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Effects of Fermented Edible Seeds and Their Products on Human Health: Bioactive Components and Bioactivities

Ren-You Gan, Hua-Bin Li, Anil Gunaratne, Zhong-Quan Sui, and Harold Corke

Abstract: There is a long history of using fermentation in food production. Edible seeds, such as certain beans and cereal grains, are important in the human diet and provide many health benefits. Various microbes, such as lactic acid bacteria, molds, and yeasts, considered as generally recognized as safe (GRAS) microbes, are commonly used to ferment edible seeds and their products. Fermentation can change bioactive components and produce new bioactivities. In order to highlight the importance of fermentation on bioactive components and bioactivities in edible seeds, this review, therefore, summarizes recent relevant studies and discusses fermentation procedures and influences of fermentation on their bioactive components and bioactivities. Overall, fermented edible seeds and their products contain enhanced bioactive components, especially γ-aminobutyric acid and natural phenolics, and they possess versatile bioactivities, such as antioxidant and anti-cancer effects, and, therefore, can be recommended as an important part of the human diet, or they can be developed into functional foods to help in the prevention of certain chronic diseases.

Keywords: anti-cancer effect, anti-hypertensive effect, antioxidant effect, beans, bioactive peptides, cereal grains, fermentation, natural phenolics, vitamins, γ-aminobutyric acid

Introduction

Fermentation, an ancient food biotechnology, is still commonly employed in the food industry to extend shelf-life as well as to improve nutritional and sensory qualities of foods (Bourdichon and others 2012). This technology mainly includes natural and inoculated fermentations. The former utilizes the endophytic microbes naturally occurring on plant-based foods to perform the fermentation process, such as to make the traditional broad bean paste in China, while the latter is commonly carried out by inoculation of generally recognized as safe (GRAS) microbes into plant-based foods or milk-based foods. Therefore, an understanding of the fermentation methods can be of importance to efficiently perform the fermentation process to develop fermented foods with health benefits.

Edible seeds, such as edible beans and cereal grains, have been reported to possess many health benefits (Saleh and others 2013; Hayat and others 2014; Rebello and others 2014). Moreover, recent studies suggest that many fermented edible seeds and their products contain enhanced bioactive components and exhibit various bioactivities. In order to better understand the fermentation procedures and to highlight the importance of the effects of fermented edible seeds and their products on health, we searched for relevant original English articles based on ISI Web of Science from 2000 to the present. In this review, we first summarize and classify the fermentation procedures for edible seeds and their products, then discuss the influences of fermentation on the various bioactive components, such as vitamins, γ-aminobutyric acid (GABA), natural phenolics, and bioactive peptides, and finally we highlight the possible benefits of fermented edible seeds and their products, such as antioxidant, anti-hypertensive, and anti-cancer effects. Therefore, this article provides a comprehensive review and updated information about the bioactive components and bioactivities of fermented edible seeds and their products.

Fermentation procedures

Based on the source of microbes involved in the fermentation process, there are natural and inoculated fermentations. In addition, fermentation can be divided into solid-state fermentation (SSF) and liquid-state fermentation (LSF) according to the water content in the system. Edible seeds commonly need to be pretreated before fermentation, such as by soaking, cracking, milling, sieving, and cooking. In many cases, these processing methods are combined together. Next, we summarize and discuss some basic principles involved in the fermentation process.

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Pretreatment of edible seeds

Before the fermentation process, edible seeds should be pretreated. Fermentation commonly requires soaked, cracked, and cooked seeds or milled flour to start SSF or LSF. Of course, seeds cannot be cooked or autoclaved before natural fermentation, since this will partly or completely kill microbes existing on seeds, leading to the failure of subsequent fermentation. On the other hand, it is better to reduce microbial populations existing on seeds before inoculated fermentation, since they would compete with and inhibit the growth of inoculated microbes during the fermentation process. For example, studies found that LAB-fermented soybeans and lentil also contain generally the same amount of aerobic mesophilic bacteria compared to LAB after 48 or 96 h of fermentation, suggesting the possible competitive relationship between aerobic mesophilic bacteria and LAB during fermentation (Fernandez-Orozco and others 2007; Torino and others 2013). Therefore, edible seeds can be dried by hot air, such as at 40 to 60 °C for 24 h, or cooked/autoclaved, before the inoculated fermentation process (Duenas and others 2005; Lee and others 2008; Limon and others 2015). Overall, pretreatment of edible seeds can enhance the efficiency of fermentation.

The starter culture and inoculum

Many diverse microbes have been used as the starter culture for fermenting edible seeds and their products, mainly GRAS microbes, such as food-grade bacteria, fungi, and yeasts. Lactic acid bacteria (LAB) are the most common bacteria used in edible seed fermentation, such as *Lactobacillus* (*Lb.*) *acidophilus*, *Lb. brevis*, *Lb. bulgaricus*, *Lb. casei*, *Lb. fermentum*, *Lb. johnsonii*, *Lb. paracasei*, *Lb. plantarum*, *Lb. reuteri*, *Lb. rhamnosus*, *Lb. rossiae*, *Lb. zeae*, *Lactococcus* (*Lc.*) *lactis*, *Bifidobacterium* (*Bb.*) *animalis, Bb. infantis, Streptococcus* (*Sc.*) *thermophilus*, and *Weissella* (*W.*) *paramesenteroides* (Coda and others 2010; Dordevic and others 2010; Hole and others 2012; Ko and others 2013; Lai and others 2013; Rizzello and others 2013; Choi and others 2014a; Zhao and Shah 2014; Jhan and others 2015; Zhang and others 2015c). In addition, *Bacillus* (*B.*) *subtilis* has also been commonly used to ferment edible seeds (Torino and others 2013; Wang and others 2014; Limon and others 2015). Additionally, fungi (molds), including *Aspergillus* (*A.*) *oryzae*, *A. awamori*, *A. sojae*, *A. niger*, *Agrocybe* (*Ac.*) *cylindracea, Cordyceps* (*C.*) *militaris*, *Coprinus* (*Cr.*) *cinereus*, *Grifola* (*G.*) *frondosa*, *Ganoderma* (*Gd.*) *austral*, *Gd. neo-japonicum*, *Gd. lucidum*, *Lentinus* (*L.*) *edodes*, *Monascus* (*M.*) *purpureus*, *M. ruber, Rhizopus* (*R.*) *azygosporus*, *R. microspores*, *R. oligosporus*, *R. oryzae*, and *Thamnidium* (*T.*) *elegans* (Rhyu and others 2000; Lee and others 2004, 2006, 2008; Fernandez-Orozco and others 2007; Cai and others 2012; Salar and others 2012; Choi and others 2014c; Starzynska-Janiszewska and others 2014; Subramaniam and others 2014; Xiao and others 2014; Gamboa-Gomez and others 2016), and yeasts, such as *Issatchenkia* (*I.*) *orientalis*, *Saccharomyces* (*S.*) *cerevisiae*, and *S. boulardii* (Rekha and Vijayalakshmi 2008; Dordevic and others 2010; Fan and others 2010), have also been employed to ferment edible seeds and their products. The diversity of starter cultures provides multiple choices for fermentation, and combinations of different starter cultures may enhance fermentation efficiency, but this topic needs further investigation.

The inoculum amount of a starter culture is an important factor for the fermentation process. For LAB fermentation, inoculation of 1% to 10% (bacteria (mL)/sample (mL or g)) of the starter culture (10^8 cfu/mL) has been commonly employed in SSF and LSF of edible seeds and their products, with 10^6 to 10^7 cfu/mL LAB in original samples (Duenas and others 2005; Torino and others 2013; Gan and others 2016b). For *B. subtilis* and fungal fermentation, inoculation of 5% (bacteria (mL)/sample (mL)) of the starter culture (10^5/g sample) has been mainly employed in SSF of edible seeds (Fernandez-Orozco and others 2007; Torino and others 2013; Limon and others 2015). Overall, the inoculum of starter cultures can vary due to different starter culture organisms and substrates, and optimization of the inoculum should be necessary to perform the fermentation efficiently.

Fermentation conditions

There are several factors, such as fermentation temperature, time, humidity, and other conditions, affecting the fermentation efficiency. Natural fermentation has been reported to control the temperature at 30, 37, or 42 °C (Elyas and others 2002; Granito and Alvarez 2006; Limon and others 2015), which is probably associated with the main microbes carried by different seeds. In addition, the temperature is commonly controlled at 37 °C for LAB fermentation (Frias and others 2005; Torino and others 2013), while fermentation using *B. subtilis* and fungi has mostly been employed at 30 °C (Fernandez-Orozco and others 2007; Lee and others 2008), probably due to the optimum growth at this temperature. For fermentation time, several hours to several days has been reported, while 48 and/or 96 h is most commonly used for edible seed fermentation. In addition, it is better to control the fermentation humidity at 90% to 95% if possible (Fernandez-Orozco and others 2007; Lee and others 2008), which can provide a relatively moist air condition for the growth of microbes. SSF of edible seeds and bean milk fermentation are generally performed quiescently, while LSF of edible seeds is commonly carried out by continuous shaking/stirring, with a speed of 200 to 450 rpm (Duenas and others 2005; Frias and others 2005; Torino and others 2013; Gan and others 2016b), which can accelerate the growth of microbes, increase the interaction between microbes and substrates, and enhance the efficiency of fermentation. Similarly, adding sugars (1% to 2%) to the fermentation system, such as glucose or sucrose (Jhan and others 2015; Gan and others 2016c), can provide an extra energy source to accelerate the growth of microbes. Moreover, fermentation can be performed under aerobic or anaerobic conditions, dependent on the species of microbes involved. For example, it is better to perform LAB fermentation in an anaerobic or microaerophilic environment. Overall, the fermentation condition is critical for the efficiency of fermentation and needs to be optimized for fermenting different products.

Treatment after fermentation

After fermentation, fermented edible seeds are commonly sterilized prior to further application. Autoclaving at 121 °C for 15 min coupled with subsequent freeze-drying is a common treatment (Gan and others 2016b). In addition, hot air drying, such as at 70 °C for 3 to 4 h, has also been used to treat fermented seeds (Elyas and others 2002). On the other hand, direct freeze-drying of fermented samples has also been reported (Frias and others 2005; Lee and others 2008; Jhan and others 2015), which can be better to retain nutritional and bioactive components. It should be mentioned that the step of sterilization after fermentation may be associated with potential food safety problems, which will be discussed in the final part of this review.

Table 1–Influences of fermentation on vitamins in edible seeds and their products.

			Vitamin content			
Edible seeds and their products	**Inoculated microbes**	**Vitamins**	**Nonfermented samples**	**Fermented samples**	**Unit**	**References**
Kidney bean (*Phaseolus vulgaris*)	Natural fermentation	Vitamin B1	0.20	0.13 to 0.17	mg/100 g DW	(Granito and others 2002)
		Vitamin B2	0.12	0.14 to 0.16	mg/100 g DW	
Lupin (*Lupinus albus* L. var. Multolupa)	Natural fermentation	Vitamin C	6.48	N.D.	mg/100 g DW	(Frias and others 2005)
		α-Tocopherol	0.19	0.25	mg/100 g DW	
		γ-Tocopherol	20.1	18.9	mg/100 g DW	
		δ-Tocopherol	0.25	0.14	mg/100 g DW	
	Lb. plantarum CECT 748	Vitamin C	6.48	N.D.	mg/100 g DW	
		α-Tocopherol	0.19	0.08	mg/100 g DW	
		γ-Tocopherol	20.1	2.35	mg/100 g DW	
		δ-Tocopherol	0.25	0.04	mg/100 g DW	
Red bean (*Phaseolus radiates*)	*B. subtilis* (BCRC 14716)	Vitamin C	5.41	192	mg/g	(Jhan and others 2015)
	and *Lb. delbrueckii* sp. bulgaricus (BCRC 14008)	Vitamin E	0.08	0.38	mg/g	
Soybean (*Glycine max* cv. Merit)	*A. oryzae* 2094^{T} (ATCC 1011)	α-Tocopherol	1.00	0.16	mg/100 g DW	(Fernandez-Orozco and others 2007)
		β-Tocopherol	0.25	0.32	mg/100 g DW	
		γ-Tocopherol	4.10	12.8	mg/100 g DW	
		δ-Tocopherol	1.65	15.8	mg/100 g DW	
	R. oryzae CECT 2340 (ATCC 24563)	α-Tocopherol	1.00	0.32	mg/100 g DW	
		β-Tocopherol	0.25	0.35	mg/100 g DW	
		γ-Tocopherol	4.10	10.9	mg/100 g DW	
		δ-Tocopherol	1.65	16.2	mg/100 g DW	
	B. subtilis CECT 39^{T} (ATCC 6051)	α-Tocopherol	1.00	0.79	mg/100 g DW	
		β-Tocopherol	0.25	0.57	mg/100 g DW	
		γ-Tocopherol	4.10	15.4	mg/100 g DW	
		δ-Tocopherol	1.65	13.4	mg/100 g DW	
	Lb. plantarum CECT 748^{T} (ATCC 14917)	α-Tocopherol	1.00	0.01	mg/100 g DW	
		β-Tocopherol	0.25	0.22	mg/100 g DW	
		γ-Tocopherol	4.10	3.34	mg/100 g DW	
		δ-Tocopherol	1.65	5.93	mg/100 g DW	
	Natural fermentation	α-Tocopherol	1.00	0.01	mg/100 g DW	
		β-Tocopherol	0.25	0.21	mg/100 g DW	
		γ-Tocopherol	4.10	3.41	mg/100 g DW	
		δ-Tocopherol	1.65	6.07	mg/100 g DW	
	Lb. plantarum CECT 748^{T} (ATCC 14917)	α-Tocopherol	1.00	0.01	mg/100 g DW	
		β-Tocopherol	0.25	0.22	mg/100 g DW	
		γ-Tocopherol	4.10	3.33	mg/100 g DW	
		δ-Tocopherol	1.65	6.17	mg/100 g DW	
	Natural fermentation	α-Tocopherol	1.00	0.01	mg/100 g DW	
		β-Tocopherol	0.25	0.21	mg/100 g DW	
		γ-Tocopherol	4.10	3.43	mg/100 g DW	
		δ-Tocopherol	1.65	6.17	mg/100 g DW	
Soymilk	*G. frondosa* GCMCC 5.00248	Thiamin	3.27	10.8	mg/L	(Yang and others 2015)
		Niacin	3.84	8.74	mg/L	
		Riboflavin	0.81	0.54	mg/L	
	Lb. casei Zhang	Vitamin B6	∼2.00	20.9	mg/L	(Li and others 2012)
	Bb. animalis V9 (CP001892)	Vitamin B6	∼2.00	18.1	mg/L	
	Lb. acidophilus NCFM	Vitamin B6	∼2.00	17.9	mg/L	
	Lb. rhamnosus GG	Vitamin B6	∼2.00	14.2	mg/L	
	Bb. animalis BB12	Vitamin B6	∼2.00	13.4	mg/L	
	Lb. casei Shirota	Vitamin B6	∼2.00	13.9	mg/L	
	Lb. acidophilus CSCC 2400	Vitamin C	431	16.2 to 227	μg/g	(Zhao and Shah 2014)
		Thiamin	35.9	41.3 to 61.1	μg/g	
		Riboflavin	196	N.D.	μg/g	
		α-Tocopherol	237	73.2 to 214	μg/g	
	Lb. paracasei CSCC 279	Vitamin C	431	70.2 to 256	μg/g	
		Thiamin	35.9	4.10 to– 14.1	μg/g	
		Riboflavin	196	179	μg/g	

(*Continued*)

Table 1–Continued.

Edible seeds and their products	Inoculated microbes	Vitamins	Vitamin content		Unit	References
			Nonfermented samples	Fermented samples		
		α-Tocopherol	237	186 to 304	μg/g	
	Lb. zeae ASCC 15820	Vitamin C	431	182 to 315	μg/g	
		Thiamin	35.9	7.20 to 16.6	μg/g	
		Riboflavin	196	185 to 186	μg/g	
		α-Tocopherol	237	343 to 361	μg/g	
	Lb. rhamnosus WQ2	Vitamin C	431	27.9 to 183	μg/g	
		Thiamin	35.9	13.8 to 30.1	μg/g	
		Riboflavin	196	N.D.	μg/g	
		α-Tocopherol	237	278 to 377	μg/g	
Buckwheat groats (*Fagopyrum esculentum* Moench)	*R. oligosporus* NRRL 2710	Thiamin	9.70	10.9	μg/g	(Malgorzata and others 2015)
		Pyridoxine	1.65	1.70	μg/g	
		Pyridoxine	120	330	μg/g	
		Vitamin C	50	110	μg/g	
		α-Tocopherol	0.73	1.10	μg/g	
		γ-Tocopherol	106	127	μg/g	
		δ-Tocopherol	2.93	3.45	μg/g	
	R. oligosporus ATCC 64063	Thiamin	0.67	1.62	mg/kg DW	(Starzynska-Janiszewska and others 2016)
		Riboflavin	0.15	1.01	mg/kg DW	

A., *Aspergillus*; *B.*, *Bacillus*; *Bb*, *Bifidobacterium*; *G.*, *Grifola*; *Lb.*, *Lactobacillus*; *R.*, *Rhizopus*; N.D., not detected. DW, dry weight.

Influences of Fermentation on Bioactive Components

Vitamins

Vitamins are important essential nutrients. Based on solubility, they can be divided into water-soluble and fat-soluble groups. The former mainly includes the vitamin B groups and vitamin C, and the latter mainly contains vitamin A, vitamin D and E groups, and vitamin K. Edible seeds, such as edible beans and cereal grains, are good natural sources of some vitamins, mainly the vitamin B and E groups (Fardet 2010; Hayat and others 2014), while fermentation has distinct influences on different vitamins in edible seeds and their products.

The vitamin B group mainly include thiamin (vitamin B1), riboflavin (vitamin B2), niacin (vitamin B3), pantothenic acid (vitamin B5), pyridoxine (vitamin B6), biotin (vitamin B7), folic acid (vitamin B9), and cobalamin (vitamin B12). Fermentation has been reported to exhibit varying effects on vitamin B members in edible seeds and their products (Table 1). Especially, fermentation by fungi and LAB, such as *G. frondosa*, *R. oligosporus*, and *Lb. acidophilus*, has been found to increase thiamin, riboflavin, niacin or pyridoxine in soymilk and buckwheat groats (Zhao and Shah 2014; Malgorzata and others 2015; Yang and others 2015; Starzynska-Janiszewska and others 2016). This suggests that some microbes may possess the capacity of producing B group vitamins, consistent with previous studies that some LAB and fungi can synthesize B vitamins (Strzelczyk and Leniarska 1985; Martens and others 2002; LeBlanc and others 2011; Capozzi and others 2012). The biosynthetic pathways of the main vitamin B group members in microbes have been reported (Magnusdottir and others 2015), and Figure 1A shows the proposed synthetic pathway of thiamin, one important B vitamin which is increased in some fermented edible seeds and their products (Table 1).

Vitamin C (also known as ascorbic acid) generally occurs at low levels in edible seeds, and fermentation can cause opposite effects on its content in different edible seeds and their products (Table 1). Fermentation was found to reduce ascorbic acid in lupin seeds and soymilk (Frias and others 2005, Zhao and Shah 2014), while increasing it in red bean and buckwheat groats (Jhan and others 2015, Malgorzata and others 2015). This discrepancy may be associated with the degradation or biosynthesis of ascorbic acid by microbes in the fermentation process, since different microbes possess the capacity of decomposing or synthesizing it (Bremus and others 2006; Linster and Van Schaftingen 2007). Several LAB have been reported to degrade ascorbic acid into simple organic acids, such as acetic and lactic acids (Montano and others 2013), while yeasts, such as *S. cerevisiae*, have been demonstrated to biosynthesize L-ascorbic acid from L-galactose (Hancock and others 2000). In addition, metabolically engineered yeasts have been reported to synthesize L-ascorbic acid from D-glucose (Branduardi and others 2007), using the synthetic pathway (Figure 1B) found in plants. On the other hand, although *R. oligosporus*-fermented buckwheat groats and *B. subtilis* combined with *Lb. bulgaricus*-fermented red bean have been reported to increase ascorbic acid compared to unfermented samples (Jhan and others 2015; Malgorzata and others 2015), whether these microbes can biosynthesize ascorbic acid needs further investigation.

E vitamins include tocopherols and tocotrienols, each with α, β, γ, and δ homolog. In most edible seeds, *γ-tocopherol* is the most abundant vitamin E, with much higher content than other tocopherols (Table 1). Fermentation has been reported to differently influence the contents of tocopherols in edible seeds and their products (Table 1), probably associated with microbes involved in the fermentation process. Fungi, such as *A. oryzae*, *R. oryzae*, and *R. oligosporus*, have been found to increase tocopherols in soybean and buckwheat groats (Fernandez-Orozco and others 2007; Malgorzata and others 2015; Starzynska-Janiszewska and others 2016). *B. subtilis* was found to significantly increase γ and δ tocopherols in soybeans (Martens and others 2002), while LAB exhibited different influences on E vitamins (Frias and others 2005; Fernandez-Orozco and others 2007; Zhao and Shah 2014). These results suggest that some microbes may biosynthesize tocopherols during the fermentation process and a possible biosynthetic pathway of *γ-tocopherol* was proposed (Figure 1C) based on a previous study (Rippert and others 2004). On the other hand, the influence of fermentation on tocotrienols has scarcely been investigated.

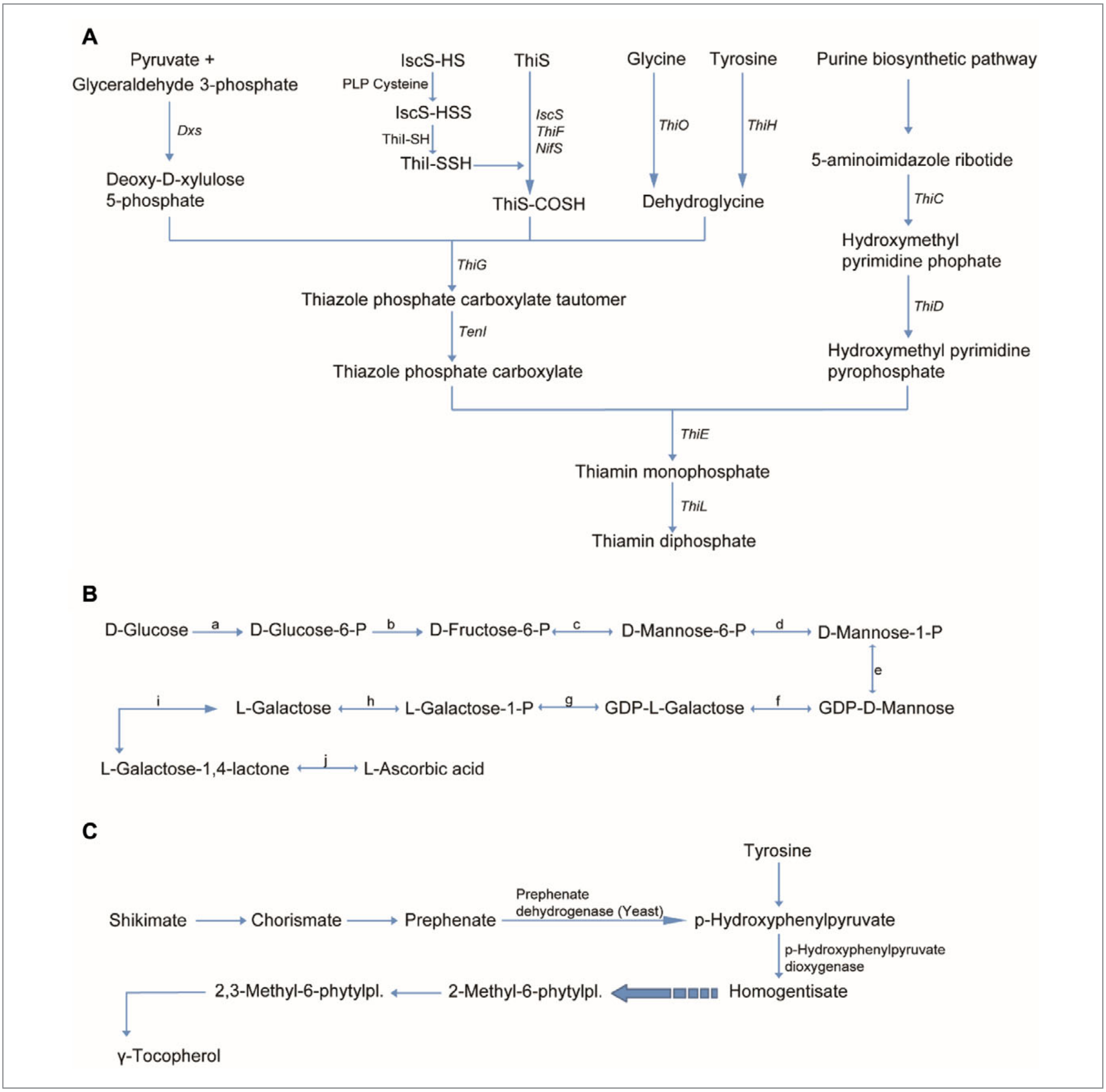

Figure 1–Proposed biosynthetic pathways of typical vitamins by microbes. (A) Proposed biosynthetic pathway of thiamin (vitamin B1), modified from Du and others (2011). Abbreviations: *Dxs*, 1-deoxy-D-xylulose 5-phosphate synthase; *IscS*, cysteine desulfurase; *NifS*, sulfur donor; *TenI*, transcriptional regulator TenI; *ThiC*, hydroxymethyl pyrimidine synthase; *ThiD*, hydroxymethyl pyrimidine (phosphate) kinase; *ThiE*, thiamin phosphate synthase; *ThiF*, adenyltransferase; *ThiG*, thiazole synthase; *ThiH*, thiazole synthase; *ThiI*, sulfur transferase; *ThiL*, thiamin phosphate kinase; *ThiO*, glycine oxidase; *ThiS*, sulfur carrier protein. (B) Proposed biosynthetic pathway of L-ascorbic acid (vitamin C), cited from Branduardi and others (2007). The enzymes a to h are as follows. a, hexokinase; b, glucose-6-phosphate isomerase; c, mannose-6-phosphate isomerase; d, phosphomannomutase; e, mannose-1-phosphate guanylyltransferase; f, GDP-mannose-3,5-epimerase; g, GDP-L-galactose phosphorylase; h, L-galactose 1-phosphate phosphatase; i, L-galactose dehydrogenase; j, L-galactono-1,4-lactone dehydrogenase. (C) Proposed biosynthetic pathway of γ-Tocopherol (vitamin E) based on a previous study (Rippert and others 2004).

In general, fermentation has distinct influences on various vitamins in edible seeds and their products, which can be associated with microbe-mediated biosynthesis or degradation of vitamins. In light of the health benefits of vitamins, it is promising to employ vitamin-producing microbes or genetically engineered microbes with enhanced vitamin-producing capacity to develop fermented edible seeds and their products rich in vitamins.

GABA

GABA, a nonprotein amino acid, is an important inhibitory neurotransmitter in the mammalian nervous system, and it plays a critical role in the regulation of blood pressure and many other physiological functions (Lee and Pan 2012; Diana and others 2014). It can be produced in plants, microorganisms, and mammals, and it is widely distributed in various foods (Jannoey and

Figure 2–Main bioactivities of fermented edible seeds and their products.

others 2010). Considering the health benefits of GABA, the need for GABA-rich foods is increasing, and various food processing methods, such as fermentation, have been employed to enhance its content (Dhakal and others 2012).

Edible seeds are natural sources of GABA, and many studies reported that fermentation can further increase GABA content in many edible seeds and their products (Table 2), such as adzuki bean, chickpea, faba bean, kidney bean, lentil, soybean, amaranth, buckwheat, millet, oat, quinoa, rice, rye, spelt, wheat, and/or their products. A variety of microorganisms has been employed in the fermentation process to enhance GABA content, and LAB are the most commonly used (Table 2). In addition, fungi and molds, such as *A. oryzae*, *R. oryzae*, and *M. purpureus*, are also used to enhance GABA content in edible seeds (Table 2).

Compared to germination where GABA is mainly synthesized by the seed itself, fermentation can accumulate GABA with the help of microorganisms. GABA is synthesized via glutamate decarboxylase (GAD)-mediated decarboxylation of glutamic acid, and GAD plays a central role in the synthesis of GABA (Battaglioli and others 2003). During the fermentation process, microbes can hydrolyze proteins and release free amino acids, such as glutamic acid, which can be used as the substrate for the synthesis of GABA by GABA-producing microbes. Many microbes have been reported to produce GAD to synthesize GABA, such as LAB and fungi (Dhakal and others 2012; Wu and Shah 2016). In addition, it is also possible that GABA can be synthesized by the endogenous GAD of seeds, since its concentration has been reported to be increased in control samples without inoculated microbes (Rizzello and others 2008; Coda and others 2010). Besides, many factors, such as fermentation temperature, pH, and fermentation time, as well as different media additives, can influence the production of GABA, as previously reviewed by Dhakal and others (2012), and not further discussed herein. Overall, fermentation is a valuable bioprocessing strategy for producing GABA-rich products.

Natural phenolics

Natural phenolics, having at least one phenol group, and existing widely in the plant kingdom, are an important category of phytochemicals. They can be classified into different subgroups based on their chemical structures, such as phenolic acids, flavonoids, and proanthocyanidins. In plants, natural phenolics may exist in soluble and bound forms. Soluble phenolics include free and conjugated forms, with the latter conjugated with organic acids or sugar groups, and are synthesized through a multi-enzyme complex localized on the cytoplasmic surface of the endoplasmic reticulum, and they subsequently transported to intracellular vacuoles and

Table 2–Influences of fermentation on GABA content in edible seeds and their products.

Edible seeds and their products	Inoculated microbes	GABA content		Unit	References
		Nonfermented samples	Fermented samples		
Chickpea (*Cicer arietinum*)	*Lb. plantarum* C48	18.0	615	mg/kg DW	(Coda and others 2010)
	Lc. lactis subsp. lactis PU1	18.0	1031	mg/kg DW	
Faba bean (*Vicia faba* L.)	*Lb. plantarum* VTT E-133328	∼50.0	∼1000	mg/kg DW	(Coda and others 2015)
Kidney bean (*Phaseolus vulgaris*)	*B. subtilis* CECT 39^{T} (ATCC 6051)	3.20	2.61 to 2.69	mg/g DW	(Limon and others 2015)
	Lb. plantarum CECT 748^{T} (ATCC 14917)	2.27	6.76 to 9.90	mg/g DW	
	Natural fermentation	2.27	7.54 to 10.6	mg/g DW	
Lentil (*Lens culinaris*)	*Lb. plantarum* CECT 748^{T} (ATCC 14917)	∼4.40	∼6.00 to 7.16	mg/g DW	(Torino and others 2013)
	Natural fermentation	∼4.40	∼7.50 to 10.4	mg/g DW	
	B. subtilis CECT 39^{T} (ATCC 6051)	∼3.20	∼4.00 to 6.54	mg/g DW	
Soybean (*Glycine max*)	*Lb. plantarum* C48	24.0	57.0	mg/kg DW	(Coda and others 2010)
	Lc. lactis subsp. lactis PU1	24.0	39.0	mg/kg DW	
	A. oryzae FMB S46471 *and L. brevis* GABA100	∼0.15	∼3.60 to 6.60	g/kg DW	(Kim and Ji 2014)
Amaranth (*Amaranthus hypocondriacus*)	*Lb. plantarum* C48	12.0	654	mg/kg DW	(Coda and others 2010)
	Lc. lactis subsp. lactis PU1	12.0	816	mg/kg DW	
Buckwheat (*Fagopyrum esculentum*)	*Lb. plantarum* C48	40.0	643	mg/kg DW	
	Lc. lactis subsp. lactis PU1	40.0	562	mg/kg DW	
Millet (*Panicum miliaceum*)	*Lb. plantarum* C48	15.0	110	mg/kg DW	
	Lc. lactis subsp. lactis PU1	15.0	231	mg/kg DW	
Oat (*Avena sativa*)	*Lb. plantarum* C48	27.0	185	mg/kg DW	
	Lc. lactis subsp. lactis PU1	27.0	206	mg/kg DW	
	A. oryzae var. effuses 3.2825	57.1	59.0 to 331	μg/g DW	(Cai and others 2014)
	A. oryzae 3.5232	57.1	59.0 to 435	μg/g DW	
	R. oryzae 3.275	57.1	59.0 to 126	μg/g DW	
Quinoa (*Chenopodium quinoa*)	*Lb. plantarum* C48	78.0	415	mg/kg DW	(Coda and others 2010)
	Lc. lactis subsp. lactis PU1	78.0	176	mg/kg DW	
Rice (*Oryza sativa*)	*Lb. plantarum* C48	12.0	24.0	mg/kg DW	
	Lc. lactis subsp. lactis PU1	12.0	30.0	mg/kg DW	
	M. purpureus CMU 001	N.M.	1.24 to 28.4	mg/g DW	(Jannoey and others 2010)
	Lc. lactis RO50	N.M.	120 to 150	mg/100 g DW	(Saikusa and others 2016)
Rye (*Secale cereale*)	Several LAB	N.M.	11.7 to 168	mg/kg DW	(Rizzello and others 2008)
	Lb. plantarum C48	12.0	39.0	mg/kg DW	(Coda and others 2010)
	Lc. lactis subsp. lactis PU1	12.0	75.0	mg/kg DW	
Spelt (*Triticum spelta*)	*Lb. plantarum* C48	3.00	72.0	mg/kg DW	
	Lc. lactis subsp. lactis PU1	3.00	259	mg/kg DW	
White wheat (*Triticum aestivum* Appulo cv)	Several LAB	N.M.	12.7 to 101	mg/kg DW	(Rizzello and others 2008a)
Common wheat (*Triticum aestivum*)	*Lb. plantarum* C48	7.00	63.0	mg/kg DW	(Coda and others 2010)
	Lc. lactis subsp. lactis PU1	7.00	70.0	mg/kg DW	
Durum wheat (*Triticum durum*)	*Lb. plantarum* C48	19.0	75.0	mg/kg DW	
	Lc. lactis subsp. lactis PU1	19.0	84.0	mg/kg DW	
Adzuki bean milk	*Lc. lactis* subsp. lactis and *L. rhamnosus* GG	∼28.0	∼68.0	mg/100 mL	(Liao and others 2013)
Black bean milk	*Lb. brevis* FPA 3709	1.07	1.34 to 4.04	mg/mL	(Ko and others 2013)
Chickpea milk	*Lb. plantarum* M-6	∼140	∼150 to 537	mg/L	(Li and others 2016)
Soymilk	A mixture of LAB	∼100	∼130 to 180	mg/g DW	(Tsai and others 2006)
	Lb. casei Zhang	∼24.5	∼43.0	mg/L	(Li and others 2012)
	Bb. animalis V9 (CP001892)	∼24.5	∼45.6	mg/L	
	Lb. acidophilus NCFM	∼24.5	∼36.0	mg/L	
	Lb. rhamnosus GG	∼24.5	∼39.0	mg/L	
	Bb. animalis BB12	∼24.5	∼39.5	mg/L	
	Lb. casei Shirota	∼24.5	∼45.0	mg/L	
Soybean paste	Natural fermentation	∼5.00	∼5.00 to 80.0	μmol/g DW	(Jung and others 2016)
Oat flakes beverage	*Lb. plantarum* LP09	∼4.00	∼5.00	mg/kg	(Nionelli and others 2014)
Rice-based sunsik	A mixture of microorganisms	26.0	66.0	mg/100 g DW	(Koh and others 2014)
Wheat-based dosa	*Lb. plantarum* MNZ	∼0.00	∼0.00 to 115	mg/kg	(Zareian and others 2015)
Wholemeal wheat	Several LAB	N.M.	11.0 to 259	mg/kg DW	(Rizzello and others 2008)

A., Aspergillus; B., Bacillus; Bb, Bifidobacterium; Lb., Lactobacillus; R., Rhizopus; N.D., not detected. DW, dry weight.

stored there, while bound phenolics are formed by the secretion of vacuolar soluble phenolics to the cell wall, where they can covalently bind with cell wall macromolecules, such as polysaccharides and proteins, as a component of plant cell walls (Agati and others 2012). Edible seeds, such as edible beans and cereal grains, have been reported to contain a variety of natural phenolics (Deng and others 2012; Gan and others 2016d). Phenolics mainly exist in the pigmented seed coats, primarily as flavonoids and proanthocyanidins (Gan and others 2016a), and many edible seeds contain a substantial level of bound phenolics, generally with much higher content than in common fruits and vegetables (Gan and others 2016a).

Recent studies indicate that fermentation can change phenolic composition and distribution of edible seeds and their products. Most studies report that fermentation increases the total phenolics content (TPC) of soluble phenolics, while having different effects on specific phenolic compounds (Table 3). This can be partly due to the metabolism of soluble phenolic compounds by microbes during the fermentation process, since many microbes, such as LAB and fungi, are able to produce different enzymes, such as β-glucosidase, esterase, and tannase, to metabolize soluble phenolics and/or phenolic polymers into free forms or degraded products (Rodriguez and others 2009; Hole and others 2012; Huynh and others 2014). For instance, fermentation of soybean and soy products by many microbes has been found to convert soybean isoflavone glucosides (such as daidzin) into their aglycones (such as daidzein). Our work (Gan and others 2016b) found that natural and LAB-mediated fermentation increased soluble TPC in mottled cowpea, accompanied with a significant increase of soluble catechin, which was speculated to be associated with the degradation of proanthocyanidins in the bean coat. Additionally, soluble phenolics can be released from bound phenolics during the fermentation process. Our work (Gan and others 2016b) also indicated that fermentation significantly increased soluble TPC in small runner bean, partly due to the release of bound phenolics. This may be related to microbe-mediated decomposition of cell wall components and subsequent release of bound phenolics, since many microbes possess various enzymes, such as cellulase, feruloyl esterase, glucosidase, xylanase, pectinase, and proteinases, which can degrade the cell wall matrix (Huynh and others 2014). Taken together, microbe-mediated metabolism of soluble phenolics and release of bound phenolics may both contribute to the increase of soluble TPC in some fermented edible seeds and their products. However, several studies also found that fermentation did not increase, or may even reduce, soluble TPC in some edible seeds and their products, such as lentil (Torino and others 2013), black soybean (Lee and others 2008), wheat (Subramaniam and others 2014), soymilk (Rekha and Vijayalakshmi 2008), buckwheat groats (Malgorzata and others 2015), and black rice bran (Yoon and others 2015), probably associated with the degradation of some phenolics during the fermentation process.

Although edible seeds contain substantial levels of bound phenolics, the influence of fermentation on TPC and phenolic composition of their bound phenolics has been not much investigated. Our recent work (Gan and others 2016b) found that fermentation exhibited different influences on bound TPC in selected edible beans. On one hand, bound TPC was found reduced in naturally fermented small runner bean and LAB-fermented lentil, small rice bean, and small runner bean, suggesting the release of bound phenolics during fermentation. On the other hand, bound TPC was found significantly increased after fermentation of some other beans, implying that bound phenolics were not released from cell walls, while becoming more available for extraction. In addition, the influence of fermentation on specific bound phenolic compounds has also been scarcely studied. We found that natural fermentation of mottled cowpea increased the contents of bound ferulic and *p*-coumaric acids and reduced the content of bound protocatechuic acid, while LAB-mediated fermentation did not evidently change them (Gan and others 2016b). Another study reported that bound ferulic acid and *p*-coumaric acid increased in LAB-fermented barley, but decreased in LAB-fermented oat groats, probably releasing from cell wall matrix and become soluble phenolics (Hole and others 2012). These limited results suggest that fermentation can, overall, improve the bioavailability of bound phenolics in edible seeds and may play an important role in gut health, therefore, more studies are needed to further investigate the specific influence of fermentation on bound phenolics in different edible seeds.

Bioactive peptides

Edible seeds, such as edible beans and cereal grains, are rich in proteins, which can be hydrolyzed into small-molecule peptides during the fermentation process. Recent studies have found that some fermented edible seeds and their products can produce bioactive peptides (Table 4), mainly antioxidant and angiotensin-converting-I-enzyme (ACE) inhibitory peptides, which are discussed below.

Antioxidant peptides exhibit various antioxidant activities, such as reducing, free radical-scavenging, inhibition of lipid peroxidation, and metal ion chelation properties, which are mainly associated with the intrinsic characteristics of peptides, such as their amino acid composition, structure, and hydrophobicity. Table 4 summarizes the main antioxidant peptides derived from fermented edible seeds and their products, and some intrinsic features and antioxidant mechanisms of antioxidant peptides have been proposed based on previous studies. (1) They, in general, contain 2 to 20 amino acids, all with molecular weight lower than 6.0 kDa (Coda and others 2012). (2) The existence of amino acids, such as A (alanine), C (cysteine), H (histidine), K (lysine), L (leucine), M (methionine), P (proline), V (valine), W (tryptophan), and Y (tyrosine), may contribute to the antioxidant activity of peptides (Sarmadi and Ismail 2010). (3) Amino acid residues, including C, D (aspartic acid), E (glutamic acid), H, K, M, R (arginine), W, and Y, can be associated with the chelating activity of antioxidant peptides (Wu and others 2014). (4) Hydrophobic amino acids can enhance the solubility of peptides in the oil environment, therefore facilitating the interaction with lipophilic radical species and polyunsaturated fatty acids (PUFAs) (Coda and others 2012). (5) The sulfur group (SH group) of cysteine and of methionine exhibits antioxidant activity, since it is able to neutralize reactive free radical species to form stable oxidation products, cystine, and methione sulfoxide, respectively (He and others 2012). (6) Histidine-containing peptides exhibit strong radical-scavenging activity due to decomposition of the imidazole ring (He and others 2012). (7) Histidine mainly acts as a chelator of metal ions at the amino terminus of peptides, while acting as an effective scavenger against various radicals at the carboxyl terminus (Coda and others 2012). (8) Peptides with aromatic amino acid residues, including F (phenylalanine), Y and W, are good donors of hydrogen and can efficiently scavenge free radicals due to their conjugated double-bond structure of a benzene ring (Zhang and others 2014). These characteristics of antioxidant peptides can be helpful for predicting other potential antioxidant peptides, and they can also provide a reference for the chemical synthesis of antioxidant peptides.

Table 3–Influences of fermentation on phenolic composition in edible seeds and their products.

Edible seeds and their products	Inoculated microbes	Extracts	TPC Nonfermented samples	TPC Fermented samples	Unit	Changes of main phenolic compounds	References
Chickpea (*Cicer arietinum* L.)	*R. oligosporus* NRRL 2710	80% Ethanol	93.0	117 to 631	mg GAE/100 g DW	N.M.	(Sanchez-Magana and others 2014)
	R. oligosporus NRRL 2710	NaOH hydrolysis	128	143 to 205	mg GAE/100 g DW	N.M.	
	C. militaris SN-18	80% Methanol	7.08	12.8	mg GAE/g DW	Shikimic acid (↑), chlorogenic acid (↑), daidzein (↑), genistein (↑), biochanin A (↑), rutin (↑), *p*-coumaric acid (↔), syringic acid (↓), ferulic acid (↓), daidzin (↓), glycitin (↓), genistin (↓), luteolin (↓)	(Xiao and others 2014)
	C. militaris SN-18	80% Ethanol	7.36	13.3	mg GAE/g DW	N.M.	
	C. militaris SN-18	Water	6.07	10.5	mg GAE/g DW	N.M.	
Common bean (*Phaseolus vulgaris*)	*Lb. plantarum* DSM 20174 and *R. microsporus* var. chinensis	PBS	1.60	1.61	mg TAE/g DW	N.M.	(Starzynska-Janiszewska and others 2014)
		80% Acetone	1.49	1.69	mg TAE/g DW		
	R. oligosporus NRRL2710	70% Acetone	~2.85	~2.00 to 2.50	mg GAE/g DW	N.M.	(Gamboa-Gomez and others 2016)
	R. oligosporus NRRL2710	70% Acetone	~2.50	~1.35 to 2.10	mg GAE/g DW	N.M.	
Black cow gram (*Lablab purpureus*)	Natural fermentation	80% Methanol	190	287	mg GAE/100 g DW	N.M.	(Gan and others 2016b)
	Lb. paracasei 279		190	277	mg GAE/100 g DW	N.M.	
	Lb. plantarum WCFS1		190	322	mg GAE/100 g DW	N.M.	
	Natural fermentation	NaOH + HCl hydrolysis	69.9	85.6	mg GAE/100 g DW	N.M.	
	Lb. paracasei 279		69.9	76.8	mg GAE/100 g DW	N.M.	
	Lb. plantarum WCFS1		69.9	90.7	mg GAE/100 g DW	N.M.	
Mottled cowpea (*Vigna unguiculata*)	Natural fermentation	80% Methanol	400	626	mg GAE/100 g DW	Catechin (↑), quercetin (↑), protocatechuic acid (↓)	(Gan and others 2016b)
	Lb. paracasei 279	80% Methanol	400	752	mg GAE/100 g DW	Protocatechuic acid (↑), catechin (↑), quercetin (↑)	
	Lb. plantarum WCFS1	80% Methanol	400	747	mg GAE/100 g DW	Protocatechuic acid (↑), catechin (↑), quercetin (↑)	
	Natural fermentation	NaOH + HCl hydrolysis	103	186	mg GAE/100 g DW	Ferulic acid (↑), *p*-coumaric acid (↑), protocatechuic acid (↓)	

(*Continued*)

Table 3–Continued.

			TPC				
Edible seeds and their products	**Inoculated microbes**	**Extracts**	**Nonfermented samples**	**Fermented samples**	**Unit**	**Changes of main phenolic compounds**	**References**
	Lb. paracasei 279	NaOH + HCl hydrolysis	103	105	mg GAE/100 g DW	Protocatechuic acid (↔), ferulic acid (↔), *p*-coumaric acid (↔)	
	Lb. plantarum WCFS1	NaOH + HCl hydrolysis	103	126	mg GAE/100 g DW	Protocatechuic acid (↔), ferulic acid (↔), *p*-coumaric acid (↓)	
Kidney bean (*Phaseolus vulgaris*)	Natural fermentation	Water	20.7	20.2 to 21.2	mg GAE/g DW	Sinapoyl aldaric acid (↑), ferulic acid (↑), catechin and its derivatives (↓), *p*-hydroxybenzoic acid (↓), sinapoyl methylaldaric acid (↓), naringenin and its derivatives (↓)	(Limon and others 2015)
	Natural fermentation	80% acetone	0.25	0.42	mg TAE/g WW	N.M.	(Oboh and others 2009)
	Natural fermentation	NaOH hydrolysis	0.32	0.17	mg TAE/g WW	N.M.	
	B. subtilis CECT 39 ^{T} (ATCC 6051)	Water	15.9	31.1 to 35.9	mg GAE/g DW	Ferulic acid and its derivatives (↑), *p*-hydroxybenzoic acid (↑), hydroxycinnamic compounds (↑), catechin (↓), *p*-coumaric acid (↓)	(Limon and others 2015)
	Lb. plantarum CECT 748 ^{T} (ATCC 14917)	Water	20.7	17.8 to 22.0	mg GAE/g DW	Sinapoyl aldaric acid (↑), catechin and its derivatives (↓), *p*-hydroxybenzoic acid (↓), sinapoyl methylaldaric acid (↓), naringenin and its derivatives (↓), ferulic acid (↓), hydroxycinnamic compounds (↓)	(Limon and others 2015)
Speckled kidney bean (*Phaseolus vulgaris*)	Natural fermentation	80% Methanol	248	441	mg GAE/100 g DW	N.M.	(Gan and others 2016b)
	Lb. paracasei 279		248	489	mg GAE/100 g DW	N.M.	
	Lb. plantarum WCFS1		248	509	mg GAE/100 g DW	N.M.	
	Natural fermentation	NaOH + HCl hydrolysis	106	110	mg GAE/100 g DW	N.M.	
	Lb. paracasei 279		106	103	mg GAE/100 g DW	N.M.	
	Lb. plantarum WCFS1		106	106	mg GAE/100 g DW	N.M.	
Lentil (*Lens culinaris*)	Natural fermentation	Water	~31.0	~28.0 to 31.0	mg GAE/g DW	N.M.	(Torino and others 2013)

(*Continued*)

Table 3–Continued.

Edible seeds and their products	Inoculated microbes	Extracts	TPC		Unit	Changes of main phenolic compounds	References
			Nonfermented samples	Fermented samples			
	B. subtilis CECT 39 ^{T} (ATCC 6051)	Water	~24.0	~35.0 to 36.0	mg GAE/g DW	N.M.	
	Lb. plantarum CECT 748 ^{T} (ATCC 14917)	Water	~31.0	~27.5 to 29.0	mg GAE/g DW	N.M.	
	Natural fermentation	80% Methanol	220	308	mg GAE/100 g DW	N.M.	(Gan and others 2016b)
	Lb. paracasei 279		220	341			
	Lb. plantarum WCFS1		220	325			
	Natural fermentation	NaOH + HCl hydrolysis	81.1	101	mg GAE/100 g DW	N.M.	
	Lb. paracasei 279		81.1	61.3			
	Lb. plantarum WCFS1		81.1	65.4			
Mung bean (*Vigna radiata*)	*Lb. plantarum* CECT 748^{T} (ATCC 14917)	Acidified 80% methanol	N.M.	N.M.	-	Catechin (↑), eriodictyol 7-O-galactoside (↑), vitexin (↑), taxifolin (↑), *p*-hydroxyphenylacetic acid (↑), eriodictyol 7-O-glucoside (↓)	(Landete and others 2015)
	C. militaris SN-18	80% methanol	1372	2972	μg GAE/g DW	Chlorogenic acid (↑), vanillic acid (↑), sinapic acid (↑), rutin (↑), luteolin (↑), shikimic acid (↔), kaempferol (↓)	(Xiao and others 2015d)
	C. militaris SN-18	80% ethanol	1480	2696	μg GAE/g DW	Chlorogenic acid (↑), vanillic acid (↑), sinapic acid (↑), rutin (↑), luteolin (↑), kaempferol (↑), shikimic acid (↔)	
	C. militaris SN-18	80% acetone	1649	3124	μg GAE/g DW	Chlorogenic acid (↑), vanillic acid (↑), sinapic acid (↑), rutin (↑), luteolin (↑), kaempferol (↑), shikimic acid (↔)	
	C. militaris SN-18	Water	1146	5680	μg GAE/g DW	Shikimic acid (↑), chlorogenic acid (↑), vanillic acid (↑), sinapic acid (↑), rutin (↑), luteolin (↑), kaempferol (↑)	
Pigeon pea (*Cajanus cajan*)	Natural fermentation	80% acetone	0.24	0.46	mg TAE/g WW	N.M.	(Oboh and others 2009)
	Natural fermentation	NaOH hydrolysis	0.58	0.34	mg TAE/g WW	N.M.	
Red bean (*Phaseolus radiatus*)	*B. subtilis* BCRC 14716 and *Lb. delbrueckii* sp. bulgaricus BCRC 14008	Water	2.30	3.25	mg GAE/g DW	N.M.	(Jhan and others 2015)

(*Continued*)

Table 3–Continued.

Edible seeds and their products	Inoculated microbes	Extracts	TPC Nonfermented samples	TPC Fermented samples	Unit	Changes of main phenolic compounds	References
	B. subtilis BCRC 14716 and *Lb. delbrueckii* sp. bulgaricus BCRC 14008	50% Ethanol	2.59	3.63	mg GAE/g DW	N.M.	
Small rice bean (*Vigna umbellata*)	Natural fermentation	80% Methanol	338	588	mg GAE/100 g DW	N.M.	(Gan and others 2016b)
	Lb. paracasei 279		338	692	mg GAE/100 g DW	N.M.	
	Lb. plantarum WCFS1		338	666	mg GAE/100 g DW	N.M.	
	Natural fermentation	NaOH + HCl hydrolysis	79.6	128	mg GAE/100 g DW	N.M.	
	Lb. paracasei 279		79.6	62.7	mg GAE/100 g DW	N.M.	
	Lb. plantarum WCFS1		79.6	70.7	mg GAE/100 g DW	N.M.	
Small runner bean (*Phaseolus coccineus*)	Natural fermentation	80% Methanol	211	360	mg GAE/100 g DW	N.M.	(Gan and others 2016b)
	Lb. paracasei 279		211	469	mg GAE/100 g DW	N.M.	
	Lb. plantarum WCFS1		211	449	mg GAE/100 g DW	N.M.	
	Natural fermentation	NaOH + HCl hydrolysis	219	132	mg GAE/100 g DW	N.M.	
	Lb. paracasei 279		219	93.8	mg GAE/100 g DW	N.M.	
	Lb. plantarum WCFS1		219	132	mg GAE/100 g DW	N.M.	
Yellow soybean (*Glycine max*)	*Lb. plantarum* KFRI 00144, *Lb. delbrueckii* subsp. latis KFRI 01181, *Bb. thermophilum* KFRI 00748, *Bb. breve* K-101	80% Ethanol	N.M.	N.M.	-	Daidzin and genistin (↓), daidzein and genistein (↑)	(Pyo and others 2005)
	Natural fermentation	80% Methanol	2.98	4.98 to 5.68	mg CE/g DW	N.M.	(Fernandez-Orozco and others 2007)
	A. oryzae 2094^{T} (ATCC 1011)	80% Methanol	2.98	3.54	mg CE/g DW	N.M.	
	R. oryzae CECT 2340 (ATCC 24563)	80% Methanol	2.98	3.43	mg CE/g DW	N.M.	
	B. subtilis CECT 39^{T} (ATCC 6051)	80% Methanol	2.98	12.5	mg CE/g DW	N.M.	
	Lb. plantarum CECT 748^{T} (ATCC 14917)	80% Methanol	2.98	5.40 to 5.51	mg CE/g DW	N.M.	

(*Continued*)

Table 3–Continued.

Edible seeds and their products	Inoculated microbes	Extracts	TPC		Unit	Changes of main phenolic compounds	References
			Nonfermented samples	Fermented samples			
	Lb. plantarum CECT 748^T (ATCC 14917)	Acidified 80% methanol	N.M.	N.M.	-	Daidzein (↑), genistein (↑), glycitin (↑), naringenin (↑), kaempferol diglucoside (↑), *p*-hydroxyphenylacetic acid (↑), daidzin (↓), genistin (↓), glycitin (↓), malonyl and acetyl daidzin (↓), malonyl and acetyl genistin (↓), malonyl glycitin (↓), eriodictyol 7-O-glucoside (↓), kaempferol glucoside (↓)	(Landete and others 2015)
	Natural fermentation	80% Methanol	219	415	mg GAE/100 g DW	N.M.	(Gan and others 2016b)
	Lb. paracasei 279		219	395	mg GAE/100 g DW	N.M.	
	Lb. plantarum WCFS1		219	384	mg GAE/100 g DW	N.M.	
	Natural fermentation	NaOH + HCl hydrolysis	42.5	69.9	mg GAE/100 g DW	N.M.	
	Lb. paracasei 279		42.5	67.0	mg GAE/100 g DW	N.M.	
	Lb. plantarum WCFS1		42.5	54.0	mg GAE/100 g DW	N.M.	
Black soybean (*Glycine max*)	*R. oryzae* BCRC 30894, *R. oligosporus* NTU-5, *R. oligosporus* BCRC 31996	80% Methanol	N.D.	2088 to 2545	µg GAE/g DW	Daidzein and genistein (↑), daidzin and genistin (↓)	(Cheng and others 2013)
	B. subtilis BCRC 14715	80% Methanol	15.9	23.4	mg GAE/g DW	N.M.	(Juan and Chou 2010)
	B. subtilis BCRC 14715	80% Ethanol	17.8	22.7	mg GAE/g DW	N.M.	
	B. subtilis BCRC 14715	80% Acetone	26.6	40.4	mg GAE/g DW	N.M.	
	B. subtilis BCRC 14715	Water	6.04	12.4	mg GAE/g DW	N.M.	
	A. awamori	Methanol	~16.4	~27.2	mg GAE/g DW	Cyaniding 3-glucoside (↑)	(Lee and others 2008)
	A. oryzae BCRC 30222	Methanol	~16.4	~17.8	mg GAE/g DW	Cyaniding 3-glucoside (↑)	
	A. sojae BCRC 30103	Methanol	~16.4	~16.6	mg GAE/g DW	Cyaniding 3-glucoside (↑)	
	R. azygosporus BCRC 31158	Methanol	~16.4	~20.0	mg GAE/g DW	Cyaniding 3-glucoside (↑)	
	Rhizopus sp. No. 2	Methanol	~16.4	~25.0	mg GAE/g DW	Cyaniding 3-glucoside (↔)	
	Natural fermentation	80% Methanol	414	547	mg GAE/100 g DW	N.M.	(Gan and others 2016b)
	Lb. paracasei 279		414	538	mg GAE/100 g DW	N.M.	
	Lb. plantarum WCFS1		414	582	mg GAE/100 g DW	N.M.	

(*Continued*)

Table 3–Continued.

Edible seeds and their products	Inoculated microbes	Extracts	TPC Nonfermented samples	TPC Fermented samples	Unit	Changes of main phenolic compounds	References
	Natural fermentation	NaOH + HCl hydrolysis	65.7	91.7	mg GAE/100 g DW	N.M.	
	Lb. paracasei 279		65.7	78.3	mg GAE/100 g DW	N.M.	
	Lb. plantarum WCFS1		65.7	85.4	mg GAE/100 g DW	N.M.	
African yam bean (*Sphenostylis stenocarpa* Harms)	Natural fermentation	80% Acetone	0.33	0.47	mg TAE/g WW	N.M.	(Oboh and others 2009)
	Natural fermentation	NaOH hydrolysis	0.26	0.20	mg TAE/g WW	N.M.	
African locust bean (*Parkia biglobosai*)	Natural fermentation	80% Acetone	0.61	0.68	mg TAE/g DW	N.M.	(Oboh and others 2008)
Barley (*Hordeum vulgare* L.)	*Lb. johnsonii* LA1, *Lb. reuteri* SD2112, *Lb. acidophilus* LA-5	50% Methanol	N.M.	N.M.	-	Ferulic acid (↑), *p*-hydroxybenzoic acid (↑)	(Hole and others 2012)
		NaOH hydrolysis	N.M.	N.M.	-	Ferulic acid (↑), *p*-coumaric acid (↑)	
	Lb. rhamnosus	70% ethanol	16.4	20.1	mg GAE/g DW	N.M.	(Dordevic and others 2010)
	S. cerevisiae	70% ethanol	16.4	18.5	mg GAE/g DW	N.M.	
Buckwheat (*Fagopyrum esculentum*)	*Lb. rhamnosus*	70% ethanol	50.7	59.4	mg GAE/g DW	N.M.	(Dordevic and others 2010)
	S. cerevisiae	70% ethanol	50.7	53.2	mg GAE/g DW	N.M.	
Maize (*Zea mays* subsp. mays)	*T. elegans* CCF-1456	Water	0.81	~1.00 to 4.00	mg GAE/g DW	N.M.	(Dey and Kuhad 2014)
	T. elegans CCF-1456	65% ethanol	327	340 to 382	µmol GAE/g DW	N.M.	(Salar and others 2012)
Oat (*Avena sativa* L.)	*A. oryzae* NCIM 1212, *A. awamori* MTCC No. 548, *R. oligosporus* NCIM 1215, *R. oryzae* RCK2012	Water	2.06	~2.30 to 6.40	mg GAE/g DW	N.M.	(Dey and Kuhad 2014)
	A. oryzae var. effuses	80% ethanol	~105	~212	mg GAE/g DW	Chlorogenic acid (↑), caffeic acid (↑), *p*-coumaric acid (↑), ferulic acid (↑)	(Cai and others 2012)
	A. oryzae	80% ethanol	~105	~186	mg GAE/g DW	Chlorogenic acid (↑), caffeic acid (↑), *p*-coumaric acid (↑), ferulic acid (↑)	
	A. niger	80% ethanol	~105	~155	mg GAE/g DW	Chlorogenic acid (↓), caffeic acid (↑), *p*-coumaric acid (↑), ferulic acid (↔)	
	A. oryzae var. effuses 3.2825, *A. oryzae* 3.5232, *R. oryzae* 3.275	80% ethanol	0.50	0.80 to 1.80	mg GAE/g DW	N.M.	(Cai and others 2014)

(*Continued*)

Table 3–Continued.

Edible seeds and their products	Inoculated microbes	Extracts	TPC		Unit	Changes of main phenolic compounds	References
			Nonfermented samples	Fermented samples			
	C. militaris SN-18	Water	5.88	14.1	mg GAE/g DW	Gallic acid (↑), *p*-hydroxybenzoic acid (↑), caffeic acid (↑), *p*-coumaric acid (↑), ferulic acid (↑), vanillin (↑), avenanthramide 2c,p,f (↑), luteolin (↑), apigenin (↑)	(Xiao and others 2015a)
		80% methanol	10.9	16.8	mg GAE/g DW		
		80% ethanol	10.1	15.0	mg GAE/g DW		
		80% acetone	12.4	19.7	mg GAE/g DW		
Brown rice (*Oryza sativa*)	*A. oryzae* NCIM 1212, *A. awamori* MTCC No. 548, *R. oligosporus* NCIM 1215, *R. oryzae* RCK2012	Water	0.79	~3.20 to 7.80	mg GAE/g DW	N.M.	(Dey and Kuhad 2014)
Rye (*Secale cereale*)	*Lb. rhamnosus*	70% ethanol	13.2	18.4	mg GAE/g DW	N.M.	(Dordevic and others 2010)
	S. cerevisiae	70% ethanol	13.2	16.2	mg GAE/g DW	N.M.	
Wheat (*Triticum aestivum* Linn.)	*C. militaris*	70 % ethanol	36.9	41.6	mg GAE/g DW	Ferulic acid (↑), *p*-coumaric acid (↑), syringic acid (↑), vanillic acid (↔), caffeic acid (↔)	(Zhang and others 2012)
	C. militaris	70 % acetone	54.2	66.4	mg GAE/g DW	Ferulic acid (↑), *p*-coumaric acid (↑), syringic acid (↑), vanillic acid (↔), caffeic acid (↔)	
Wheat (*Triticum durum*)	*Lb. rhamnosus*	70% ethanol	16.2	20.7	mg GAE/g DW	N.M.	(Dordevic and others 2010)
	S. cerevisiae	70% ethanol	16.2	18.4	mg GAE/g DW	N.M.	
Wheat (*Triticum* spp.)	*A. oryzae* NCIM 1212, *A. awamori* MTCC No. 548, *R. oligosporus* NCIM 1215, *R. oryzae* RCK2012	Water	0.81	~2.30 to 11.6	mg GAE/g DW	N.M.	(Dey and Kuhad 2014)
	Gd. austral (KUM60813)	Water	27.4	22.6	mg GAE/g DW	N.M.	(Subramaniam and others 2014)
		Ethanol	56.0	49.7	mg GAE/g DW	N.M.	
	Gd. neo-japonicum (KUM61076)	Water	27.4	32.6	mg GAE/g DW	N.M.	
		Ethanol	56.0	61.4	mg GAE/g DW	N.M.	
	Gd. lucidum (VITA GL)	Water	27.4	17.7	mg GAE/g DW	N.M.	
		Ethanol	56.0	32.9	mg GAE/g DW	N.M.	
Adlay (*Coix lachryma-jobi*)	*B. subtilis* BCRC 14718	Methanol	8.58	13.3	mg GAE/g DW	N.M.	(Wang and others 2014)
	Lb. plantarum	Methanol	8.58	11.9	mg GAE/g DW	N.M.	
Bambara groundnut (*Vigna subterranea*)	Natural fermentation	80% Acetone	0.60	0.75	mg TAE/g WW	N.M.	(Oboh and others 2009)
	Natural fermentation	NaOH hydrolysis	0.29	0.27	mg TAE/g WW	N.M.	

(*Continued*)

Table 3–Continued.

Edible seeds and their products	Inoculated microbes	Extracts	TPC		Unit	Changes of main phenolic compounds	References
			Nonfermented samples	Fermented samples			
Chestnut (*Castanea crenata*)	*B. subtilis* BCRC 14718	Methanol	13.0	19.7	mg GAE/g DW	N.M.	(Wang and others 2014)
	Lb. plantarum	Methanol	13.0	15.3	mg GAE/g DW	N.M.	
Lotus seed (*Nelumbo nucifera*)	*B. subtilis* BCRC 14718	Methanol	17.5	28.7	mg GAE/g DW	N.M.	
	Lb. plantarum	Methanol	17.5	24.6	mg GAE/g DW	N.M.	
Walnut (*Juglans regia*)	*B. subtilis* BCRC 14718	Methanol	22.8	33.9	mg GAE/g DW	N.M.	
	Lb. plantarum	Methanol	22.8	28.6	mg GAE/g DW	N.M.	
Mung bean milk	*Lb. plantarum* WCFS1	THF	29.1	30.7 to 33.6	mg GAE/100 mL	N.M.	(Gan and others 2016c)
		Acidic methanol	12.6	15.9 to 17.4	mg GAE/100 mL	Vitexin and isovitexin (↔)	
Soymilk	*Lb. acidophilus* B4496 + *S. boularidii*	Water	26.6	23.4	mg GAE/100 mL	Daidzein (↑), genistein (↑), daidzin (↓), genistin (↓)	(Rekha and Vijayalakshmi 2008)
	Lb. bulgaricus CFR 2028 + *S. boularidii*	Water	26.6	11.9	mg GAE/100 mL		
	Lb. casei B1922 + *S. boularidii*	Water	26.6	12.8	mg GAE/100 mL		
	Lb. plantarum B4495 + *S. boularidii*	Water	26.6	12.8	mg GAE/100 mL		
	Lb. helviticus B4526 + *S. boularidii*	Water	26.6	12.6	mg GAE/100 mL		
	Lb. rhamnosus CRL981	Acidified acetonitrile solution	N.M.	N.M.	–	Daidzein (↑), genistein (↑), daidzin (↓), genistin (↓)	(Marazza and others 2009, 2012)
	Sc. thermophilus CCRC 14085 and *Bb. infantis* CCRC 14603	80% Methanol	11.3	12.6	mg GAE/g DW	N.M.	(Lai and others 2013)
		50% Acetone	10.6	12.7	mg GAE/g DW	N.M.	
		Water	4.60	5.96	mg GAE/g DW	N.M.	
	Lb. acidophilus CSCC 2400	80% Methanol + Hexane	47.0	47.4 to 59.5	mg GAE/100 mL	Gallic acid (↑), ferulic acid (↑), chlorogenic acid (↑), daidzein (↑), glycitein (↑), genistein (↑), catechin (↓), daidzin (↓), glycitin (↓), genistin (↓),	(Zhao and Shah 2014)
	Lb. paracasei CSCC 279	80% Methanol + Hexane	47.0	47.1 to 57.9	mg GAE/100 mL		
	Lb. zeae ASCC 15820	80% Methanol + Hexane	47.0	39.7 to 57.3	mg GAE/100 mL		
	Lb. rhamnosus WQ2	80% Methanol + Hexane	47.0	46.9 to 63.8	mg GAE/100 mL		
	Lb. plantarum WCFS1	THF	28.1	30.0 to 32.1	mg GAE/100 mL	N.M.	(Gan and others 2016c)
		Acidic methanol	14.4	18.9 to 20.5			

(*Continued*)

Table 3–Continued.

Edible seeds and their products	Inoculated microbes	Extracts	TPC Nonfermented samples	TPC Fermented samples	Unit	Changes of main phenolic compounds	References
Black soymilk	*Sc. thermophilus* S10	80% Ethanol	∼62.5	89.7	mg GAE/100 g DW	Daidzein (↑), genistein (↑), daidzin (↓), genistin (↓)	(Lee and others 2015)
Soy germ	*A. niger* M46	70% Methanol	∼12.0	∼33.0 to 38.0	mg GAE/g DW	Daidzein (↑), daidzin (↓), glycitin (↓), genistin (↓), acetyl daidzin (↓), acetyl glycitin (↓)	(Sheih and others 2014)
Soy whey	*Lb. plantarum* B1-6	80& Ethanol	52.8	64.7	mg GAE/g	Daidzein (↑), genistein (↑), daidzin (↓), genistin (↓)	(Xiao and others 2015b)
Buckwheat groats	*R. oligosporus* NRRL 2710	80% methanol	7.19	5.15	mg RUE/g DW	Rutin (↓)	(Malgorzata and others 2015)
	R. oligosporus ATCC 64063	50% Acetone	6.18	7.47	mg GAE/g DW	N.M.	(Starzynska-Janiszewska and others 2016)
		PBS (0.1 M, pH 7.4)	3.00	4.66	mg GAE/g DW	N.M.	
Oat flakes	*Lb. plantarum* LP09	80% Methanol	0.46	0.62	mmol GAE/L	N.M.	(Nionelli and others 2014)
Oat groats	*Lb. johnsonii* LA1, *Lb. reuteri* SD2112, *Lb. acidophilus* LA-5	50% Methanol	N.M.	N.M.	–	Caffeic acid (↑), ferulic acid (↑), sinapic acid (↑)	(Hole and others 2012)
	Lb. reuteri SD2112, *Lb. acidophilus* LA-5, *Lb. plantarum* WCFS1, *Lb. fermentum* NCDO 1750	NaOH hydrolysis	N.M.	N.M.	–	Ferulic acid (↓), *p*-coumaric acid (↓)	
Black rice bran	*B. subtilis* KU3	Fermented supernatant	172	139	mg GAE/g DW	N.M.	(Yoon and others 2015)

A., *Aspergillus*; *B.*, *Bacillus*; *Bb*, *Bifidobacterium*; *C.*, *Cordyceps*; *Gd.*, *Ganoderma*; *Lb.*, *Lactobacillus*; *R.*, *Rhizopus*; *S.*, *Saccharomyces*; *Sc.*, *Streptococcus*; *T.*, *Thamnidium*; N.M., not measured; DW, dry weight; WW, wet weight; CE, catechin equivalent; GAE, gallic acid equivalent; TAE, tannic acid equivalent; RUE, rutin equivalent.

Table 4–Bioactive peptides in fermented edible seeds and their products.

Edible seeds and their products	Inoculated microbes	Bioactive peptides	Information of peptides	References
Chickpea (*Cicer arietinum*)	*Lb. plantarum* C48 and *Lb. brevis* AM7	Lunasin-like polypeptides	Name: Leucoagglutinating phytohemagglutinin; MW: 29.5 kDa; AA sequence: MASSKFFTVLFLVLLTHANSSNDIYFNFQRFNETNLILQRDASVSSSGQLRLTNLNGNGEPRVGSLGRAFYSAPIQIWDNTTGTVASFATSFTFNIQVPNNAGPADGLAFALVPVGSQPKDKGGFLGLFDGSNSNFHTVAVEFDTLYNKDWDPTERHIGIDVNSIRSIKTTRWDFVNGENAEVLIYDSSTNLLVASLVYPSQKTSFIVSDTVDLKSVLPEWVSVGFSATTGINKGNVETNDVLSWSFASKLSDGTTSEGLNLANLVLNKIL Name: Pathogenesis related protein; MW: 16.9 kDa; AA sequence: MGVFTFEQETASTVPPAKLYKAMVKDADVIIPKAVDAIKTVETVEGNGGPGTIKKLTFVEGGQTLYVLHKIEAIDEANLGYNYSIVGGAGLSETVERYHFEAKLCEGPNGGSIGKVSVKYQTKGDAKPNEKEVQEGKAKGDALFKAIEGYVLANPNYN Name: Seed linoleate 9S-lipoxygenase-3; MW: 97.6 kDa; AA sequence: MFSGVTGILNRGHKIKGTVVLMRKNVLDINSLTTVGGVIGQGFDILGSTVDNLTAFLGRSVSLQLISATKPDATGKGKLGKATFLEGIISSLPTLGAGQSAFKIHFEWDDDMGIPGAFYIKNFMQTEFFLVSLTLDDIPNHGSIYFVCNSWIYNAKHHKIDRIFFANQTYLPSETPAPLVHYREEELNNLRGDGTGERKEWERIYDYDVYNDLGNPDSGENHARPVLGGSETYPYPRRGRTGRKPTRKDPNSESRSDYVYLPRDEAFGHLKSSDFLTYGLKAVSQNVVPALESVFFDLNFTPNEFDSFDEVHGLYEGGIKLPTNILSQISPLPVLKEIFRTDGENTLKYPPPKVIQVSRSGWMTDEEFAREMLAGVNPNVICCLQEFPPRSKLDSQIYGDHTSKISKEHLEPNLEGLTVEEAIQNKKLFLLDHHDSIMPYLRRINSTSTKAYATRTILFLNNNQNLKPLAIELSLPHPQGDEHGAVSYVYQPALEGVESSIWLLAKAYVIVNDSCYHQLVSHWLNTHAVVEPFVIATNRHLSCLHPIYKLLYPHYRDTMNINSLARLSLVNDGGIIEKTFLWGRYSMEMSSKVYKNWVFTEQALPADLIKRGMAIEDPSSPCGVKLVVEDYPYAVDGLEIWAIIKTWVQDYVSLYYTSDEKLRQDSELQAWWKELVEVGHGDKKNEPWWPKMQTREDLIEVCSIVIWTASALHAAVNFGQYSYGGLILNRPTLSRRFMPEKGSAEFEELVKSPQKAYLKTITPKFQTLIDLSVIEILSRHASDELYLGERDNPNWTSDKRALEAFKKFGNKLAEIEKKLTQRNNDEKLRNRHGPVEMPYTLLYPSSKEGLTFRGIPNSISI	(Rizzello and others 2015)
Kidney bean (*Phaseolus vulgaris*)	*Lb. plantarum* C48 and *Lb. brevis* AM7	Lunasin-like polypeptides	Name: Subtilisin inhibitor 1; MW: 10.4 kDa; AA sequence: QEQGTNPSQEQNVPLPRNYKQALETNTPTKTSWPELVGVTAEQAETKIKEEMVDVQIQVSPHDSFVTADYNPKRVRLYVDESNKVTRTPSIGName: Legumin A2; MW: 59.6 kDa; AA sequence: MATKLLALSLSFCFLLLGGCFALREQPEQNECQLERLNALEPDNRIESEGGLIETWNPNNKQFRCAGVALSRATLQHNALRRPYYSNAPQEIFIQQGNGYFGMVFPGCPETFEEPQESEQGEGRRYRDRHQKVNRFREGDIIAVPTGIVFWMYNDQDTPVIAVSLTDIRSSNNQLDQMPRRFYLAGNHEQEFLRYQHQQGGKQEQENEGNNIFSGFKRDFLEDAFNVNRHIVDRLQGRNEDEEKGAIVKVKGGLSIISPPEKQARHQRGSRQEEDEDEDEERQPRHQRGSRQEEEEDEDEERQPRHQRRRGEEEEEDKKERRGSQKGKSRRQGDNGLEETVCTAKLRLNIGPSSSPDIYNPEAGRIKTVTSLDLPVLRWLKLSAEHGSLHKNAMFVPHYNLNANSIIYALKGRARLQVVNCNGNTVFDGELEAGRALTVPQNYAVAAKSLSDRFSYVAFKTNDRAGIARLAGTSSVINNLPLDVVAATFNLQRNEARQLKSNNPFKFLVPARQSENRASA Name: Phaseolin; MW: 47.5 kDa; AA sequence: MMRARVPLLLLGILFLASLSASFATSLREEEESQDNPFYFNSDNSWNTLFKNQYGHIRVLQRFDQQSKRLQNLEDYRLVEFRSKPETLLLPQQADAELLLVVRSGSAILVLVKPDDRREYFFLTSDNPIFSDHQKIPAGIFYLVNPDPKEDLRIIQLAMPVNNPQIHEFFLSSTEAQQSYLQEFSKHILEASFNSKFEEINRVLFEEEGQQEGVIVNIDSEQIKELSKHAKSSSRKSLSKQDNTIGNEFGNLTERTDNSLNVLISSIEMEEGALFVPHYYSKAIVILVVNEGEAHVELVGPKGNKETLEYESYRAELSKDDVFVIPAAYPVAIKATSNVNFTGFGINANNNNRNLLAGKTDNVISSIGRALDGKDVLGLTFSGSGDEVMKLINKQSGSYFVDAHHHQQEQQKGRKGAFVY	(Rizzello and others 2015)
Lentil (*Lens culinaris*)	*Lb. plantarum* C48 and *Lb. brevis* AM7	Lunasin-like polypeptides	N.M.	(Rizzello and others 2015)

(*Continued*)

Table 4–Continued.

Edible seeds and their products	Inoculated microbes	Bioactive peptides	Information of peptides	References
Mung bean (*Vigna radiata*)	*Lb. plantarum* B1-6	ACE-inbibitory peptides	N.M.	(Wu and others 2015)
Navy bean (*Phaseolus vulgaris*)	Different LAB	ACE-inbibitory peptides	N.M.	(Rui and others 2015)
Pea (*Pisum sativum*)	*Lb. plantarum* 299v	ACE-inbibitory peptides	MW: 1.59 kDa; AA sequence: KEDDEEEEQGEEE	(Jakubczyk and others 2013)
	Lb. plantarum C48 and *Lb. brevis* AM7	Lunasin-like polypeptides	Name: Provicilin; MW: 31.5 kDa; AA sequence: DNAEIEKILLEEHEKETHHRRGLRDKRQQSQEKNVIVKVSKKQIEELSKNAKSSSKKSVSSRSEPFNLKSSDPIYSNQYGKFFEITPKKNPQLQDLDIFVNYVEIKEGSLWLPHYNSRAIVIVTVNEGKGDFELVGQRNENQQGLREEDDEEEEQREEETKNQVQSYKAKLTPGDVFVIPAGHPVAVRASSNLNLLGFGINAENNQRNFLAGEEDNVISQIQKQVKDLTFPGSAQEVDRLLENQKQSYFANAQPQQRETRSQEIKEHLYSILGAF Name: Seed linoleate 9S-lipoxygenase-2; MW: 97.1 kDa; AA sequence: MFPNVTGLLNKGHKIRGTVVLMRKNVLDFNTIVSIGGGNVHGVIDSGINIIGSTLDGLTAFLGRSVSLQLISATKSDANGKGKVGKDTFLEGVLASLPTLGAGESAFNIHFEWDHEMGIP121GAFYIKNYMQVEFFLKSLTLEDVPNHGTIRFVCNSWVYNSKLYKSPRIFFANKSYLPSETPSPLVKYREEELQTLRGDGTGERKLHERIYDYDVYNDLGNPDHGEHLARPILGGSSTHPYPRRGRTGRYPTRKDPNSEKPATETYVPRDENFGHLKSSDFLAYGIKSVSQCVVPAFESAFDLNFTPNEFDSFQDVRNLFEGGIKLPLDVISTLSPLPVVKEIFRTDGEQVLKFTPPHVIRVSKSAWMTDEEFAREMLAGVNPCMIRGLQEFPPKSNLDPAEYGDHTSKISVDVLNLDGCTIDEALASGRLFILDYHDTFIPFLRRINETSAKAYATRTILFLKENGTLKPVAIELSLPHPDGDKSGFVSKVILPADEGVESTIWLLAKAYVVVNDSCYHQLMSHWLNTHAVIEPFVIATNRQLSVVHPINKLLAPHYRDTMMNINALARDSLINANGLIERSFLPSKYAVEMSSAVYKYWVFTDQALPNDLIKRNMAVKDSSSPYGLRLLIEDYPYAVDGLEIWTAIKTWVQDYVSLYYATDNDIKNDSELQHWWKEVVEKGHGDLKDKPWWPKLQTFDELVEVCTIIIWTASALHAAVNFGQYPYGGLILNRPTLSRRLLPEEGTAEYDEMVKSSQKAYLRTITPKFQTLIDLSVIEILSRHASDEVYLGQRENPHWTSDSKALQAFQKFGNKLAEIEAKLTNKNNDPSLYHRVGPVQLPYTLLHPSSKEGLTFRGIPNSISI Name: Seed biotin-containing protein SBP65; MW: 59.5 kDa; AA sequence: MASEQLSRRENITTERKIQNAEDSVPQRTTHFELRETHELGPNFQSLPRNENQAYLDRGARAPLSANVSESYLDRARVPLNANIPEHRVREKEDFGGVRDMGKFQMESKGGNKSLAEDRETLDTRSRMVTGTPHIKEASGKGQVVEERERARERAMEEEEKRLTMEEISKYRNQAQQSALEALSAAQEKYERAKQATNETLRNTTQAAQEKGEAAQAKDATFEKTQQGYEMTGDTVSNSARTASEKAAQAKNTTLGKTQQGYEATRDTVSNAARTAAEYATPAAEKARCVAVQAKDVTLETGKTAAEKAKCAAEIAAKVAVDLKEKATVAGWTASHYATQLTVDGTRAAANAVEGAVGYVAPKASELAAKSVETVKGLAASAGETAKEFTARKKEESWREYEAKRASQLQEGEEILPSTGGIGKVLPSGERTQAQGTNLQEKVQGKGSDILGAVTETVSDIGSSMIKPIDNANTKVKEHGGTTITPKGQDAGGVLDAIGETIAEIAHTTKVIVVGEDDEVEKSMQKNIGSDSHSLDRAKHEGYRAPKNNVS Name: Albumin-1 C; MW: 13.9 kDa; AA sequence: MASVKLASLIVLFATLGMFLTKNVGAISCNGVCSPFDIPPCGSPLCRCIPAGLVIGNCRNPYGVFLRTNDEHPNLCESDADCRKKGSGTFCGHYPNPDIEYGWCFASKSEAEDVFSKITPKDLLKSVSTA	(Rizzello and others 2015)

(*Continued*)

Table 4–Continued.

Edible seeds and their products	Inoculated microbes	Bioactive peptides	Information of peptides	References
	Lb. rhamnosus BGT10	Antioxidant peptides	N.M.	(Stanisavljevic and others 2015)
Grass pea (*Lathyrus sativus*)	*Lb. plantarum* C48 and *Lb. brevis* AM7	Lunasin-like polypeptides	N.M.	(Rizzello and others 2015)
Soybean (*Glycine max*)	Different LAB	Cancer preventive peptide	Name: Lunasin; Amino acid sequence: with immunoreactive epitope RGDDDDDDDDD	(Rizzello and others 2012)
Soymilk	A mixture of LAB	ACE-inbibitory peptides	N.M.	(Tsai and others 2006)
Soy sauce	Natural fermentation	ACE-inbibitory peptides	Amino acid sequence: SY and GY	(Nakahara and others 2012)
Soy protein	*Lb. casei* spp. pseudoplantarum	ACE-inbibitory peptides	N-terminal AA sequence: LIVTQ	(Vallabha and Tiku 2014)
Amaranth (*Amaranthus*)	Different LAB	Cancer preventive peptide	Name: Lunasin; Amino acid sequence: with immunoreactive epitope RGDDDDDDDDD	(Rizzello and others 2012)
Barley (*Hordeum vulgare* L.)	Different LAB	Cancer preventive peptide	Name: Lunasin; Amino acid sequence: with immunoreactive epitope RGDDDDDDDDD	(Rizzello and others 2012)
Rapeseed (*Brassica napus*)	*B. subtilis* 10160	Antioxidant peptides	N.M.	(He and others 2012)
Rye (*Secale cereal*)	A mixture of LAB	Antioxidant peptides	Amino acid sequence: VFVDEGLEVLGWRPVPFNVSVVGRNAK (MW: 2.98 kDa); RLSLPAGAPVTVAVSP (MW: 1.54 kDa); NANGELCPNNMCCSQWGYCGLGSEFCGNGCQSGACCPEK (MW: 4.03 kDa); LCPVHRAADL (MW: 1.10 kDa); PAEMVAAALDR (MW: 1.48 kDa); KVALMSAGSMH (MW: 1.13 kDa); DLADIPQQQRLMAGLALVVATVIFLK (MW: 2.82 kDa); KNGSIFNSPSATAATIIHGHNYSGLAYLDFVTSK (MW: 3.58 kDa); GTIFFSQEGDGPTSVTGSVSGLKPGLHGFHVHALGDTTNGCMSTGPHFNPTGK (MW: 5.34 kDa)	(Coda and others 2012)
Rye malt sourdoughs	Different LAB	ACE-inbibitory peptides	Amino acid sequences: LQP, LLP, VPP, and IPP	(Hu and others 2011)
Rye malt and flour	*Lb. reuteri*	Taste-active γ-glutamyl-dipeptides	Amino acid sequence: γ-EV, γ-EM, γ-EE, γ-EL, γ-EF, γ-EI	(Zhao and Gänzle 2016)

(*Continued*)

Table 4–Continued.

Edible seeds and their products	Inoculated microbes	Bioactive peptides	Information of peptides	References
Spelt (*Triticum spelta*)	A mixture of LAB	Antioxidant peptides	Amino acid sequence: AIAGAGVLSGYDQLQILFFGK (MW: 2.17 kDa); GNQEKVLELVQR (MW: 1.41 kDa): PAGSAAGAAP (MW: 0.77 kDa); EALEAMFL (MW: 0.92 kDa); AAGAAAAARSAGQCGR (MW: 1.39 kDa); ITFAAYRR (MW: 1.00 kDa); HPVPPKKK (MW: 0.91 kDa)	(Coda and others 2012)
Wholemeal wheat sourdough	A mixture of LAB	ACE-inbibitory peptides	Amino acid sequence: DPVAPLQRSGPEI (MW: 1.15kDa); PVAPQLSRGLL (MW: 1.15 kDa); ELEIVMASPP (MW: 1.08 kDa); QILLPRPGQAA (MW: 1.16kDa); PVAPLQRSGPE (MW: 1.15 kDa); PRSGNVGESGL (MW: 1.15 kDa); VAPSRPTPR (MW: 1.08 kDa); DIIIPD (MW: 1.16 kDa); PRSGNVGESGLID (MW: 1.30 kDa); DPVAPLQRSGPEI (MW: 1.15 kDa); DPVAPLQRSGPEIP (MW: 1.26 kDa); PVAPLPRKGS (MW: 1.02 kDa); DPVAPLQRSGPE (MW: 1.02 kDa); SFTAGARTFNFDENPCDYFQGGKIKAT (MW: 2.98 kDa)	(Rizzello and others 2008)
Whole wheat	A mixture of LAB	Antioxidant peptides	Amino acid sequence: MAPAAVAAAEAGSK (MW: 1.24 kDa); DNIPIVIR (MW: 0.94 kDa)	(Coda and others 2012)
Wheat (Kamut)	A mixture of LAB	Antioxidant peptides	Amino acid sequence: YEWEPTVPNFDVAKDVTDM (MW: 2.26 kDa); GVSNAAVVAGGH (MW: 1.04 kDa); DAQEFKR (MW: 0.89 kDa); PPGPGPGPPPPPGAAGRGGGG (MW: 1.70 kDa); HKEMQAIFDVYIMFIN (MW: 2.00 kDa); TGGGSTSSSSSSSSSLGGGASRGSVVEAAPPATQGAAAANA-PAVPVVVVDTQEAGIR (MW: 5.02 kDa); DTAAGYVAPPDPAVSTGDYGLAGAEAPHPHESAVMSGAAAAAVAPGGEAYTR (MW: 4.92 kDa)	(Coda and others 2012)
Wholemeal wheat	Different LAB	Cancer preventive peptide	Name: Lunasin; Amino acid sequence: with immunoreactive epitope RGDDDDDDDDD	(Rizzello and others 2012)
Wheat germ	*Lb. plantarum* LB1 and *Lb. rossiae* LB5	Anti-fungal peptides	Amino acid sequence: VLHEPLF (MW: 0.85 kDa); YNNPIIYVTENGIAEGNNKSLPITEAL (MW: 2.95 kDa); ALKAAPSPA (MW: 0.82 kDa); AILIIVMLFGR (MW: 1.24 kDa); AAAAVFLSLLAVGHCAAADFNATDADADFAGNGVDFNSSDAAVYWGPWTKAR (MW: 5.29 kDa)	(Rizzello and others 2011)
Wheat germ	*B. Subtilis* B1	Antioxidant peptides	N.M.	(Niu and others 2013)
Casein miso paste based on rice and soybean	*A. oryzae* and *S.cerevisiae*	ACE-inbibitory peptides	Amino acid sequence: VPP and IPP	(Inoue and others 2009)
Peanut meal	*B. subtilis*	Antioxidant peptides	Amino acid sequence: YP	(Zhang and others 2014)
Walnut protein meal	*B. subtilis* GIM 1.135	Antioxidant peptides	N.M.	(Wu and others 2014)

The amino acid sequences of peptides were expressed by the manner of single-letter. Common amino acid abbreviations: A, alanine; C, cysteine; D, aspartic acid; E, glutamic acid; F, phenylalanine; G, glycine; H, histidine; I, isoleucine; K, lysine; L, leucine; M, methionine; N, asparagine; P, proline; Q, glutamine; R, arginine; S, serine; T, threonine; V, valine; W, tryptophan; Y, tyrosine. Other abbreviations: *A.*, *Aspergillus*; *B.*, *Bacillus*; *Lb.*, *Lactobacillus*; *S.*, *Saccharomyces*; N.M., not measured; MW, molecular weight; AA, amino acid.

In addition, fermentation can also produce peptides with ACE-inhibitory activity in edible seeds and their products (Table 4), with some features of ACE-inhibitory peptides summarized below. In general, ACE-inhibitory peptides have a low molecular weight. Many ACE-inhibitory peptides consist of 2 to 12 amino acids, and peptides with molecular weight about 0.8 to 0.9 kDa exhibit the highest ACE-inhibitory activity in LAB-fermented soymilk (Tsai and others 2006). Rizzello and others (2008) stated that most ACE-inhibitory peptides in LAB-fermented wholemeal wheat sourdough had molecular weights less than 1.6 kDa. In addition, the existence and position of some special amino acids in peptides can also influence the ACE-inhibitory activity. Peptides containing VAP (valine-alanine-proline) epitope were reported to possess strong ACE-inhibitory effect (Rizzello and others 2008). Vallabha and Tiku (2014) suggested that glutamine at the C-terminal had a more potent effect than other residues, and leucine (a branch-chained amino acid) at the N-terminal was more effective than glycine to bind with ACE. Ondetti and Cushman (1982) suggested that C-terminal arginine with a positive charge on the ε-amino group significantly contributed to ACE-inhibitory activity. Therefore, understanding these characteristics can be helpful for predicting potential ACE-inhibitory peptides from natural sources.

Besides, fermented edible seeds and their products also contain other bioactive peptides, such as taste-active peptides (Zhao and Gänzle 2016) and lunasin-like peptides (Rizzello and others 2015), which may possess anti-cancer effects (Rizzello and others 2012). In general, fermented edible seeds and their products are good sources of various bioactive peptides. However, bioactive peptides have only been reported in a limited number of fermented edible seeds up to now, and the identification of specific bioactive peptides, including their amino acid sequences, has also been scarcely reported. Therefore, more studies are needed to further explore bioactive peptides and their identities in fermented edible seeds and their products.

Other bioactive components

Many other bioactive components have been found in fermented edible seeds and their products, especially in yeast-fermented rice. A variety of bioactive compounds have been reported in *Monascus* spp.-fermented rice, such as monascin, ankaflavin, rubropunctatin, monascorburin, rubropunctamine, monascorburamine, two furanoisophthalides, monapurfluores A and B, monascopyridine A, B, C, and D, monasfluores A and B, xanthomonasin A and B, monascumic acid, and monacolin K (Wild and others 2003; Akihisa and others 2005a,b; Chen and Hu 2005; Hsu and others 2010), which exhibited different bioactivities, such as anti-cancer, anti-inflammatory, and hypolipidemic effects. Similarly, *Monascus* spp.-fermented monascal waxy corn and soybean also contained increased contents of monacolin K (also known as mevinolin and lovastatin) compared to unfermented samples (Pyo and Lee 2007; Kongbangkerd and others 2014), which was positively associated with the increased antioxidant effect of samples. In addition, fermented wheat germ has been found to produce benzoquinones with anti-cancer effect (Comin-Anduix and others 2002; Mueller and others 2011, Rizzello and others 2013).

Overall, fermented edible seeds and their products contain various bioactive components, especially vitamins, GABA, natural phenolics, and bioactive peptides, and these bioactive components endow the fermented products with versatile bioactivities, as discussed in the following section. In the future, bioactive components in other fermented edible seeds and their products can be explored to provide a basis for the development of fermented functional foods.

Bioactivities of fermented edible seeds and their products

A large number of studies demonstrate that fermented edible seeds and their products exhibit manifold bioactivities (Figure 1), such as antioxidant, anti-hypertensive, and anti-cancer effects.

Antioxidant effect

The influence of fermentation on the antioxidant effect of edible seeds and their products has been extensively investigated *in vitro*. Various antioxidant effects, such as free radical-scavenging, and reducing and metal-chelating effects, have been reported to be increased in the hydrophilic extracts of most fermented edible seeds and their products compared to unfermented samples (Table 5). The increase of antioxidant effect is mainly due to the increased antioxidant levels in fermented samples, mainly antioxidant phenolics and peptides (Table 3 and 4). However, the influence of fermentation on antioxidant effect in the lipophilic and bound extracts of edible seeds and their products has been scarcely investigated. Unlike the hydrophilic extract commonly prepared by polar solutions, such as ethanol and methanol water solutions, the lipophilic extract needs to be prepared by nonpolar solutions, such as *n*-hexane or tetrahydrofuran, and the bound extract needs to be hydrolyzed by acidic, alkaline, or enzymatic solutions. Our previous study found that fermented and nonfermented soybean and mung bean milks exhibited much higher ABTS and DPPH free radical-scavenging effect in their lipophilic extracts than their hydrophilic extracts, and fermentation had different effects on antioxidant effect in their lipophilic and hydrophilic extracts (Gan and others 2016c). In addition, we also found that some edible beans exhibited substantial antioxidant effects in their bound extracts, while fermentation had varying effects on antioxidant effect in their bound extracts (Gan and others 2016b). These results suggest that ignoring the lipophilic or bound extracts may significantly underestimate the total antioxidant effect in some fermented edible seeds and their products.

On the other hand, fermentation was also reported to decrease antioxidant effect in the hydrophilic extract of some edible seeds (Table 5), such as lentil (Gan and others 2016b), black cow gram (Gan and others 2016b), common bean (Gamboa-Gomez and others 2016), soybean (Fernandez-Orozco and others 2007; Gan and others 2016b), wheat (Dordevic and others 2010), buckwheat (Dordevic and others 2010), and buckwheat groats (Malgorzata and others 2015). The reduction of antioxidant effect may be partly associated with the reduction of reduced glutathione and related antioxidant enzyme activities in these fermented samples, such as fermented soybeans (Fernandez-Orozco and others 2007), and may also be associated with the degradation of antioxidant phenolics into phenolic compounds with lower antioxidant effect in these fermented samples. This may explain why fermentation generally increased TPC in these samples, but reduced their antioxidant effect. Overall, fermentation has different influences on antioxidant effect in edible seeds and their products, probably associated with different fermentation methods, different antioxidant components in samples as well as different extraction and evaluation methods for antioxidant effect.

Anti-hypertensive effect

Hypertension is one of the most important risk factors for cardiovascular diseases. Blood pressure is tightly controlled by the

Table 5–Influences of fermentation on antioxidant effect in edible seeds and their products.

Edible seeds and their products	Inoculated microbes	Extracts	Antioxidant assay	Antioxidant effect: Nonfermented samples	Antioxidant effect: Fermented samples	Unit	References
Chickpea (*Cicer arietinum* L.)	*R. oligosporus* NRRL 2710	80% Ethanol	ABTS	14.8	17.2 to 68.4	μmol TE/g DW	(Sanchez-Magana and others 2014)
			ORAC	30.3	34.6 to 100	μmol TE/g DW	
		NaOH hydrolysis	ABTS	18.2	19.1 to 28.7	μmol TE/g DW	
			ORAC	21.9	25.4 to 45.9	μmol TE/g DW	
	C. militaris SN-18	80% Methanol	DPPH	5.56^a	1.21^a	mg/mL	(Xiao and others 2014)
			ABTS	3.61^a	0.94^a	mg/mL	
			RP	14.6^a	4.15^a	mg/mL	
		80% Ethanol	DPPH	4.67^a	1.35^a	mg/mL	
			ABTS	3.34^a	0.98^a	mg/mL	
			RP	12.8^a	5.61^a	mg/mL	
		Water	DPPH	N.D.^{a}	3.08^a	mg/mL	
			ABTS	5.25^a	3.97^a	mg/mL	
			RP	10.2^a	5.38^a	mg/mL	
Common bean (*Phaseolus vulgaris* L., Bayo Victoria)	*R. oligosporus* (NRRL2710)	70% Acetone	DPPH	~2.00^a	~7.00 to 10.4^a	μg/μL	(Gamboa-Gomez and others 2016)
			LDL	~0.28^a	~0.48 to 1.48^a	μg/μL	
			HRSP	~3.30^a	~0.70 to 4.20^a	μg/μL	
Common bean (*Phaseolus vulgaris* L., Pinto durango)	*R. oligosporus* (NRRL2710)	70% Acetone	DPPH	~2.10^a	~7.40 to 9.70^a	μg/μL	
			LDL	~0.41^a	~1.15 to 1.74^a	μg/μL	
			HRSP	~0.50^a	~2.20 to 4.70^a	μg/μL	
Common bean (*Phaseolus vulgaris*)	*Lb. plantarum* DSM 20174 and *R. microsporus* var. chinensis	Phosphate buffer	ABTS	16.4	18.8	μmol TE/g DW	(Starzynska-Janiszewska and others 2014)
		80% Acetone	DPPH	3.73	4.70	μmol TE/g DW	
Black cow gram (*Lablab purpures*)	Natural fermentation	80% Methanol	FRAP	14.9	13.8	μmol Fe (II)/g DW	(Gan and others 2016b)
			ABTS	12.9	10.9	μmol TE/g DW	
		NaOH + HCl hydrolysis	FRAP	5.13	6.87	μmol Fe (II)/g DW	
			ABTS	3.52	4.45	μmol TE/g DW	
	Lb. paracasei 279	80% Methanol	FRAP	14.9	17.7	μmol Fe (II)/g DW	
			ABTS	12.9	12.5	μmol TE/g DW	
		NaOH + HCl hydrolysis	FRAP	5.13	5.94	μmol Fe (II)/g DW	
			ABTS	3.52	4.13	μmol TE/g DW	
	Lb. plantarum WCFS1	80% Methanol	FRAP	14.9	18.7	μmol Fe (II)/g DW	
			ABTS	12.9	13.2	μmol TE/g DW	
		NaOH + HCl hydrolysis	FRAP	5.13	6.46	μmol Fe (II)/g DW	

(*Continued*)

Table 5–Continued.

Edible seeds and their products	Inoculated microbes	Extracts	Antioxidant assay	Antioxidant effect: Nonfermented samples	Antioxidant effect: Fermented samples	Unit	References
Mottled cowpea (*Vigna unguiculata*)	Natural fermentation	80% Methanol	ABTS FRAP	3.52 23.1	4.18 29.6	µmol TE/g DW µmol Fe (II)/g DW	(Gan and others 2016b)
		NaOH + HCl hydrolysis	ABTS FRAP	23.9 8.93	28.0 17.8	µmol TE/g DW µmol Fe (II)/g DW	
	Lb. paracasei 279	80% Methanol	ABTS FRAP	5.35 23.1	12.9 40.1	µmol TE/g DW µmol Fe (II)/g DW	
		NaOH + HCl hydrolysis	ABTS FRAP	23.9 8.93	29.4 8.59	µmol TE/g DW µmol Fe (II)/g DW	
	Lb. plantarum WCFS1	80% Methanol	ABTS FRAP	5.35 23.1	5.55 38.1	µmol TE/g DW µmol Fe (II)/g DW	
		NaOH + HCl hydrolysis	ABTS FRAP	23.9 8.93	28.9 9.81	µmol TE/g DW µmol Fe (II)/g DW	
Kidney bean (*Phaseolus vulgaris*)	Natural fermentation	Water	ABTS ORAC	5.35 ~120	6.08 ~130	µmol TE/g DW mmol TE/g DW	(Limon and others 2015)
	B. subtilis CECT 39 ^{T} (ATCC 6051)	Water	ORAC	~170	~500 to 550	mmol TE/g DW	
	Lb. plantarum CECT 748 ^{T} (ATCC 14917)	Water	ORAC	~120	~115 to 130	mmol TE/g DW	
Speckled kidney bean (*Phaseolus vulgaris*)	Natural fermentation	80% Methanol	FRAP	11.5	16.9	µmol Fe (II)/g DW	(Gan and others 2016b)
		NaOH + HCl hydrolysis	ABTS FRAP	13.1 6.17	19.1 6.92	µmol TE/g DW µmol Fe (II)/g DW	
	Lb. paracasei 279	80% Methanol	ABTS FRAP	4.89 11.5	4.70 24.0	µmol TE/g DW µmol Fe (II)/g DW	
		NaOH + HCl hydrolysis	ABTS FRAP	13.1 6.17	24.0 5.99	µmol TE/g DW µmol Fe (II)/g DW	
	Lb. plantarum WCFS1	80% Methanol	ABTS FRAP	4.89 11.5	4.23 21.9	µmol TE/g DW µmol Fe (II)/g DW	
		NaOH + HCl hydrolysis	ABTS FRAP	13.1 6.17	22.6 6.26	µmol TE/g DW µmol Fe (II)/g DW	
Lentil (*Lens culinaris*)	Natural fermentation	Water	ABTS ORAC	4.89 ~0.26	4.08 ~0.25 to 0.30	µmol TE/g DW mmol TE/g DW	(Torino and others 2013)
	B. subtilis CECT 39 ^{T} (ATCC 6051)	Water	ORAC	~0.15	~0.21 to 0.23	mmol TE/g DW	
	L. plantarum CECT 748 ^{T} (ATCC 14917)	Water	ORAC	~0.26	~0.27 to 0.30	mmol TE/g DW	
Lentil (*Lens culinaris*)	Natural fermentation	80% Methanol	FRAP	11.2	10.5	µmol Fe (II)/g DW	(Gan and others 2016b)
		NaOH + HCl hydrolysis	ABTS FRAP	12.8 6.30	11.0 8.72	µmol TE/g DW µmol Fe (II)/g DW	

(*Continued*)

Table 5–Continued.

Edible seeds and their products	Inoculated microbes	Extracts	Antioxidant assay	Antioxidant effect: Nonfermented samples	Antioxidant effect: Fermented samples	Unit	References
			ABTS	4.50	5.62	μmol TE/g DW	
	Lb. paracasei 279	80% Methanol	FRAP	11.2	16.1	μmol Fe (II)/g DW	
			ABTS	12.8	13.3	μmol TE/g DW	
		NaOH + HCl hydrolysis	FRAP	6.30	4.47	μmol Fe (II)/g DW	
			ABTS	4.50	3.40	μmol TE/g DW	
	Lb. plantarum WCFS1	80% Methanol	FRAP	11.2	14.5	μmol Fe (II)/g DW	
			ABTS	12.8	12.5	μmol TE/g DW	
		NaOH + HCl hydrolysis	FRAP	6.30	5.16	μmol Fe (II)/g DW	
			ABTS	4.50	3.63	μmol TE/g DW	
Lupin (*Lupinus albus*)	Natural fermentation	PBS	ABTS	71.4	55.1 to 71.8	μmol TE/g DW	(Frias and others 2005)
	Lb. plantarum CECT 748	PBS	ABTS	71.4	75.2	μmol TE/g DW	
Mung bean (*Vigna radiata*)	*C. militaris* SN-18	80% methanol	DPPH	~720	~1040	μg VcE/g DW	(Xiao and others 2015d)
			ABTS	~1000	~3750	μg VcE/g DW	
			FRAP	~7.30	~8.50	μmol Fe (II)/g DW	
			RP	~400	~800	μg VcE/g DW	
			Iron-chelating	~2.50	~10.5	μmol EDTA-2Na/g DW	
		80% ethanol	DPPH	~650	~750	μg VcE/g DW	
			ABTS	~1120	~3500	μg VcE/g DW	
			FRAP	~6.20	~7.00	μmol Fe (II)/g DW	
			RP	~440	~750	μg VcE/g DW	
			Iron-chelating	~4.60	~10.0	μmol EDTA-2Na/g DW	
		80% acetone	DPPH	~1050	~1055	μg VcE/g DW	
			ABTS	~1560	~3350	μg VcE/g DW	
			FRAP	~9.30	~10.0	μmol Fe (II)/g DW	
			RP	~680	~850	μg VcE/g DW	
			Iron-chelating	~3.70	~9.20	μmol EDTA-2Na/g DW	
		water	DPPH	~600	~1460	μg VcE/g DW	
			ABTS	~1050	~3750	μg VcE/g DW	
			FRAP	~5.00	~16.0	μmol Fe (II)/g DW	
			RP	~310	~1280	μg VcE/g DW	
			Iron-chelating	~3.50	~4.70	μmol EDTA-2Na/g DW	
Red bean (*Phaseolus radiatus*)	*B. subtilis* (BCRC 14716) and *Lb. delbrueckii* sp. bulgaricus (BCRC 14008)	Water	DPPH	84.6[a]	22.4[a]	mg/mL	(Jhan and others 2015)
		Water	Iron-chelating	N.D.[a]	> 1000 [a]	mg/mL	
		50% Ethanol	DPPH	56.0[a]	16.6[a]	mg/mL	
		50% Ethanol	Iron-chelating	N.D.[a]	75.3[a]	mg/mL	
Small rice bean (*Vigna umbellata*)	Natural fermentation	80% Methanol	FRAP	19.8	21.3	μmol Fe (II)/g DW	(Gan and others 2016b)
			ABTS	20.0	21.5	μmol TE/g DW	
		NaOH + HCl hydrolysis	FRAP	6.04	11.5	μmol Fe (II)/g DW	

(*Continued*)

Table 5–Continued.

Edible seeds and their products	Inoculated microbes	Extracts	Antioxidant assay	Antioxidant effect: Nonfermented samples	Antioxidant effect: Fermented samples	Unit	References
			ABTS	4.60	7.50	μmol TE/g DW	
	Lb. paracasei 279	80% Methanol	FRAP	19.8	29.7	μmol Fe (II)/g DW	
			ABTS	20.0	25.7	μmol TE/g DW	
		NaOH + HCl hydrolysis	FRAP	6.04	4.26	μmol Fe (II)/g DW	
			ABTS	4.60	3.48	μmol TE/g DW	
	Lb. plantarum WCFS1	80% Methanol	FRAP	19.8	29.4	μmol Fe (II)/g DW	
			ABTS	20.0	25.7	μmol TE/g DW	
		NaOH + HCl hydrolysis	FRAP	6.04	5.11	μmol Fe (II)/g DW	
			ABTS	4.60	4.05	μmol TE/g DW	
Small runner bean (*Phaseolus coccineus*)	Natural fermentation	80% Methanol	FRAP	11.1	11.7	μmol Fe (II)/g DW	(Gan and others 2016b)
			ABTS	12.2	14.8	μmol TE/g DW	
		NaOH + HCl hydrolysis	FRAP	20.7	9.16	μmol Fe (II)/g DW	
			ABTS	13.2	5.63	μmol TE/g DW	
	Lb. paracasei 279	80% Methanol	FRAP	11.1	18.5	μmol Fe (II)/g DW	
			ABTS	12.2	20.3	μmol TE/g DW	
		NaOH + HCl hydrolysis	FRAP	20.7	5.46	μmol Fe (II)/g DW	
			ABTS	13.2	4.04	μmol TE/g DW	
	Lb. plantarum WCFS1	80% Methanol	FRAP	11.1	18.9	μmol Fe (II)/g DW	
			ABTS	12.2	18.9	μmol TE/g DW	
		NaOH + HCl hydrolysis	FRAP	20.7	9.08	μmol Fe (II)/g DW	
			ABTS	13.2	6.27	μmol TE/g DW	
Soybean (*Glycine max*)	Natural fermentation	80% Methanol	ABTS	63.0	44.6 to 57.6	μmol TE/g DW	(Fernandez-Orozco and others 2007)
	A. oryzae 2094^{T} (ATCC 1011)	80% Methanol	ABTS	63.0	38.0	μmol TE/g DW	
	R. oryzae CECT 2340 (ATCC 24563)	80% Methanol	ABTS	63.0	46.7	μmol TE/g DW	
	B. subtilis CECT 39^{T} (ATCC 6051)	80% Methanol	ABTS	63.0	131	μmol TE/g DW	
	Lb. plantarum CECT 748^{T} (ATCC 14917)	80% Methanol	ABTS	63.0	54.5 to 57.4	μmol TE/g DW	
	Natural fermentation	80% Methanol	PRTC	2.54	2.22 to 3.40	μmol TE/g DW	
	A. oryzae 2094^{T} (ATCC 1011)	80% Methanol	PRTC	2.54	4.59	μmol TE/g DW	
	R. oryzae CECT 2340 (ATCC 24563)	80% Methanol	PRTC	2.54	6.77	μmol TE/g DW	
	B. subtilis CECT 39^{T} (ATCC 6051)	80% Methanol	PRTC	2.54	9.23	μmol TE/g DW	
	Lb. plantarum CECT 748^{T} (ATCC 14917)	80% Methanol	PRTC	2.54	3.60 to 4.25	μmol TE/g DW	
Yellow soybean (*Glycine max*)	Natural fermentation	80% Methanol	FRAP	7.08	4.37	μmol Fe (II)/g DW	(Gan and others 2016b)

(*Continued*)

Table 5–Continued.

Edible seeds and their products	Inoculated microbes	Extracts	Antioxidant assay	Antioxidant effect Nonfermented samples	 Fermented samples	Unit	References
			ABTS	9.53	4.62	μmol TE/g DW	
		NaOH + HCl hydrolysis	FRAP	2.10	3.50	μmol Fe (II)/g DW	
			ABTS	1.24	1.79	μmol TE/g DW	
	Lb. paracasei 279	80% Methanol	FRAP	7.08	4.64	μmol Fe (II)/g DW	
			ABTS	9.53	3.47	μmol TE/g DW	
		NaOH + HCl hydrolysis	FRAP	2.10	3.39	μmol Fe (II)/g DW	
			ABTS	1.24	1.76	μmol TE/g DW	
	Lb. plantarum WCFS1	80% Methanol	FRAP	7.08	4.48	μmol Fe (II)/g DW	
			ABTS	9.53	3.58	μmol TE/g DW	
		NaOH + HCl hydrolysis	FRAP	2.10	2.86	μmol Fe (II)/g DW	
			ABTS	1.24	1.91	μmol TE/g DW	
Black soybean (*Glycine max*)	*B. subtilis* BCRC 14715	80% Methanol	DPPH	1.56[a]	0.83[a]	mg/mL	(Juan and Chou 2010)
		80% Ethanol	DPPH	1.48[a]	0.91[a]	mg/mL	
		80% Acetone	DPPH	0.94[a]	0.65[a]	mg/mL	
		Water	DPPH	2.28[a]	1.65[a]	mg/mL	
		80% Methanol	Iron-chelating	4.52[a]	2.17[a]	mg/mL	
		80% Ethanol	Iron-chelating	8.97[a]	4.57[a]	mg/mL	
		80% Acetone	Iron-chelating	12.0[a]	8.30[a]	mg/mL	
		Water	Iron-chelating	16.1[a]	14.2[a]	mg/mL	
Black soybean (*Glycine max*)	*A. awamori*	Methanol	DPPH	1.95[a]	0.70[a]	mg/mL	(Lee and others 2008)
	A. oryzae BCRC 30222	Methanol	DPPH	1.95[a]	1.39[a]	mg/mL	
	A. sojae BCRC 30103	Methanol	DPPH	1.95[a]	1.24[a]	mg/mL	
	R. azygosporus BCRC 31158	Methanol	DPPH	1.95[a]	1.58[a]	mg/mL	
	Rhizopus sp. No. 2	Methanol	DPPH	1.95[a]	2.11[a]	mg/mL	
	A. awamori	Methanol	Iron-chelating	2.68[a]	1.19[a]	mg/mL	
	A. oryzae BCRC 30222	Methanol	Iron-chelating	2.68[a]	1.54[a]	mg/mL	
	A. sojae BCRC 30103	Methanol	Iron-chelating	2.68[a]	1.67[a]	mg/mL	
	R. azygosporus BCRC 31158	Methanol	Iron-chelating	2.68[a]	1.82[a]	mg/mL	
	Rhizopus sp. No. 2	Methanol	Iron-chelating	2.68[a]	3.11[a]	mg/mL	
Black soybean (*Glycine max*)	Natural fermentation	80% Methanol	FRAP	17.5	13.6	μmol Fe (II)/g DW	(Gan and others 2016b)
			ABTS	15.4	10.6	μmol TE/g DW	
		NaOH + HCl hydrolysis	FRAP	3.75	9.15	μmol Fe (II)/g DW	
			ABTS	2.59	5.21	μmol TE/g DW	
	Lb. paracasei 279	80% Methanol	FRAP	17.5	16.8	μmol Fe (II)/g DW	

(*Continued*)

Table 5–Continued.

Edible seeds and their products	Inoculated microbes	Extracts	Antioxidant assay	Antioxidant effect		Unit	References
				Nonfermented samples	Fermented samples		
			ABTS	15.4	11.8	μmol TE/g DW	
		NaOH + HCl hydrolysis	FRAP	3.75	5.88	μmol Fe (II)/g DW	
			ABTS	2.59	3.55	μmol TE/g DW	
	Lb. plantarum WCFS1	80% Methanol	FRAP	17.5	17.8	μmol Fe (II)/g DW	
			ABTS	15.4	12.2	μmol TE/g DW	
		NaOH + HCl hydrolysis	FRAP	3.75	6.27	μmol Fe (II)/g DW	
			ABTS	2.59	3.65	μmol TE/g DW	
Barley (*Hordeum vulgare*)	*Lb. rhamnosus*	70% ethanol	FRAP	15.6	20.0	nmol Fe (II)/mg DW	(Dordevic and others 2010)
	S. cerevisiae	70% ethanol	FRAP	15.6	19.8	nmol Fe (II)/mg DW	
Buckwheat (*Fagopyrum esculentum*)	*Lb. rhamnosus*	70% ethanol	DPPH	76.7	63.4^{a}	μg/mL	
			FRAP	49.4	51.5	nmol Fe (II)/mg DW	
	S. cerevisiae	70% ethanol	DPPH	76.7	66.3^{a}	μg/mL	
			FRAP	49.4	49.8	nmol Fe (II)/mg DW	
Maize (*Zea mays* subsp. mays)	*A. oryzae* NCIM 1212, *A. awamori* MTCC No. 548, *R. oligosporus* NCIM 1215, *R. oryzae* RCK2012	Water	ABTS	4.85	~3.00 to 13.0	μmol TE/g DW	(Dey and Kuhad 2014)
			DPPH	1.84	~2.00 to 5.80	μmol TE/g DW	
	T. elegans CCF-1456	65% Ethanol	ABTS	~15.5	~18.0 to 24.0	μmol TE/g DW	(Salar and others 2012)
			DPPH	~12.0	~12.5 to 14.0	μmol TE/g DW	
Oat (*Avena sativa* L.)	*A. oryzae var. effuses 3.2825, A. oryzae 3.5232, R. oryzae 3.275*	80% Ethanol	CVA	~1.60	~5.50 to 7.00	Q1200, μC	(Cai and others 2014)
			ORAC	~240	~350 to 430	μmol TE/g DW	
	A. oryzae NCIM 1212, *A. awamori* MTCC No. 548, *R. oligosporus* NCIM 1215, *R. oryzae* RCK2012	Water	ABTS	4.90	~6.00 to 20.5	μmol TE/g DW	(Dey and Kuhad 2014)
			DPPH	2.98	~2.50 to 9.50	μmol TE/g DW	
	C. militaris SN-18	water	DPPH	9.13^{a}	5.86^{a}	mg/mL	(Xiao and others 2015a)
			ABTS	3.62^{a}	1.18^{a}	mg/mL	
			RP	16.7^{a}	8.10^{a}	mg/mL	
			Iron-chelating	17.4^{a}	9.14^{a}	mg/mL	
		80% methanol	DPPH	3.71^{a}	2.78^{a}	mg/mL	
			ABTS	1.80^{a}	0.83^{a}	mg/mL	
			RP	6.83^{a}	4.32^{a}	mg/mL	
			Iron-chelating	15.5^{a}	2.90^{a}	mg/mL	
		80% ethanol	DPPH	2.96^{a}	2.77^{a}	mg/mL	

(*Continued*)

Table 5–Continued.

Edible seeds and their products	Inoculated microbes	Extracts	Antioxidant assay	Antioxidant effect: Nonfermented samples	Antioxidant effect: Fermented samples	Unit	References
			ABTS	2.11[a]	0.94[a]	mg/mL	
			RP	6.23[a]	3.75[a]	mg/mL	
			Iron-chelating	8.03[a]	4.71[a]	mg/mL	
		80% acetone	DPPH	2.54[a]	2.26[a]	mg/mL	
			ABTS	1.65[a]	0.85[a]	mg/mL	
			RP	4.49[a]	3.41[a]	mg/mL	
			Iron-chelating	0.88[a]	0.56[a]	mg/mL	
Brown rice (*Oryza sativa*)	*A. oryzae* NCIM 1212, *A. awamori* MTCC No. 548, *R. oligosporus* NCIM 1215, *R. oryzae* RCK2012	Water	ABTS	4.30	~7.50 to 18.0	μmol TE/g DW	(Dey and Kuhad 2014)
			DPPH	1.15	~2.40 to 4.80	μmol TE/g DW	
Black rice bran	*B. subtilis* KU3	Fermented super-natant	DPPH	0.58[a]	0.70[a]	mg/mL	(Yoon and others 2015)
			CBA	52.9[a]	47.8[a]	mg/mL	
Rye (*Secale cereale*)	*Lb. rhamnosus*	70% ethanol	FRAP	8.94	13.9	nmol Fe (II)/mg DW	(Dordevic and others 2010)
	S. cerevisiae	70% ethanol	FRAP	8.94	10.7	nmol Fe (II)/mg DW	
Wheat (*Triticum durum*)	*Lb. rhamnosus*	70% ethanol	FRAP	12.2	15.1	nmol Fe (II)/mg DW	
	S. cerevisiae	70% ethanol	FRAP	12.2	12.3	nmol Fe (II)/mg DW	
Wheat (*Triticum* spp.)	*A. oryzae* NCIM 1212, *A. awamori* MTCC No. 548, *R. oligosporus* NCIM 1215, *R. oryzae* RCK2012	Water	ABTS	3.85	~8.00 to 19.5	μmol TE/g DW	(Dey and Kuhad 2014)
			DPPH	1.29	~3.70 to 8.60	μmol TE/g DW	
	G. gargal	Methanol	DPPH	57.6[a]	0.56[a]	mg/mL	(Postemsky and Curvetto 2014)
			RP	55.0[a]	0.55[a]	mg/mL	
	G. sordulenta	Methanol	DPPH	57.6[a]	5.80[a]	mg/mL	
			RP	55.0[a]	4.20[a]	mg/mL	
	G. frondosa	Methanol	DPPH	57.6[a]	0.81[a]	mg/mL	
			RP	55.0[a]	0.64[a]	mg/mL	
	Gd. australe (KUM60813)	Ethanol	DPPH	12.4	15.0	mg AAE/g DW	
			FRAP	2.19	1.05	mg Fe (II)/g DW	
			ABTS	8.74	9.73	mg TE/g DW	
	Gd. neo-japonicum (KUM61076)	Ethanol	DPPH	12.4	21.7	mg AAE/g DW	
			FRAP	2.19	2.41	mg Fe (II)/g DW	
			ABTS	8.74	9.47	mg TE/g DW	
	Gd. lucidum (VITA GL)	Ethanol	DPPH	12.4	6.61	mg AAE/g DW	
			FRAP	2.19	0.80	mg Fe (II)/g DW	
			ABTS	8.74	14.2	mg TE/g DW	
Wheat (*Triticum aestivum* Linn.)	*C. militaris*	70% Ethanol	DPPH	0.08[a]	0.06[a]	mg/mL	(Zhang and others 2012)

(*Continued*)

Table 5–Continued.

Edible seeds and their products	Inoculated microbes	Extracts	Antioxidant assay	Antioxidant effect		Unit	References
				Nonfermented samples	Fermented samples		
			HRSP	0.21^a	0.11^a	mg/mL	
			Iron-chelating	0.61^a	0.26^a	mg/mL	
			RP	0.52^a	0.58^a	mg/mL	
		70% Acetone	DPPH	$< 0.05^a$	$< 0.05^a$	mg/mL	
			HRSP	0.12^a	0.07^a	mg/mL	
			Iron-chelating	0.29^a	0.21^a	mg/mL	
			RP	0.23^a	0.13^a	mg/mL	
		Water	DPPH	0.38^a	0.32^a	mg/mL	
			HRSP	0.76^a	0.61^a	mg/mL	
			Iron-chelating	0.79^a	0.44^a	mg/mL	
			RP	$> 0.80^a$	$> 0.80^a$	mg/mL	
Adlay (*Coix lachryma-jobi*)	*B. subtilis* BCRC 14718	Methanol	DPPH	3.12	1.19	mg/mL	(Wang and others 2014)
			Iron-chelating	10.1	6.15	mg/mL	
	Lb. plantarum	Methanol	DPPH	3.12	2.24	mg/mL	
			Iron-chelating	10.1	8.09	mg/mL	
Chestnut (*Castanea crenata*)	*B. subtilis* BCRC 14718	Methanol	DPPH	2.43	1.89	mg/mL	
			Iron-chelating	6.83	5.73	mg/mL	
	Lb. plantarum	Methanol	DPPH	2.43	2.31	mg/mL	
			Iron-chelating	6.83	6.51	mg/mL	
Lotus seed (Nelumbo nucifera)	*B. subtilis* BCRC 14718	Methanol	DPPH	2.93	1.67	mg/mL	
			Iron-chelating	15.8	11.3	mg/mL	
	Lb. plantarum	Methanol	DPPH	2.93	1.83	mg/mL	
			Iron-chelating	15.8	12.0	mg/mL	
Walnut (Juglans regia)	*B. subtilis* BCRC 14718	Methanol	DPPH	1.92	0.80	mg/mL	
			Iron-chelating	7.70	6.83	mg/mL	
	Lb. plantarum	Methanol	DPPH	1.92	0.89	mg/mL	
			Iron-chelating	7.70	6.71	mg/mL	
Soymilk	*Lb. acidophilus* CCRC 14079	N.M.	RP	3.81	8.28	μmol CE/L	(Wang and others 2006)
	Sc. thermophiles CCRC 14085	N.M.	RP	3.81	7.86	μmol CE/L	
	Bb. infantis CCRC 14633	N.M.	RP	3.81	7.97	μmol CE/L	
	Bb. longum B6	N.M.	RP	3.81	8.31	μmol CE/L	
	Lb. acidophilus CSCC 2400	80% Methanol + Hexane	RP	1.00	0.81 to 1.20	mg AAE/100 mL	(Zhao and Shah 2014)
	Lb. paracasei CSCC 279	80% Methanol + Hexane	RP	1.00	0.58 to 1.10	mg AAE/100 mL	

(*Continued*)

Table 5–Continued.

Edible seeds and their products	Inoculated microbes	Extracts	Antioxidant assay	Antioxidant effect: Nonfermented samples	Antioxidant effect: Fermented samples	Unit	References
	Lb. zeae ASCC 15820	80% Methanol + Hexane	RP	1.00	0.64 to 1.21	mg AAE/100 mL	
	Lb. rhamnosus WQ2	80% Methanol + Hexane	RP	1.00	0.74 to 1.60	mg AAE/100 mL	
	Lb. plantarum CCFM8610	Unknown	RP	25.0	117	umol CE/L	(Zhai and others 2015)
	Lb. bulgaricus CCFM8004	Unknown	RP	25.0	81.5	umol CE/L	
Soy germ	*A. niger* M46	70% Methanol	HRSP	164^a	0.8^a	ug/mL	(Sheih and others 2014)
Soy whey	*Lb. plantarum* B1-6	80& Ethanol	ABTS	0.72^a	0.19^a	mg/mL	(Xiao and others 2015b)
			RP	1.36^a	1.16^a		
			HRSP	0.12^a	0.03^a		
			SASP	2.71^a	2.30^a		
Buckwheat groats (*Fagopyrum esculentum* Moench)	*R. oligosporus* NRRL 2710	80% methanol	ABTS	22.9	15.7	μmol TE/g DW	(Malgorzata and others 2015)
			ACL PCL	17.3	11.2	μmol TE/g DW	
			ACW PCL	3.97	4.57	μmol TE/g DW	
Buckwheat groats (*Fagopyrum esculentum*)	*R. oligosporus* ATCC 64063	50% Acetone	DPPH	9.46	10.8	μmol TE/g DW	(Starzynska-Janiszewska and others 2016)
		PBS (0.1 M, pH 7.4)	ABTS	27.2	42.7	μmol TE/g DW	

AAE, ascorbic acid equivalent; ABTS, ABTS free radical scavenging value; CVA, Cyclic voltammetry assay; DPPH, DPPH free radical scavenging value; ORAC, oxygen radical absorbance capacity; RP, reducing power; HRSP, hydroxyl radical scavenging capacity; SASP, superoxide anion scavenging capacity; CBA, β-carotene bleaching assay; ACL PCL, lipophilic-based superoxide anion radicals scavenging value; ACW PCL, hydrophilic-based superoxide anion radicals scavenging value. CE, cysteine equivalent; TE, trolox equivalent; VcE/AAE, vitamin C/Ascorbic acid equivalent; DW, dry weight; N.M., not measured. *A., Aspergillus; B., Bacillus; Bb, Bifidobacterium; C., Cordyceps; G., Grifola; Gd., Ganoderma; Lb., Lactobacillus; R., Rhizopus; S., Saccharomyces; Sc., Streptococcus; T., Thamnidium.* ^{a} EC_{50} value.

Table 6–Anti-hypertensive effect of fermented edible seeds and their products.

Edible seeds and their products	Inoculated microbes	Anti-hypertensive effect	Main anti-hypertensive components	References
Chickpea (*Cicer arietinum* L.)	*C. militaris* SN-18	Inhibit ACE activity *in vitro*	Potential ACE-inhibitory peptides	(Xiao and others 2015c)
Lentil (*Lens culinaris* L.)	*Lb. plantarum* CECT 748^T	Inhibit ACE activity *in vitro*	Potential ACE-inhibitory peptides	(Torino and others 2013)
Mung bean (*Vigna radiata*)	*Lb. plantarum* B1-6	Inhibit ACE activity *in vitro*	Potential ACE-inhibitory peptides	(Wu and others 2015)
Pea seeds (*Pisum sativum* var. Bajka)	*Lb. plantarum* 299v.	Inhibit ACE activity *in vitro*	ACE-inhibitory peptides	(Jakubczyk and others 2013)
Soybean (*Glycine max*)	*M. pilosus* KFRI-1140	Inhibit ACE activity *in vitro*	Potential ACE-inhibitory peptides	(Pyo and Lee 2007)
Soy protein	*Lb. casei* spp. pseudoplantarum	Inhibit ACE activity *in vitro*	ACE-inhibitory peptides	(Vallabha and Tiku 2014)
Black soybean (*Glycine max*)	*B. subtilis* BCRC 14715 and *Bacillus* sp. CN11	Inhibit ACE activity *in vitro*	Potential ACE-inhibitory peptides, nicotiamide, isoflavone aglycones and other flavonoids	(Juan and others 2010)
A mixture of black beans, soybeans, and wheat bran (1:1:1, w/w/w)	*B. subtilis* B060	Lower blood pressure in hypertensive rats	GABA and nattokinase	(Suwanmanon and Hsieh 2014)
Navy bean (*Phaseolus vulgaris*) milk	Different LAB	Inhibit ACE activity *in vitro*	ACE-inhibitory peptides	(Rui and others 2015)
Soymilk	A mixture of LAB	Inhibit ACE activity *in vitro* and Lower blood pressure in hypertensive rats	ACE-inhibitory peptides and GABA	(Tsai and others 2006)
	Different LAB	Inhibit ACE activity *in vitro*	N.M.	(Ewe and others 2011)
	Lb. plantarum TWK10	Inhibit ACE activity and lower blood pressure in hypertensive rats	N.M.	(Liu and others 2016)
Soy yogurt	Different LAB	Inhibit ACE activity *in vitro*	Potential ACE-inhibitory peptides	(Donkor and others 2005)
Soy flour sourdoughs	Different LAB	Inhibit ACE activity *in vitro*	Potential ACE-inhibitory peptides	(Omedi and others 2016)
Tofuyo (based on soybean)	Unknown	Inhibit ACE activity *in vitro*	ACE-inhibitory peptides	(Kuba and others 2003)
Casein miso paste (based on rice and soybean)	*A. oryzae*	Lower blood pressure in hypertensive rats	ACE-inhibitory peptides	(Inoue and others 2009)
A *dosa* made of wheat and rice flour	*Lb. plantarum* MNZ	Inhibit ACE activity *in vitro* and Lower blood pressure in hypertensive rats	GABA and potential bioactive peptides	(Zareian and others 2015)
White wheat, wholemeal wheat and rye	Different LAB	Inhibit ACE activity *in vitro*	ACE-inhibitory peptides	(Rizzello and others 2008)

N.M., not mentioned; ACE, angiotensin converting-I-enzyme; GABA, γ-aminobutyric acid; LAB, lactic acid bacteria; *Lb., lactobacillus; A., Aspergillus; B., Bacillus; C., Cordyceps; M., Monascus.*

renin–angiotensin–aldosterone system in humans. As a central component of the system, ACE functions to convert angiotensin I into angiotensin II, which is able to increase blood pressure by directly causing blood vessels to constrict (Skeggs and others 1956). As a result, ACE plays a central role in the control of blood pressure, and natural or synthetic compounds with ACE-inhibitory activity have been reported to lower blood pressure in experimental animals and humans (Fang and others 2008).

Recent studies demonstrate that some fermented edible seeds and their products exhibit anti-hypertensive effects *in vitro* and *in vivo*. A variety of fermented edible seeds and their products, mainly edible bean products, such as fermented chickpea, lentil, mung bean, pea, soybean, soymilk, and navy bean milk, have been reported to possess ACE-inhibitory activity *in vitro* or lower blood pressure in animal models (Table 6). However, the anti-hypertensive effect of fermented grains has been less investigated. Their bioactive components, such as GABA, ACE-inhibitory peptides, nattokinase, vitamins, and various antioxidant phenolics, can be responsible for the anti-hypertensive effect (Kim and others 2008; Lee and Pan 2012; Huang and others 2013). Especially, GABA and ACE-inhibitory peptides are found in many fermented edible seeds and their products (Table 2 and 4), which have been reported to be predominantly responsible for their anti-hypertensive effect (Table 6). As a result, fermented edible seeds and their products can be an important dietary component consumed by people to prevent hypertension. In addition, in light of the importance of cereal grains as staple foods for humans, more studies are needed to investigate the potential anti-hypertensive effect of fermented cereal grains in the future.

Anti-cancer effect

The anti-cancer effect has been investigated in different fermented edible seeds and their products, such as fermented soybean, black bean, green bean, soymilk, wheat germ, and rice (Table 7). LAB and fungi are the main inoculated microbes to produce anti-cancer products. Various bioactive compounds, such as natural phenolics, peptides, amino acids, benzoquinones, GABA, polysaccharides, monacolin K, and vitamin E, have been suggested to be potential anti-cancer components. Below, we highlight the anti-cancer effect of *S. cerevisiae*-fermented wheat germ and *A. oryzae*-fermented brown rice and rice bran, which have been extensively investigated for their anti-cancer effect.

S. cerevisiae-fermented wheat germ was first produced by Dr. Mate Hidvegi in the early 1990s with anti-cancer effect in animal models and cancer patients, and subsequently developed into a commercial product, with the brand name Avemar (Demidov and others 2008; Rizzello and others 2013). This fermented wheat germ has been reported to exhibit anti-cancer effect on a variety of cancer cells, such as leukemia, lymphoid, pediatric, colon, skin melanoma, ovarian, and liver cancer/tumor cells *in vitro* and *in vivo* (Table 7). Two benzoquinones, 2-methoxy benzoquinone (2-MBQ) and 2,6-dimethoxy-benzoquinone (2,6-DMBQ), have

Table 7–Anti-cancer effect of fermented edible seeds and their products.

Edible seeds and their products	Inoculated microbes	Possible effective components	Actions and potential mechanisms	References
Soybean, black bean, and green bean mixture	*Lb. paracasei* and *S. cerevisiae*	Isoflavones	Induce cancer cell apoptosis *in vitro* and inhibit tumor xenografts *in vivo*	(Chia and others 2013)
Italian legumes	*Lb. plantarum* C48 and *Lb. brevis* AM7	Lunasin-like polypeptides	Inhibit cancer cell proliferation *in vitro*	(Rizzello and others 2015)
Soybean and mung bean	*Rhizopus* sp. 5351	GABA, free amino acids and phenolics	Induce cytotoxicity by blocking G0/G1 cell cycle phase and inducing apoptosis *in vitro*	(Ali and others 2016)
Soymilk	*Sc. thermophilus* 14085 and *Bb. infantis* 14603	Phenolics	Inhibit cancer cell proliferation *in vitro*	(Lai and others 2013)
Wheat germ	*S. cerevisiae*	Benzoquinones	Inhibit proliferation and induce apoptosis in Jurkat T-cell leukemia tumor cells *in vitro*	(Comin-Anduix and others 2002)
	S. cerevisiae	2,6-DMBQ	Induce apoptosis and reduce MHC class I expression in lymphoid tumor cells *in vitro*	(Fajka-Boja and others 2002)
	S. cerevisiae	N.M.	Reduce chemotherapy-induced febrile neutropenia in pediatric cancer patients	(Garami and others 2004)
	S. cerevisiae	N.M.	Inhibit proliferation, and induced both necrosis and apoptosis in human HT-29 colon cancer cells *in vitro*	(Illmer and others 2005)
	S. cerevisiae	N.M.	Induce apoptosis and inhibit ribonucleotide reductase in human HL-60 promyelocytic leukemia cells *in vitro*	(Saiko and others 2007)
	S. cerevisiae	N.M.	Improve the survival of high-risk skin melanoma patients	(Demidov and others 2008)
	S. cerevisiae	N.M.	Attenuate the growth and induce apoptosis in human H9 lymphoma cells *in vitro*	(Saiko and others 2009)
	S. cerevisiae	2-MBQ and 2,6-DMBQ	Induce apoptosis in a variety of cancer cells *in vitro*	(Mueller and others 2011)
	S. cerevisiae	2,6-DMBQ	Inhibit proliferation and potentiate cisplatin-induced apoptosis human ovarian cancer cells *in vitro*	(Judson and others 2012)
	Lb. plantarum LB1 and *Lb. rossiae* LB5	2-MBQ and 2,6-DMBQ	Inhibit cancer cell proliferation *in vitro*	(Rizzello and others 2013)
	S. cerevisiae	N.M.	Induce cell death and enhance cytotoxicity of cisplatin and 5-fluorouracil on human liver cancer cells *in vitro*	(Tai and others 2013)
	S. cerevisiae	N.M.	Inhibit proliferation and induce apoptosis in human ovarian cancer cells *in vitro*	(Wang and others 2015)
	Lb. plantarum dy-1 (LFWGE).	2,6-DMBQ	Inhibit proliferation and induce apoptosis in human HT-29 colon cancer cells *in vitro*	(Zhang and others 2015a)
	Lb. plantarum dy-1 (LFWGE).	N.M.	Induce colon cancer cell apoptosis in xenograft mouse model	(Zhang and others 2015b)
	S. cerevisiae	2,6-DMBQ	Inhibit proliferation *in vitro*, probably associated with the induction of autophagy	(Otto and others 2016)
Brown rice and rice bran	*A. oryzae*	N.M.	Inhibit the formation of AOM-induced aberrant crypt foci and tumors in the colon of F344 rats	(Katyama and others 2002)
	A. oryzae	N.M.	Decrease the incidence and multiplicity of hepatocellular carcinoma in F344 rats	(Katayama and others 2003)
	A. oryzae	N.M.	inhibit NMBA-induced esophageal tumor development in rats possibly through inhibition of cell proliferation	(Kuno and others 2004)
	A. oryzae	N.M.	Inhibit chemical-induced urinary bladder carcinogenesis in mice through anti-proliferative mechanisms	(Kuno and others 2006)
	A. oryzae	N.M.	Suppress the development of 4-NQO-induced oral carcinogenesis in rats via inhibiting proliferation and scavenging free radicals	(Long and others 2007)
	A. oryzae	N.M.	Inhibit MNNG-induced development of gastric tumors in rats	(Tomita and others 2008)
	A. oryzae	N.M.	Inhibit NNK-induced pulmonary tumorigenesis in A/J mice via induction of Cyp2a5 in the lung and the reduced proliferation rate of tumor cells	(Phuttraphadoong and others 2009)
	A. oryzae	N.M.	Inhibit inflammation-related colorectal carcinogenesis in Apc(Min/+) mice	(Phutthaphadoong and others 2010)
	A. oryzae	N.M.	Inhibit N-nitrosobis (2-oxopropyl) amine-induced pancreatic tumorigenesis in male hamsters	(Kuno and others 2015)
	A. oryzae	Vitamin E and phenolic acids	Decrease the incidence and progression of prostate carcinogenesis in rats	(Kuno and others 2016)
	A. oryzae	N.M.	Induce apoptosis of human acute lymphoblastic leukemia cells *in vitro*	(Horie and others 2016)
Rice bran	*L. edodes*	Polysaccharides	Inhibit the growth of B16/B16 melanoma xenograft in mice via enhancing natural killer cell activity	(Kim and others 2007)
Brown rice	*A. oryzae*	N.M.	Induce apoptosis of human HCT116 colorectal cancer cells in vitro by activating mitochondrial pathway	(Itoh and others 2012)
Rice	*M. purpureus* NTU 803	Monacolin K and phenolics	Induce apoptosis and cell cycle arrest at G2/M phase in human MCF-7 breast cancer cells *in vitro*	(Lee and others 2013)
Black rice bran	*B. subtilis* KU3	Phenolics	Inhibit proliferation *in vitro*	(Yoon and others 2015)

A., *Aspergillus*; *B.*, *Bacillus*; *Bb.*, *Bifidobacterium*; *L.*, *Lentinus*; *Lb.*, *Lactobacillus*; *M.*, *Monascus*; *S.*, *Saccharomyces*; *Sc.*, *Streptococcus*; 2-MBQ, 2-methoxy benzoquinone; 2,6-DMBQ, 2,6-dimethoxy-1,4-benzoquinone; 4-NQO, 4-nitroquinoline 1-oxide; AOM, azoxymethene; GABA, γ-aminobutyric acid; MHC, major histocompatibility complex; MNNG, N-methyl-N′-nitro-N-nitrosoguanidine; NMBA, N-nitrosomethylbenzylamine; NNK, 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone; N.M., not mentioned;

Table 8–Other bioactivities of fermented edible seeds and their products.

Bioactivities	Edible seeds and their products	Inoculated microbes	Possible effective components	Actions and potential mechanisms	References
Anti-depressant effect	Black soybean milk	*Lb. brevis* FPA 3709	GABA	Reduce the duration of immobility in rats	(Ko and others 2013)
Anti-diabetic effect	Soybean and rice bran	*Bacillus* spp.	N.M.	Reduce serum glucose, HbA1c and triglyceride in diabetic mice and stimulate glucose uptake via activation of PI3K/Akt signaling in C2C12 cells *in vitro*	(Lim and Lee 2010)
	Mung bean	*Rhizopus* sp. strain 5351	GABA and free amino acids	Reduce blood sugar and lipids, and improve insulin secretion and antioxidant level in diabetic mice	(Yeap and others 2012)
	Soymilk	*Lb. rhamnosus* CRL981	Isoflavone aglycones	Ameliorate hyperglycemia, lipid profiles and increase antioxidant enzyme activities in diabetic mice	(Marazza and others 2013)
	Bambara groundnut, African locust bean, and soybeans	Natural fermentation	Bioactive polypeptides and flavonoids	Ameliorate hyperlipidemia and inhibit ACE activity in streptozotocin-induced diabetic rats	(Ademiluyi and Oboh 2015)
	Wheat	*Gd. neo japonicum* (KUM61076)	N.M.	Possess insulin-like potential *in vitro*	(Subramaniam and others 2015)
	Rice	mutant *M. purpureus* 254	N.M.	Lower blood glucose and alter lipid profiles in diabetic rats	(Rajasekaran and Kalaivani 2015)
Anti-fungal effect	Wheat germ	*Lb. plantarum* LB1 and *Lb. rossiae* LB5	Organic acids and peptides	Inhibit various fungi isolated from bakeries	(Rizzello and others 2011)
Anti-inflammatory effect	Wheat germ	N.M.	N.M.	Alleviate severe rheumatoid arthritis in patients	(Balint and others 2006)
	Brown rice	*A. oryzae*	N.M.	Inhibit colonic inflammation in rat colon by decreasing the ulcer and erosion area and myeloperoxidase activity in the colonic mucosa	(Kataoka and others 2008)
	Rice bran	*I. orientalis* MFST1	N.M.	Suppress allergic and inflammatory reactions through inhibition of degranulation, histamine release, and pro-inflammatory cytokine production from mast cells	(Fan and others 2010)
	Brown rice and rice bran	*A. oryzae*	N.M.	Inhibit inflammatory cell infiltration in mice	(Onuma and others 2015)
Anti-obesity effect	Rice bran	*I. orientalis* MFST1	Phenolics	Ameliorate oxidative stress-induced insulin resistance in 3T3-L1 adipocytes *in vitro*	(Kim and Han 2011)
	Soymilk	*Lb. paracasei* subsp paracasei NTU 101	N.M.	Reduce body weight and lipogenesis in obese rats	(Cheng and others 2015)
	Soybean	*B. subtilis* MORI	Isoflavones	Inhibit the differentiation of 3T3-L1 preadipocytes and facilitate its glucose utilization	(Hwang and others 2015)
Anti-stress and fatigue effects	Rice bran	*S. cerevisae* IFO 2346	N.M.	Inhibit major changes in the weight of the adrenal, thymus, spleen and thyroid and prolong the swimming time in rats and mice	(Kim and others 2001, Kim and others 2002)
Anti-trypanosomal activity	Wheat germ	*S. cerevisiae*	Glycoside, alkaloids and saponins	Decrease in the proliferation of *T. brucei*, and extend the surviving days of *T. brucei*-infected rats	(Yusuf and Ekanem 2010)
Cardiovascular protective effect	Red rice	*M. ruber* IFO32318	N.M.	Induce NO-mediated endothelium-dependent relaxation of rat thoracic aorta	(Rhyu and others 2000)
	Rice	*Monascus* spp.	N.M.	Suppress hypertriglyceridemia and hyperlipidemia in rats fed with high-fructose diet	(Wang and others 2000)
	A mixture of coffee bean, soybean and rice bran	*B. subtilis* Natto	N.M.	Inhibit the TBARS formation and atherosclerotic lesions in the aorta of rabbits	(Naito and others 2003)
	Rice	*M. purpureus*	N.M.	Reduce serum TC, TG, LDL-C and ameliorate the severity of atherosclerosis in cholesterol fed rabbits	(Wei and others 2003)
	Brown rice	*Lb. acidophilus* KCTC 2182	N.M.	Lower plasma and hepatic TG, TC, LDL-C and VLDL-C, and increase HDL-C in cholesterol-fed rats	(Baek and others 2005)
	Rice	*Basidiomycota* (sangwhang) and *M. ruber*	N.M.	Improve the lipid metabolism and reduce oxidative stress in high-cholesterol-fed rats via upregulating the hepatic antioxidant enzymes	(Jang and others 2007)
	Wheat germ	N.M.	N.M.	Attenuate chronic hypertension, diabetes or metabolic syndrome-induced cardiovascular symptoms along with metabolic abnormalities	(Iyer and Brown 2011)

(*Continued*)

Table 8–Continued.

Bioactivities	Edible seeds and their products	Inoculated microbes	Possible effective components	Actions and potential mechanisms	References
	Rice	*M. purpureus*	Naturally occurring statin	Inhibit TNFα-induced upregulation of MMP2 and 9 and intracellular ROS in human aortic smooth muscle cells *in vitro*	(Lin and others 2011)
	Rice bran and soybean	*Bacillus* spp.	N.M.	Decrease total lipids and triglyceride in the serum and liver of rats fed with high fat diet	(Lim and others 2011)
	Indian rice	*M. purpureus* MTCC 1090	N.M.	Ameliorate lipid profiles and oxidative stress markers in high cholesterol diet fed rats	(Rajasekaran and Kalaivani 2011)
	Rice	*M. purpureus*	Antioxidants and amino acids	Reduce the cholesterol level enhance the antioxidant level in hypercholesterol mice	(Yeap and others 2014)
	Wheat powder	*Lactobacilli* and natural yeast strains	Phenolics, lipoic acid, tocopherols and polyunsaturated fatty acids	Improve blood lipids and oxidative status in healthy rabbits	(Pozzo and others 2015)
	Mung bean	*Rhizopus* sp. strain 5351	GABA and phenolics	Increase antioxidant activity, reduce blood lipids and regulate atherosclerosis related gene expression in hypercholesterolemic mice	(Yeap and others 2015)
Gastrointestinal protective effect	Brown rice	*A. oryzae*	Nucleobases	Improve the incidence rate of diarrhea, increase the protein content in small intestinal mucosa, and improve the survival rate in methotrexate-treated rats	(Ochiai and others 2013)
Hepatoprotective effect	Waxy brown rice	*Cr. cinereus*	N.M.	Inhibit carbon tetrachloride induced hepatotoxicity in rats	(Lee and others 2004)
	Brown rice and rice bran	*A. oryzae*	N.M.	Inhibit acute hepatitis in Long-Evans Cinnamon rats via protecting the liver against free radicals induced by copper accumulation in the liver	(Shibata and others 2006)
	Waxy brown rice	*Ac. cylindracea*	N.M.	Attenuate carbon tetrachloride-induced hepatotoxicity in rats	(Lee and others 2006)
	Rice	*M. purpureus* NTU 568	Monacolin K, GABA, dimerumic acid and various pigments	Attenuate oxidative stress, inflammatory response, and steatosis in mice with alcoholic liver disease	(Cheng and Pan 2011)
	Soymilk	*Sc. thermophilus* grx02	Phenolics	Ameliorate alcohol-induced liver damage in mice by lowering ALT, AST and enhancing ADH and SOD activity as well as GSH content	(Xu and others 2012)
	Mung bean	*Rhizopus* sp. strain 5351	GABA and amino acids	Improve antioxidant activity, serum markers (ALT, AST, TG and TC) and NO level in ethanol-induced liver damage of mice	(Ali and others 2013)
	Rice bran	*Bacillus* species	N.M.	Ameliorate CCl4-induced hepatic fibrosis in mice	(Park and others 2014)
	Thai glutinous rice	*M. purpureus* CMU 002U	N.M.	Reduce blood and hepatic cholesterol and hepatic steatosis in hypercholesterolemic rats	(Bunnoy and others 2015)
Laxative effect	Rice	*S. cerevisiae* and *W. paramesenteroides*	N.M.	Exhibit a laxative effect without causing diarrhea in rats with loperamide-induced constipation	(Choi and others 2014a)
	Rice	N.M.	N.M.	Ameliorate loperamide-induced constipation in rats	(Choi and others 2014b)
Immunomodulatory effect	Rice bran	*S. cerevisiae*	N.M.	Activate macrophage and enhance secretion of hematopoietic growth factors from Peyer's patch cells of mice	(Koh and others 2003)
	Rice bran	*L. edodes*	Arabinoxylan	Increase IFN-γ production without causing adverse effects in health people	(Choi and others 2014c)
	Wheat germ	N.M.	N.M.	Induce a better immune response compared to pigs exposed to T-2 toxin	(Arpad and others 2009)
	Wheat germ	N.M.	N.M.	Enhance the blastogenic response of lymphocytes to nonspecific mitogens, phagocytic activity and phagocytic index in pigs	(Rafai and others 2011)
	nonsalty soybean powder	N.M.	Phenolics	Stimulate the cellular immune response, but suppress the acquired humoral immune response in C3H/HeN mice	(Karasawa and others 2013)

(*Continued*)

Table 8–Continued.

Bioactivities	Edible seeds and their products	Inoculated microbes	Possible effective components	Actions and potential mechanisms	References
	Soybean	*Lb. paracasei*, *Lb. bulgaricus* and *S. cerevisiae*	Isoflavones	Induce T-cell proliferation, enhance the function of Th1 cells and activity of NK cells in mice	(Chin and others 2015)
	Mung bean and soybean	*Rhizopus* sp. 5351	GABA, free amino acids and phenolics	Induce splenocyte proliferation and enhance the levels of serum IL-2 and IFN-γ *in vitro*	(Ali and others 2016)
Neuroprotective effect	Chickpea milk	*Lb. plantarum* M-6	GABA	Inhibit $MnCl_2$-induced PC12 cell death partially by retaining the integrity of cell membrane	(Li and others 2016)
	Soymilk	*Lb. plantarum* TWK10	N.M.	Improve learning and memory in rats	(Liu and others 2016)
	Rice	*M. purpureus* NTU 568	DFC, DMA	Ameliorate 6-hydroxydopamine-induced neurotoxicity in SH-SY5Y cells and the rat model of Parkinson's disease	(Tseng and others 2016a, Tseng and others 2016b)
Heavy metal protective effect	Soymilk	*Lb. plantarum* CCFM8610	Isoflavone aglycones	Increase fecal Cd excretion, reduce tissue Cd burden, alleviate tissue oxidative stress in mice	(Zhai and others 2015)
DNA protective effect	Chickpea, mung bean, oats (Avena sativa L.)	*C. militaris* SN-18	Phenolics	Inhibit hydroxyl radical-induced supercoiled DNA strand scission *in vitro*	(Xiao and others 2014, Xiao and others 2015a, Xiao and others 2015d)
	Soy whey	*Lb. plantarum* B1–6	Phenolics, especially isoflavone aglycones	Inhibit hydroxyl radical-induced supercoiled DNA strand scission *in vitro*	(Xiao and others 2015b)
Regulation of gut microbiota	Brown rice	*A. oryzae*	N.M.	increase the number of lactobacilli species already resident in the rat intestine	(Kataoka and others 2007)
Regulation of sleep	Rice germ	N.M.	GABA	Counter the sleep disturbance induced by caffeine in mice	(Mabunga and others 2015)
Reproductive protective effect	Rice	*M. purpureus*	N.M.	Prevent Zn deficiency-induced testis and sperms injury in rats	(Lee and others 2011)
Skin protective effect	Rice bran	*Lb. rhamnosus* and *S. cerevisiae*	N.M.	Inhibit α-MSH-Induced Melanogenesis in B16F1 Melanoma via downregulating MITF Expression	(Chung and others 2009)
	Rice bran	*Lb. rhamnosus* and *S. cerevisiae*	N.M.	Increase the synthesis of type I collagen, decrease the expression of MMP-1, and inhibit the production of IL-1α in UV-B irradiated human fibroblasts *in vitro*	(Seo and others 2010)
	Soymilk	*Lb. plantarum* TWK10	Isoflavone aglycones	Inhibit mushroom tyrosinase activity and melanin production in B16F0 melanocytes	(Chen and others 2013)

A., Aspergillus; Ac., Agrocybe; B., Bacillus; Bb., Bifidobacterium; C., Cordyceps; Cr., Coprinus; Gd., Ganoderma; I., Issatchenkia; L., Lentinus; M., Monascus; S., Saccharomyces; Sc., Streptococcus; T., Trypanosoma; W., Weissella; ACE, angiotensin converting-I-enzyme; ADH, alcohol dehydrogenase; ALT, alanine transaminase; AST, aspartate transaminase; Cd, cadmium; DFC, deferricoprogen; DMA, dimerumic acid; DMBQ, 2,6-dimethoxy-1,4-benzoquinone; GABA, γ-aminobutyric acid; GSH, glutathione; HDL-C, high-density lipoprotein cholesterol; IFN-γ, interferon γ; IL-2, interleukin-2; LDL-C, low-density lipoprotein cholesterol; MITF, microphthalmia-associated transcription factor; MHC, histocompatibility complex class; MMP, matrix metalloproteinase; NK cells, natural killer cells; NO, nitric oxide; SOD, superoxide dismutase; ROS, reactive oxygen species;TBARS, thiobarbituric acid reactive substances; TC, total cholesterols; TG, triglycerides; Th1 cells, T helper type 1 cells; VLDL-C, very low-density lipoprotein cholesterol; N.M., not mentioned.

been reported as the main anti-cancer compounds in it (Mueller and others 2011; Rizzello and others 2013). *S. cerevisiae*-fermented wheat germ exhibits different actions on cancer cells (Table 7). It can inhibit cancer cell proliferation, induce cancer cell necrosis and apoptosis, potentiate the efficiency of chemotherapy, as well as improve the survival of cancer patients. For the anti-cancer mechanism, it can mainly induce cell cycle arrest and activate apoptotic signaling. Studies found that it inhibited the G1 phase cell-cycle progression in HT-29 cells (Illmer and others 2005), blocked cell cycle from G2–M to G0–G1 phase in human HL-60 promyelocytic leukemia cells (Saiko and others 2007), and activated caspase-3 and caspase-7-dependent apoptotic signaling in human ovarian cancer cells (Wang and others 2015). In addition, LAB-fermented wheat germ has also been reported to exhibit anti-cancer effect (Rizzello and others 2013; Zhang and others 2015a,b).

A. oryzae-fermented brown rice and rice bran is another extensively investigated food with anti-cancer effect. It has also been reported to inhibit various cancer cells *in vitro* and *in vivo* (Table 7), mainly by inhibiting cancer cell proliferation and inducing cancer cell apoptosis. Kuno and others (2016) reported that it controlled the growth of prostate tumor *in vivo* by activating AMP-activated protein kinase (AMPK) signaling. Another study suggested that it induced the apoptosis of human acute lymphoblastic leukemia cells probably through the death receptor-mediated apoptotic pathway (Horie and others 2016). However, its anti-cancer components have not been clarified, with vitamin E and phenolic acids having been suggested to be responsible for its anti-cancer effect (Kuno and others 2016). In addition, fermented common rice, black rice, and their brans have also been reported to possess anti-cancer effects on different cancer cells (Table 7).

Overall, fermented wheat and rice, especially their germ and bran, can be excellent anti-cancer foods consumed by humans for the prevention and treatment of cancer. On the other hand, the anti-cancer effect of other fermented edible beans, grains, and their products has been less investigated, and future studies are required to investigate their anti-cancer effect and anti-cancer components.

Other bioactivities

Fermented edible seeds and their products have also been reported to possess many other bioactivities (Table 8), such as anti-depressant, anti-diabetic, anti-fungal, anti-inflammatory, anti-obesity, anti-stress and -fatigue, anti-trypanosomal, cardiovascular protective, gastrointestinal protective, hepatoprotective, neuroprotective, reproductive protective, skin protective, DNA-protective, heavy metal protective, laxative, immunomodulatory, gut microbiota regulatory, and sleep regulatory effects. Likewise, bioactive components, including GABA, phenolics, bioactive peptides, naturally occurring statins, nucleobases, amino acids, tocopherols, polyunsaturated fatty acids, monacolin K, dimerumic acid, and arabinoxylan, have been proposed to be associated with the bioactivities (Table 8).

In general, fermented edible seeds and their products possess versatile bioactivities, implying that they should have comprehensive health benefits. Therefore, it is recommended to consume fermented edible seeds and their products as a part of the diet to prevent chronic diseases such as cancer and cardiovascular diseases.

Potential problems of food safety

Although fermented edible seeds and their products have been demonstrated to contain a variety of bioactive components and to confer a great number of health benefits, their potential safety problem cannot be ignored. However, it should be pointed out that there are few studies focused on the potential safety problems of fermented products. On one hand, fermented seed products without sterilization may contain pathogenic microbes or those with potential pathogenic risk, especially naturally fermented products. For example, naturally fermented and LAB-fermented soybeans and lentils have been reported to contain substantial numbers of aerobic mesophilic bacteria (Fernandez-Orozco and others 2007; Torino and others 2013), which may include pathogenic bacteria and increase the risk of food poisoning. On the other hand, microbes may release toxic or harmful substances during fermentation, which may be harmful for health and cannot be excluded without toxicological analysis. Recent emerging food technologies, such as ultraviolet radiation, pulsed electric field, and high-pressure processing, have been reported to inactivate *Bacillus* spores (Soni and others 2016), and these technologies may also be employed to treat fermented products. Therefore, from a food safety viewpoint, fermented products may be processed to kill microbes in them and/or toxicological analysis may be undertaken prior to further applications. However, it should also be pointed out that some fermented products, such as yogurt, known as safe and requiring a live culture (such as LAB) to provide the full health benefits, on the contrary, require maximization of the viability of their live cultures.

Conclusions

Fermented edible seeds and their products generally contain increased bioactive components, such as some vitamins, GABA, natural phenolics, and bioactive peptides, compared to unfermented materials. More importantly, they exhibit various bioactivities, such as antioxidant, anti-hypertensive, and anti-cancer effects, suggesting that they may have potential and comprehensive health benefits. Therefore, it is highlighted that fermented edible seeds and their products are excellent natural sources of bioactive components and can be recommended for consumption as a part of dietary components and developed into functional foods to prevent chronic diseases.

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Author Contributions

R.Y.G and H.C initially constructed and prepared the manuscript draft, and H.B.L, A.G, Z.Q.S, and H.C edited and revised the final manuscript.

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