunasin (Rizzello et al., 2012b), the most widely studied peptide for its anticancer activities. Selected lactic acid bacteria had the capacity to release antioxidant BP from spelt and kamut during sourdough fermentation (Gobbetti et al., 2014). The ex vivo antioxidant activity of these BP was comparable to that of  $\alpha$ -tocopherol.

## 6. Legumes

After cereals, *Leguminosae* are the second most popular food crop worldwide. The global value for leguminous crops is ca. 31 billion US

dollars per year (Abate et al., 2011). A growing interest to include legumes in the diet and to prepare legume-based novel foods has emerged. According to World Health Organization, legumes are essential components of the daily diet, which provide proteins, dietary fibers (DF), vitamins, minerals, oligosaccharides and phenolics. The frequent consumption of legumes decreases the risk of CDV, type 2 diabetes, some types of cancer, and overweight and obesity. Instead of these potential benefits, the world consumption of legumes is below than the recommended dose (McCrorry et al., 2010). Legume fermentation is traditional in many countries, especially outside of Europe. It brings a number of advantages by enhancing sensory features, improving nutritional value and decreasing ANF.

One of the most suitable option to increase the consumption of legumes in the daily diet is to use their flours in the formulas for making baked goods and to improve their sensory and functional features through sourdough fermentation. The careful selection of legumes, based on their nutritional complementarity, is also of pivotal importance. Table 1 summarizes the most relevant effects of sourdough fermentation on legume flours. Although the addition of soybean to bread undoubtedly improves the nutritional value, its level is usually limited because the detrimental effects on bread rheology and flavor. Adding soybean flour for making wheat sourdough bread resulted in a product with lower volume with respect to the conventional counterpart but the acceptance by consumers was good. The sour flavor hid the off flavor of soybean (Peñaloza-Espinosa et al., 2011). The potential of sourdough fermentation by *Lb. plantarum* and *Lactobacillus brevis* has exploited on nineteen traditional and certified Italian legumes, belonging to *Phaseolus vulgaris*, *Cicer arietinum*, *Lathyrus sativus*, *Lens culinaris* and *Pisum sativum* species (Curiel et al., 2015). Compared to doughs without bacterial inoculum, the concentrations of FAA, soluble fibers, and total phenols increased. The content of raffinose decreased up to ca. 64%. Almost all fermented legumes increased antioxidant and

**Table 1**

Main nutritional and functional advantages related to the use of sourdough biotechnology for legume flours fermentation and production of legume-enriched wheat bread.

Legume flour	Fermenting agent	Effects	References
Bean, chickpea, grass pea, lentil, pea (local cultivars)	<i>L. plantarum</i> C48, <i>L. brevis</i> AM7	Increase of phytase activity and free amino acids, GABA, soluble fibers, and total phenols concentrations. Decrease of raffinose and condensed tannins concentrations	Curiel et al. (2015)
Cowpeas Grass pea	<i>L. plantarum</i> ATCC 14917 <i>L. plantarum</i> DSM 20174	Changes in phenolic composition and improved antioxidant activity Decrease of phytic acid concentration and trypsin inhibitory activity	Dueñas et al. (2005) Starzyńska-Janiszewska and Stodolak (2011)
Faba bean	Type I sourdough and <i>L. plantarum</i> DPPMF B24W	Decrease of vicine and convicine concentration, trypsin inhibitor activity, starch hydrolysis index. Increase of protein digestibility, free amino acids and GABA concentrations. Decrease of RFOs during sourdough fermentation	Rizzello et al. (2016b); Coda et al. (2015a); Coda et al. (2017)
Kidney beans Lentils	<i>L. plantarum</i> ATCC 14917 <i>Bacillus subtilis</i> ATCC 6051, <i>L. plantarum</i> ATCC 14917	Synthesis of GABA and ACE-inhibitory peptides Increase of free amino acids, GABA, and total phenolic compounds and ACE-inhibitory activity	Limón et al. (2015) Torino et al. (2013)
Chickpea	<i>L. plantarum</i> C48 and <i>Lactococcus lactis</i> subsp. <i>lactis</i> PU1	Increase of free amino acid and GABA concentrations; decrease of the starch hydrolysis index (HI) of the fortified wheat bread	Coda et al. (2010)
Soybean	Type I sourdough	Improved nutritional quality, as estimated by Protein Efficiency Ratio (PER); Net Protein Ratio (NPR), Apparent Digestibility (AD), true digestibility, of the fortified wheat bread	Peñaloza-Espinosa et al. (2011)
Lupine	<i>Pediococcus acidilactici</i> M1807	Decrease of the trypsin inhibitor activity; increase of protein digestibility of the fortified wheat bread	Bartkiene et al. (2011)
Chickpea/lentil/bean (mixture)	Type I sourdough	Increase of free amino acid concentration; increase of the antioxidant and phytase activities of the fortified wheat bread	Rizzello et al. (2014)
Faba bean	<i>Pediococcus pentosaceus</i> 102	Increase of protein content and digestibility, free amino acids, nutritional indexes and decrease of the predicted glycemic index in faba bean sourdough bread	Coda et al. (2017)

phytase activities. Kidney beans fermented by *Lb. plantarum* exhibited potential antihypertensive activity because the synthesis of GABA and the release of ACE-inhibitory peptides (Limón et al., 2015). The sourdough fermentation of lentils and chickpea also favored high levels of GABA (Torino et al., 2013). Fermentation of cowpeas with *Lb. plantarum* led to changes in phenolic composition and improved antioxidant activity (Dueñas et al., 2005). Type I sourdough, containing legumes flours, was prepared and propagated (Rizzello et al., 2014). The lactic acid bacteria microbiota consisted mainly of species of lactobacilli, which slightly differ from those most commonly found in cereal sourdoughs. Bread making was using 15% (w/w) of legume (chickpea, lentil and bean) flours and sourdoughs. Compared to yeasted breads and breads made with wheat flour alone, the sourdough fermentation with legume flours ensured higher levels of FAA, and phytase and antioxidant activities, and improved in vitro protein digestibility. According to levels of carbohydrates, DF and resistant starch, sourdough breads enriched with legumes also showed lower values of GI. The manufacture of sourdough bread, with the supplementation by whole meal *Lupinus angustifolius* and *Lupinus luteus* flours, enhanced the nutritional value without showing sensory and rheology differences (Bartkiene et al., 2011). Fermentation improved protein extraction, decreased ATIs activity, and increased protein digestibility. Lupine is a valuable source of protein with good nutritional balance of essential amino acids, but also with higher DF (27–31% of the kernel weight) than most of the other legumes. Bread prepared by adding lupine flour decreased blood pressure and CVD (Lee et al., 2009). Currently, the gluten-free market offers a range of products, whose consumption is safe for celiac disease patients. Nevertheless, challenges for optimal formulation remain on the way in terms of appreciable texture, flavor, and adequate nutritional features. Within that framework, legumes have recently attracted attention as structure- and texture-forming agents, as source of nutrients and bioactive compounds, and as a low-GI ingredient (Melini et al., 2017).

The presence of ANF in several legume species is one of the major limiting factor for their dietary exploitation. Some of these ANF are heat-labile (e.g., protease inhibitors and lectins) and thus thermal treatments would remove the negative effect during consumption. On

the other hand, others (e.g., phytic acid, raffinose, tannins, saponins) are heat stable. This is the case of faba bean, which contains vicine and convicine, trypsin inhibitor activity, condensed tannins and phytic acid. In particular, divicine and isouramil, active aglycone derivatives of vicine and convicine, are toxic to human carriers of a genetic deficiency of the erythrocyte located glucose-6-phosphate dehydrogenase, causing the hemolytic anemia disease known as favism (Crépon et al., 2010). De-hulling, soaking, germination, air classification, extrusion and heat or enzyme treatments have been used to reduce or eliminate ANF, but fermentation gave the most promising perspectives. Sourdough fermentation of faba bean decreased the content of vicine and convicine by > 91% and significantly reduced trypsin inhibitor activity and condensed tannins (ca. 40% on the protein-rich fraction) (Coda et al., 2015a, 2017). The degradation of the pyrimidine glycosides was complete after 48 h of fermentation and the aglycone derivatives were not detectable. Ex-vivo assays on human blood confirmed the lack of toxicity of fermented faba bean flour (Rizzello et al., 2016a). The sourdough fermentation of grass pea caused the partial or complete elimination of  $\alpha$ -galactosides, tannins, phytic acid and trypsin inhibitor activity (Starzyńska-Janiszewska and Stodolak, 2011). Compared to raw seeds, fermentation resulted in reduced levels of  $\beta$ -N-oxalyl-L- $\alpha$ - $\beta$ -diaminopropionic acid (ca. 10%) and trypsin inhibitors (ca. 30%) (Starzyńska-Janiszewska and Stodolak, 2011). The levan sucrose activity of lactobacilli converted or hydrolyzed raffinose family oligosaccharides (RFOs) during sourdough fermentation (Teixeira et al., 2012). Treatment with  $\alpha$ -galactosidase or sourdough lactic acid bacteria markedly decreased the concentration of RFOs in legumes (Rizzello et al., 2014; Teixeira et al., 2012).

## 7. By-products and pseudo-cereals

Refined cereal flours contain almost exclusively endosperm seed. Bran and germ (embryo) are milling by-products despite the high DF content and the presence of a variety of functional compounds. Currently, the major part of these milling by-products is used for livestock feed and only a small amount has a utilization as food ingredient (Coda et al., 2015b).

**Table 2**

Main nutritional and functional advantages related to the use of sourdough biotechnology for milling by-products fermentation and its use in bread making.

By-product	Fermenting agent	Effects	References
Wheat bran	<i>Lactobacillus brevis</i> E95612, <i>Kazachstania exigua</i> C81116 and enzymes (Depol 740 L and Grindamyl 1000)	Improved antioxidant activity, in vitro protein digestibility and peptides and FAA concentration.	Coda et al. (2014)
Wheat germ	<i>L. plantarum</i> LB1, <i>L. rossiae</i> LB5	Increase of FAA, in vitro protein digestibility, total phenols, and phytase and antioxidant activities. Decrease of the concentration of raffinose. Ex vivo activity for anti-proliferative, anti-metastatic and immunological effects.	Rizzello et al. (2010a, 2010b, 2013)
Wheat/oat bran (mixture)	<i>L. delbrueckii</i> subsp. <i>bulgaricus</i> 397, <i>L. curvatus</i> 2768	Improvement of the nutritional profile of the protein fraction	Zalán et al. (2015)
Durum wheat bran (micronized fractions)	<i>L. sanfranciscensis</i> DE9, <i>L. plantarum</i> 3DM	Increase of FAA, total phenols and dietary fiber and phytase and antioxidant activities in fortified bread.	Rizzello et al. (2012a)
Wheat bran	<i>S. cerevisiae</i> and cell-wall-degrading enzymes (xylanase, cellulose, $\beta$ -glucanase, and feruloyl-esterase)	Increased levels of folates, free phenolic acids, and soluble arabinoxylans of bread. Increase of the in vitro and in vivo bioavailability of phenolic acids and their metabolites, having <i>ex vivo</i> immunomodulatory effects in fortified bread.	Katina et al. (2012); Mateo Anson et al. (2011)
Rye bran	<i>S. cerevisiae</i> and enzymes (Depol 740 L and Grindamyl 1000)	Increase of soluble fiber content, release of protein from aleurone cells, ferulic acid and short chain fatty acids in fortified wheat bread.	Nordlund et al. (2013)

Different processing techniques may enhance the biological value of bran, also eliminating or reducing some technological drawbacks such as loss of volume in baked goods and unappealing taste. Notwithstanding the importance of milling protocols for having bran particles with different dimensions that variously influence the manufacture of baked goods, bran sourdough fermentation, also in combination with enzymes, is one of the optimized tools for the above purposes (Coda et al., 2015b). Table 2 summarizes the most relevant effects of sourdough fermentation on bran and germ utilization. Sourdough fermentation of wheat and rye bran was successful to improve loaf volume, crumb structure, flavor and shelf life of bread (Hartikainen et al., 2014). In particular, the pungent flavor or bitter aftertaste of bran attenuated. Sourdough fermentation of wheat bran with *Lb. brevis* and *Kazachstania exigua* improved the antioxidant activity, content of peptides and FAA, and in vitro protein digestibility (Coda et al., 2014). Other sourdough species such as *Lactobacillus delbrueckii* subsp. *bulgaricus* and *Lactobacillus curvatus* improved the protein profiles and the shelf life of the sourdough bread made with a mixture of wheat and oat bran (Zalán et al., 2015). Phytase activation and decrease of starch digestibility, which lowers the glycemic response, are other effects (Coda et al., 2015b). Fractions from debranning of durum wheat have subjected to micronization and air fractionation, obtaining coarse and fine fractions, which differed for particle size, total dietary fiber, protein and fat. *Lactobacillus sanfranciscensis* and *Lb. plantarum* were the starters to ferment soft wheat doughs, containing 5% of the above fractions. Compared to wheat flour alone, these supplementations increased the concentration of FAA, total phenols and dietary fiber as well as the phytase and antioxidant activities of doughs. The rheology and sensory properties of breads containing bran fractions improved also (Rizzello et al., 2012a). Enzymes with various carbohydrate-degrading activities favored the growth and acidification of *Lb. brevis* by increasing the content of fermentable sugars of bran-enriched mixtures (Katina et al., 2012). Xylanase,  $\beta$ -glucanase,  $\alpha$ -amylase, cellulase and ferulic acid esterase, in combination with *Saccharomyces cerevisiae*, brought to an enhanced in vitro and in vivo bioavailability of phenolic acids and their metabolites, which had *ex vivo* immunomodulatory effects (Mateo Anson et al., 2011). A similar effect was observed when rye bran was fermented with cell-wall hydrolyzing enzymes and *S. cerevisiae* (Nordlund et al., 2013). As the noblest fraction of the kernel, the germ contains  $\alpha$ -tocopherol, vitamins, minerals, phytochemicals and proteins with high biological value. Nevertheless, germ also contains triglycerides and lipase and lipoxygenase activities. The presence of this substrate and related enzymes favors the sensitivity of flour to oxidation during storage and bread making. Sourdough fermentation was a promising process to inactivate germ lipase activities, thus allowing its use as an ingredient in baked good formulas. Germ

autochthonous lactic acid bacteria (*Lb. plantarum* and *Lactobacillus rossiae*) were the starters for making the sourdough-fermented wheat germ. The lipase activity markedly decreased and most of the volatile compounds derived from lipid oxidation were absent during storage for 40 days. Fermentation of wheat germ increased by ca. 50% the content of FAA. The concentration of raffinose decreased and the in vitro protein digestibility, total phenols, and phytase and antioxidant activities increased (Rizzello et al., 2010b). After this stabilization, the manufacture of a wheat bread included the sourdough-fermented wheat germ. Compared to the conventional counterpart, the concentration of FAA and the in vitro protein digestibility increased as well as the antioxidant activity. The sourdough-fermented wheat germ also positively influenced bread volume and rheology features (Rizzello et al., 2010a). Quinones present in wheat germ are responsible for anti-proliferative, anti-metastatic and immunological effects. Lactic acid bacteria, previously selected based on  $\beta$ -glucosidase activity, released non-glycosylated and physiologically active 2-methoxy benzoquinone, and 2,6-dimethoxybenzoquinone during wheat germ sourdough fermentation (Rizzello et al., 2013). The sourdough-fermented preparation markedly affected the proliferation of human ovarian carcinoma cells A2780, and colorectal carcinoma cells HT-29 and HCT-8. The values of IC<sub>50</sub> ranged from 0.105  $\pm$  0.005 to 0.556  $\pm$  0.071 mg/ml, with a median value 0.302 mg/ml. These results were comparable to those found for other well-known pharmaceutical preparations, disclosing the use of sourdough-fermented wheat germ as an ingredient, nutritional supplement and/or anticancer drug.

In spite of the huge amount produced, wheat and rye are not typical cereals in developing countries, where other crops comprise the local diet (Coda et al., 2010). Research on minor, ethnic and ancient grains has received worldwide interest. Pseudo-cereals such as buckwheat, quinoa and amaranth have nutritional and textural features making them suitable for replacing, at least in part, traditional cereal-based products. Sourdough fermentation is a suitable biotechnology option to incorporate nutrient-dense grains for enhancing the overall quality of wheat bread. Buckwheat is rich in antioxidants (mainly rutin and quercetin), lysine and micronutrients, and has cholesterol-lowering and prebiotic activities. Bread prepared from buckwheat flour had significant higher contents of oleic acid, magnesium and DF with respect to wheat bread (Alvarez-Jubete et al., 2010). Nonetheless, the manufacture of wheat bread enriched with buckwheat is challenging because of technological issues and increased contents of phytate and tannins, which decrease the protein digestibility and confer bitterness (Lin et al., 2009). One way for enhancing palatability, digestibility and baking performances of buckwheat flour is the preparation of buckwheat sourdough. Fermentation hydrolyzed the main buckwheat storage proteins, and reduced the phytate and tannin contents of buckwheat

flour, as already observed in sorghum. The addition of buckwheat sourdough improved the rheology features of the wheat dough, by inducing a more resistant gluten network, and positively influencing the nutritional value in terms of phenol contents (Moroni et al., 2012). FAO selected quinoa as one of the crops that are destined to offer food security in the 21st century. The high nutritional value of quinoa seeds is mainly due to the high concentrations of proteins, minerals, and vitamins. Quinoa proteins are rich in amino acids like lysine, threonine and methionine, which complement the cereal profile. Autochthonous lactic acid bacteria were the starters to ferment quinoa flour for exploiting the antioxidant potential. As in vitro shown towards DPPH and ABTS radicals, the scavenging activity of water/salt-soluble extracts from fermented doughs was significantly higher than that of non-inoculated doughs. These extracts contained a mixture of peptides, which were resistant to digestive enzymes, showed typical sequences of antioxidant compounds and had antioxidant activity towards human keratinocytes. Autochthonous *Lb. plantarum* and *Lb. rossiae* strains were the selected starters to prepare type I quinoa sourdough (Rizzello et al., 2016b). Compared to non-fermented flour, organic acids, FAA, DF, total phenols, phytase and antioxidant activities, and in vitro protein digestibility increased during fermentation. This sourdough was the starter (20%, w/w) for making a wheat bread. Compared to baker's yeast wheat breads manufactured with or without quinoa flour, the use of quinoa sourdough improved the chemical, textural, and sensory features of wheat bread, showing better performances than simple quinoa flour. Protein digestibility and quality, and the rate of starch hydrolysis were other nutritional features that markedly improved (Rizzello et al., 2016b). The cultivation of amaranth extended in Central and South America since centuries. The flour contains 13–15.5% protein, and an elevated ratio of lysine and methionine (Ruiz Rodriguez et al., 2016). Besides the high vitamin and mineral contents, amaranth is a source of BP. The food industry today is looking for the selection of sourdough lactic acid bacteria starters to ferment amaranth flour (Ruiz Rodriguez et al., 2016). The fermentation of amaranth flour with selected *Lb. plantarum* and *Lc. lactis* strains allowed the synthesis of very elevated concentrations (ca. 600 mg/kg) of GABA (Coda et al., 2010). Besides, lunasin and various lunasin fragments were found in amaranth sourdoughs fermented with the selected proteolytic strains of *Lb. curvatus* and *Lb. brevis* (Rizzello et al., 2012b).

## 8. Conclusion

An abundant literature shows the versatile functional/nutritional features of sourdough fermentation. As described in this review, salt reduction in baked goods, IBS diet management, synthesis of phytochemicals and exploitation of non-conventional flours with high nutritional value are some of the most recent examples. According to a critical approach that does not consider this biotechnology as the unique solution to optimize all processes, it is, however, fundamental to treasure historical and cultural events. In the era where food processing sustainability and naturalness, and waste reduction have recommended, the potential of sourdough fermentation needs a fully exploitation. Future efforts should be focused on targeted processes and optimally selected sourdough lactic acid bacteria and yeasts, depending on the functional/nutritional characteristics of the raw material and those desired in the food product.

## Funding sources

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

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