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Review article

γ-Aminobutyric acid found in fermented foods and beverages: current trends

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ABSTRACT

γ-aminobutyric acid (GABA) is synthesised by glutamic acid decarboxylase which catalyses the decarboxylation of L-glutamic acid. L-glutamic acid is formed by α-ketoglutarate in the TCA cycle by glutamic acid dehydrogenase (GDH). GABA is found in the human brain, plants, animals and microorganisms. GABA functions as an antidepressant, antihypertensive, antidiabetic and immune system enhancer and has a good effect on neural disease. As GABA have pharmaceutical properties, conditions for GABA production need to be established. Microbiological GABA production is more safe and eco-friendly rather than chemical methods. Moreover, it is easier to control conditions of production using microorganisms compared to production in plants and animals. GABA production in fermented foods and beverages has the potential to be optimised to increase the functional effect of fermented foods and beverages.

1. Introduction

The synthesis of γ-aminobutyric acid (GABA), a non-protein amino acid with four carbon atoms, is catalysed by the enzyme glutamic acid decarboxylase (GAD) and the cofactor pyridoxal-5-phosphate (PLP) from L-glutamate [1, 2, 3]. GABA has been isolated from many sources, such as tea leaves, mulberry leaves, tomato, animals, lactic acid bacteria (LAB), yeasts and moulds [1, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19]. GABA is also found in fermented foods and beverages such as *tempe*/fermented soybean, *dadih*/fermented buffalo milk, *asam durian*/fermented durian, *tape singkong*/-fermented cassava, *ikan budu*/fermented fish, sake, yogurt-sake, sourdough, mulberry beer, kimchi and zlatar cheese [9, 11, 16, 19, 20, 21, 22, 23].

γ-aminobutyric acid has potential health benefits such as antidepressant, sedative, antihypertensive, antidiabetic, anticarcinogenic and immune system enhancer [14, 24, 25, 26, 27, 28, 29]. In microorganisms, GABA is involved in spore germination and causes acid resistance in bacteria [30]. In animals, GABA performs essential activities as an inhibitory neurotransmitter on several routes, namely the central nervous system and peripheral tissue. GABA also has a good effect on patients with Huntington, Parkinson's, Alzheimer's, stiff-person syndrome and schizophrenia [3].

γ-aminobutyric acid production using plants and animals is not easy. GABA concentration is low in plants and the production mechanism is unclear [31]. In contrast, GABA production using microorganisms has been studied extensively. The factors which influence GABA production are easily controlled, so that researchers mostly focused on GABA production using microorganisms [3]. Moreover, GABA production using microorganisms is safe and eco-friendly compared to chemical methods [3, 31, 32].

Microorganisms are found everywhere; however, they are mainly isolated from fermented foods and beverages. Fermentation involves bacteria, yeasts and moulds, which produce GABA. Microorganism-based GABA production in fermented food has immense prospects [32]. The availability of nutrients in food, along with microorganisms, allows the natural synthesis of GABA. All it needs to do is optimize the fermentation process in fermented foods to maximize the GABA content.

γ-aminobutyric acid was first discovered in plants in 1949 by Steward [33]. The earliest finding was in the form of alpha butyric acid in potatoes [34]. There is 79122 research papers and 18047 article reviews with numerous topics relating to GABA, such as its existence in plants, animals, microorganisms, fermented food and beverages, extraction and

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purification, as well as numerous clinical trials of GABA against diseases. The main focus of this article is the existence of GABA in fermented foods and beverages which is contributed by microorganisms.

2. γ-aminobutyric acid metabolic pathway

In microorganisms, glucose metabolism produces several metabolites; one of which is GABA. Glucose is converted to pyruvate during glycolysis. Thereafter, pyruvate is converted to acetyl-CoA, which reacts with oxaloacetate and enters the TCA cycle forming citrate. Citrate is converted to isocitrate and α-ketoglutarate, which can be converted to GABA by several microorganisms via glutamic acid dehydrogenase (GDH) and GAD, as shown in Figure 1 [33].

The formation of GABA by the TCA cycle via glutamate is called the GABA shunt [33]. The α-ketoglutarate from the TCA cycle is converted to glutamate by GDH and then converted to GABA by decarboxylation. The reaction is irreversible, catalysed by GAD and needs pyridoxal phosphate (PLP) as a cofactor [2, 33, 34, 35].

The GABA shunt may degrade GABA by γ-aminobutyric acid aminotransferase (GABA-AT) and semialdehyde dehydrogenase (SSADH). These enzymes convert GABA to succinate, which then enters the TCA cycle. The first is a reversible reaction by GABA-AT and produces succinic semialdehyde (SSA) and the second reaction converts SSA to succinate by SSADH [33]. The TCA cycle occurs in the mitochondria whereas the formation of GABA from glutamate occurs in the cytosol, as GABA is transformed by GABA-AT and SSADH, it goes back to the mitochondria [36].

3. Microorganisms roles in γ-aminobutyric acid production

γ-aminobutyric acid synthesis of L-glutamate in metabolism is catalyzed by the GAD enzyme. As shown in Table 1, GAD can be produced by many microorganism like LAB, yeasts and fungi [15, 32, 37, 38, 39, 40, 41].

LAB, such as *Streptococcus thermophilus*, *Lactobacillus brevis, L. paracasei, L. fitsaii, L. plantarum* and *Bifidobacterium adolescentis*, have GAD enzyme activity and are widely used for GABA production. These bacteria are commonly isolated from fermented foods and beverages such as koumiss, kimchi, zlatar cheese and kung-som; however, some bacteria have been isolated from fresh ocean fish, fish intestine and infant faeces [1, 12, 13, 14, 16, 42, 43, 44].

Glutamic acid decarboxylase has also been identified in yeasts such as *Saccharomyces cerevisiae* and *Kluyveromyces marxianus* isolated from fermented product [16, 45]. *S. cerevisiae* had lower activity than *L. plantarum*, this may be caused by the utilization of GABA by *S. cerevisiae* as nitrogen source [16, 18]. However coculture *L. plantarum* and *S. cerevisiae* had highest activity to produce GABA than single culture *L. plantarum* nor *S. cerevisiae* in mulberry beer [16]. Wild yeast, such as *Kazachstania unispora*, *Sporobolomyces carnicolor, Sporobolomyces ruberrimus, Nakazawaea holstii* and *Pichia scolyti*, isolated from wild flowers, also have GAD activity [15].

Aspergillus oryzae is a mould used to ferment rice-*koji* fermentation for brewing *sake*. *A. oryzae* generates GABA [18]. *Rhizopus oligosporus* and *R. oryzae* are moulds used to prepare *tempe* (fermented soybean) generating 1.770 mg/100 g GABA for *R. microsporus* var. *oligosporus* IFO 32002 and 770 mg/100 g GABA for *R. oryzae* IFO 4705 and *R. oryzae* IFO 5438 [19]. LABs are the most studied GABA producers, because they are economically viable as starters and generate higher GABA than other producers [3].

A number of factors, namely temperature, pH, substrate and culture time influence the amount of GABA produced during microbial fermentation (Table 2). According to [1], the optimum fermentation temperature for GABA synthesis is 30 °C, whereas that according to [22] is 37 °C. The optimal conditions for GABA synthesis by *L. brevis* are pH 3.5–5, in GM broth containing 1% glucose, 2.5% yeast extract, 2 ppm Tween 80, 2 ppm CaCO3, MnSO4, 10 μM PLP and 650 mM MSG [46]. However, according to Lim et al. [12], the optimal conditions for GABA synthesis by *Enterococcus faecium* are pH 7.74, with substrate containing 2.14% (w/v) maltose, 4.01% (w/v) tryptone and 2.38% (w/v) MSG. The growth of *E. faecium* increased proportionally to the initial pH, of which the experimental pH is in the range 4–8. Likewise, the formation of GABA increased with the increasing number of *E. faecium*, but at a pH of more than 7.5 the formation of GABA decreased.

pH is a crucial factor in GABA biosynthesis, GAD in LAB is only active under acidic conditions and loses its activity at a pH > 5 [8]. GAD activity is optimum at pH 4.5 [22]. GABA biosynthesis causes an increase in pH and acid is adding during the fermentation process to maintain pH [8]. In addition, the activities of enzymes that decompose GABA, such as GABA transaminases and SSADH [2], must be considered [18]. The optimum pH for fermentation varies: for *L. plantarum* pH 5 and *L. brevis* pH 3.5–5, with an optimum at 4.74, are optimal [12, 20, 46].

During fermentation, *Saccharomyces cerevisiae* may consume GABA using SSADH at pH 8.40, thereby reducing the amount of GABA produced [18]. In *Pseudomonas*, GABA is used as a substrate at pH 8.5 by GABA transaminase, which is inhibited by adding a buffer [8].

Media composition also affects GABA biosynthesis. GABA production by *L. paracasei* and *L. brevis* increases upon adding glutamate [8]. Addition of glutamate to yogurt-*sake* fermented by *Streptococcus thermophilus* Hp increases the concentration of GABA. The use of compared to *sake*, *amazake*, a substitute for *sake*, produces a higher concentration of GABA [22] The addition of glutamate produces curd that is rich in GABA [20].

Fermentation temperature is important for GABA production [16]. Fermentation temperature affects the growth of microorganisms. For *L. brevis* the optimum temperature is 30 °C, *S. thermophilus* Hp 37 °C and *L. plantarum* 30°C–36 °C [1, 16, 20, 22, 23].

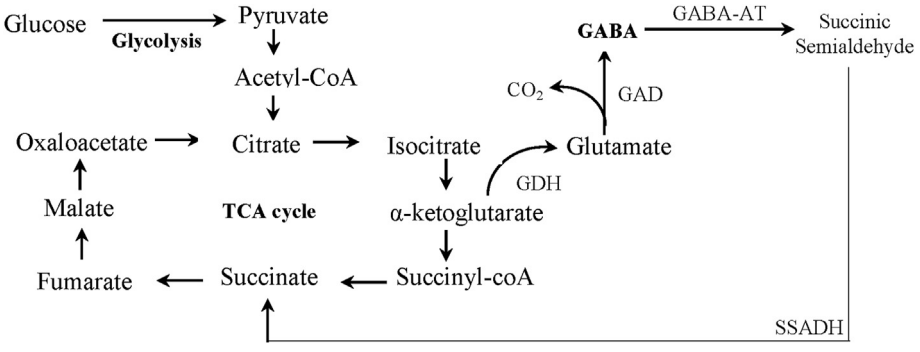

Figure 1. Metabolic pathway of GABA production from the TCA cycle [2, 33]. TCA, tricarboxylic acid cycle; GDH, glutamate dehydrogenase; GAD, glutamate decarboxylase; GABA, γ-aminobutyric acid; GABA-AT, γ-aminobutyric acid aminotransferase; SSADH, succinic semialdehyde dehydrogenase.

Table 1. γ-aminobutyric acid (GABA) production by microorganisms.

Microorganism	Species	Amount of GABA	Reference
LAB	*Streptococcus thermophilus* Hp	3,894 ± 132 μM	[22]
	S. thermophilus	2.8–8.3 g/L	[44]
	S. thermophilus QYW-LYS1	2.905 g/L	[59]
	Lactobacillus brevis DPC6108	11.01–32.32 mg/mL	[10]
	L. brevis RK03	62.523 mg/L	[1]
	L. brevis FPA 3709	2.45 ± 0.30 mg/mL	[14]
	L. brevis HYE1	14.64–18.97 mM	[12]
	L. brevis IFO-12005	10.18 mM	[13]
	L. paracasei NFRI 7415	302 mM	[60]
	L. fitsaii CS3	1,280–10,500 mg/kg	[61]
	L. plantarum C48	504 mg/kg	[23]
	Bifidobacterium adolescentis	<0.5 mM	[43]
Yeasts	*Kazachstania unispora*, *Sporobolomyces carnicolor*, *Sporobolomyces ruberrimus*, *Nakazawaea holstii*, *Pichia scolyti*	ND	[15]
	Pichia silvicola UL6-1	134.4–136.5 μg/mL	[41]
	Sporobolomyces carnicolor 402-JB-1	179.2–200.8 μg/mL	
	Saccharomyces cerevisiae	ND	[16]
Moulds	*Aspergillus oryzae*	ND	[18]
	Rhizopus microsporus var. *oligosporus* IFO 32002	1,740 mg/100 g	[19]
	Rhizopus oryzae IFO 4705	770 mg/100 g	
	Aspergillus oryzae	435.2 μg/g	[62]

*ND = not defined.

Table 2. Optimum fermentation conditions.

Microorganism	Source	Fermentation Media	γ-aminobutyric 2acid production	Reference
Lactobacillus brevis RK03	Ocean fish from the fish markets in Taiwan	GM broth containing 1% glucose; 2.5% yeast extract; 2 ppm each of CaCO3, MnSO4 and Tween 80 and 10 μM pyridoxal phosphate (PLP)	62,523 mg/L	[1]
L. brevis FPA 3709	Fish intestine	MRS broth, 5% mono sodium glutamate (MSG), at 37 °C for 48 h	2.45 ± 0.30 mg/mL	[14]
L. brevis DPC6108	Infant faeces	MRS supplemented with 30 mg/mL MSG, cultured anaerobically at 37 °C for 72 h	28.02 mg/mL	[10]
L. fermentum NBRC 3956	Fermented Thai foods	MRS broth, pH 6.5, 40 °C and 10 d incubation	12 mg/mL	[63]
L. paracasei NFRI 7415	Funa-sushi (fermented fish from Japan)	MRS broth with pyridoxal phosphate, 500 mM glutamate, pH maintained at 5.0, 30 °C	302 mM	[60]
L. pentosus SS6	Fermented mulberry fruits	10% saccharose, 6% peptone, 1.6% K2HPO4, 1% L-sodium glutamate and a 60% water, fermented for 36 h at 35 °C	ND	[7]

*ND = not defined.

Time of fermentation influences GABA production, i.e., longer the fermentation time, higher is the GABA concentration. *L. plantarum* DSM19463 and *L. paracasei* NFRI 7415 need 72 and 144 h to produce 4.83 mM and 60 mM GABA, respectively [8]. *L. plantarum* needs 84 h to produce 211.169 mM GABA in *dadih* [20] and *L. lactis* needs 24 h to produce 1,031 mg/kg in mulberry beer [16].

γ-aminobutyric acid synthesis by microorganisms is affected by temperature, pH, substrate and culture time [1, 8, 12, 16, 18, 20, 22, 46, 46]. Numerous studies have shown that the addition of glutamate can increase the formation of GABA [8, 20, 22]. Apart from affecting the amount of GABA, these factors also affect the degradation of GABA by GABA-AT and SSADH which are active at pH above 8 [8], [18]. So that fermentation process optimisation is needed.

4. Optimisation of γ-aminobutyric acid production in fermented foods and beverages

The amount of GABA in some fermented foods and beverages is small. The fermentation process needs to be optimised to produce higher amounts of GABA. Optimisation studies have included stages such as (1) isolating and purifying microorganisms from fermented foods and beverages; (2) identifying GAD activity in the selected colony; (3) identifying the name of the microorganism that produced the highest amount of GABA; (4) optimising the growth of the selected microorganism; (5) and producing fermented foods and beverages using the selected microorganism under optimum growth conditions [22].

Table 3. Optimisation of fermentation process in fermented food.

Fermented Product [Reference]	Microorganism	Source	Fermentation condition	γ-aminobutyric acid production
Tempe [19]	*Rhizopus microsporus var. oligosporus* IFO 32002 and 32003	Ikeda Food Res. Co.	Aerobic cultivation at 30 °C for 20–22 h and anaerobic cultivation at 30 °C for 20 h	1,740 mg/100 g (Dry Basis)
Sourdough [23]	*Lactobacillus plantarum* C48	Cheese	Flour supplemented with 0.1 mM pyridoxal 5 phosphate, starter 5 × 107 CFU/g, at 30 °C for 24 h	504 mg/kg
Kung-som [42, 61]	*L. futsaii* CS3	Kung-som	Starter culture 8 log CFU/g, supplemented with 0.5% MSG	10.130 mg/kg
Yogurt-*sake* [22]	*Streptococcus thermophilus* Hp	Yogurt-*sake*	T 37 °C for 5 d, supplemented with 380 μM glutamate	424 μM
Yogurt-*amazake* [22]	*S. thermophilus* Hp	Yogurt-*sake*	T 37 °C for 5 d	1,096 μM
Yogurt [52]	*S. thermophilus* APC151	Digestive tract of fish	Milk consisted of 14% (w/v) skim milk, supplemented with 2.25 mg/mL MSG at 42 °C for 48 h.	2 mg/mL
Fermented milk [44]	*S. thermophilus*	*koumiss* dairy products	T 43 °C for 48 h, supplemented with 10% skim milk powder and 15 g/L MSG	8.3 mg/L
Black soybean milk [14]	*Lactobacillus brevis* FPA 3709	Fish intestine	T 37 °C, t 48 h, supplemented with 1% MSG, 1% brown sugar and 0.1% peptone	2.45 ± 0.30 mg/mL
Shochu kasu [13]	*L. brevis IFO-12005*	ND	*Sochu kasu* (pH 5.2) with 1% inoculum and 10.50 mM free glutamic acid, at 30 °C for 2 d	10.18 mM
Mulberry beer [16]	*Saccharomyces cerevisiae* SC125	Shichuan *Paocai*	T 30 °C, t 72 h, supplemented with 5 g/L glutamate	2.42 g/L
	L. plantarum BC114	Fermented vegetable		

*ND = not defined.

Isolation and purification aim to identify one indigenous microorganism and test its ability to produce the desired compound, which is GABA in this case. GABA producers can be isolated from fermented foods or beverages [7, 11, 21, 22, 47].

The stages for microorganism isolation include sample preparation, inoculation and incubation. Thereafter, the LAB colony with a clear area around it in MRS (de Man Rogosa and Sharpe) agar media is selected and screened for its ability to produce GABA. The selection of microorganisms that produce high levels of GABA is needed by the fermented food industry, especially for functional food production [11]. Microorganisms isolated from fermented foods and beverages are *Lactobacillus plantarum*, *L. pentosus* SS6, *L. brevis*, *L. brevis*, *Leuconostoc mesenteroides*, *L. lactis* and *Streptococcuse thermophillus* Hp [7, 9, 11, 16, 20, 22].

Kimchi is a fermented South Korean food that is traditionally made from vegetables such as *baechu* cabbage (Chinese cabbage), cucumber, radish and green onion with red paper powder, garlic, ginger and *jeotgal* (fermented seafood) [48, 49, 50]. *Kimchi* is fermented by LAB, which have GAD activity. *Lactobacillus plantarum* is an LAB with GAD activity and is predominantly used for *kimchi* preparation. *L. brevis*, *Leuconostoc mesenteroides, Leuconostoc lactis* and *Weissella viridescens* can also be isolated from kimchi and have GAD activity [11].

Lactobacillus plantarum can also be isolated from fermented buffalo milk called *dadih*, which originates from West Sumatra [16, 20]. *Dadih* is fermented in bamboo covered with banana leaves. Fermentation is done by several LAB, such as *L. brevis*, *L. paracasei, L. pentosus, L. plantarum* and *Lactococus lactis* [51]. Harnentis et al. [20] isolated 10 LAB from *dadih*, of which *L. plantarum* N5 could generate the highest amount of GABA, compared to the others.

LAB with GAD activity is also found in zlatar cheese and yogurt-*sake*. Twenty-five strains of LAB have been isolated in zlatar cheese, of which 15 have GAD activity. *L. brevis* BGZLS10-17 is a LAB with GAD activity and the potential as a probiotic [9]. Moreover, 11 strains of LAB have been isolated from yogurt-*sake* and the highest GABA producer is identified as *S. thermophilus* Hp, which produced 3,000 μM GABA after 54 h of incubation [22].

As a small amount of GABA is produced by the spontaneous fermentation of food and beverages, several optimisations have been done. Table 3 shows the optimisations done for fermenting foods and beverages. *Tempe* is indigenous Indonesian food made from soybean that is rich in glutamic acid and is fermented using *Rhizopus spp*. Fermentation of soybean by *R. microsporus* var. *oligosporus* IFO 32002 at 30 °C for 20–22 h and 20 h under aerobic and anaerobic conditions, respectively, generates the highest content of GABA, at 1,740 mg/100 g (dry basis) [19].

Optimisations have also been done with *L. plantarum* C48 and *Lactococcus lactis* subsp. *lactis* PU1 for sourdough bread preparation. Optimum fermentation requires *L. plantarum* C48 at 5×10^7 CFU/g with an addition of 0.1 mM PLP for 24 h at 30 °C. Fermentation of buckwheat, amaranth, chickpea and quinoa flour at a ratio of 1:1:5.3:1 under these conditions generates 504 mg/kg GABA [23]. For the preparation of *kung-som* or fermented shrimp, which originates from Thailand, *Lactobacillus futsaii* CS3, used as starter at 8 log CFU/g, supplemented with 0.5% MSG, generates 10.130 mg/kg GABA [42].

Streptococcus thermophilus has GAD activity, was isolated from dairy products and is used as a starter in fermented milk and yogurt. The use of *S. thermophilus* in fermented milk generates 2.8 g/L GABA after 48 h of fermentation. Higher levels of GABA can be achieved by co-culturing with *Lactobacillus rhamnosus*, which produces 8.3 g/L of GABA [44]. In yogurt, *S. thermophilus* APC151 used as starter, with 2.25 mg/mL MSG, generates 2 mg/mL of GABA [52]. In yogurt-*sake*, *S. thermophilus* Hp generates 424 μM of GABA under fermentation conditions, at 37 °C for 5 d, with the addition of 380 μM glutamate. Moreover, 1,096 μM GABA can be generated under the same conditions without the addition of glutamate in yogurt-*amazake*. The amount of GABA in yogurt-*amazake* is higher than yogurt-*sake*. This is caused by the difference in glutamic acid content. A total of 2,709 μM glutamic acid in *amazake* results in higher GABA synthesis [22].

For black soybean milk, *L. brevis* FPA 3709, cultured with 1% MSG, 1% brown sugar and 0.1% peptone at 37 °C for 48 h, generates 4.01 mg/mL GABA. Compared to soybean and red soybean, black soybean generates the highest amount of GABA [14]. For *shochu kasu, L. brevis* IFO-12005 requires up to 1% of 10.50 mM free glutamic acid at 30 °C for 2 d to generate 10.18 mM GABA [13].

The use of *Saccharomyces cerevisiae* SC125 and *L. plantarum* BC114 in mulberry beer fermentation at 300 °C for 72 h, supplemented with 5 g/L

Table 4. Functional effect of γ-aminobutyric acid (GABA).

Functional effect	Object	GABA dosage	Reference
Antihypertensive	Rats	Single dose of 0.05–5.00 mg/kg	[25]
		Single dose of GABA-rich tomato containing 3.6–17.9 mg of GABA	[17]
		Single dose of mulberry leaf containing 3.8 ± 0.71 mg/g of GABA (20 mg/kg body weight)	[6]
		Daily intake of fermented beans containing 0.4–2 g/kg GABA and nattokinase for 8 weeks	[53]
	Human	Daily intake of 50 g cheese containing 16 mg of GABA for 12 weeks	[26]
		Twice daily intake of GABA-rich *Chlorella* containing 20 mg of GABA for 12 weeks	[54]
Antidiabetic	Rats	Daily intake of tea extracts containing 3.01 or 30.1 μg of GABA for 6 weeks	[55]
		ND	[29]
		Daily intake of 6 mg/mL GABA in drinking water for 6 weeks	[57]
	Human	Twice daily intake of GABA and injection of GAD	[64]
		Daily intake of 2 g of GABA once or three times/d for 7 d	[56]
Renal Protection	Rats	Dose of 100 or 500 mg/kg daily via a stomach tube for 100 consecutive days	[58]
Anticancer	Human	ND	[28]
Relaxation	Human	Dose of 100 mg of GABA in 200 mL distilled water	[24]
Immunity enhancer	Human	ND	

*ND = not defined.

glutamate, generates 2.42 g/L of GABA. The fermentation also increases volatile compounds and increases the concentration of fruity esters [16].

There has been optimisation of GABA formation in fermented products. The optimisation is done by conditioning the fermentation process according to the optimal conditions of selected indigenous microorganism as starter culture which has GAD activity. Also, the addition of PLP, glutamate, and MSG were used to increase the concentration of GABA in fermented products [16, 22, 23, 42, 52]. The amount of GABA in fermented products needs to be considered in order to provide its functionality.

5. Functional effects of γ-aminobutyric acid

GABA is a bioactive materials, found in the brain, and acts as an inhibitory neurotransmitter. Studies show that GABA performs multiple physiological functions (Table 4).

GABA has a hypotensive effect on spontaneously hypertensive rats [14, 25]. A significant decrease in blood pressure is detected 4–8 h after the administration of 0.05–5.00 mg/kg of GABA [25]. Suwanmanon and Hsieh [53] also reported that the GABA and nattokinase lowered blood pressure in spontaneously hypertensive rats. In men with slight hypertension, the daily intake of GABA-rich cheese, which contains 16 mg of GABA, decreases mean blood pressure and systolic blood pressure [26]. In individuals with high-normal blood pressure and borderline hypertension, consumption of the GABA-rich chlorella dietary supplement significantly decreases systolic and diastolic blood pressure [54].

GABA exhibits antidiabetic activities in rats and human. GABA-rich tea, containing 3.01 or 30.1 μg of GABA, lowers blood glucose level in diabetic rats [55]. Oral doses of GABA increase insulin secretion [29, 56, 57]. The consumption of GABA significantly increases the secretion of insulin in normal rats; however, the secretion of insulin is not significant in diabetic rats. The role of GABA in increasing insulin secretion is unknown; speculation is that (1) GABA plays a role in the regulation of insulin synthesis, (2) GABA is an energy source in beta cells and (3) GABA is an insulin stabiliser [29].

In chronic renal failure, GABA ameliorates renal dysfunction, inhibits disease progression, regulates blood pressure and improves lipid profile. The administration of GABA also decreases oxidative stress induced by renal failure by increasing the activity of antioxidative enzymes [58]. In patient with cholangiocarcinoma or bile duct cancer, GABA inhibits the growth of cancer cells [28].

The oral administration of GABA significantly increases alpha waves and reduces beta waves in the human brain, thereby inducing relaxation and reducing anxiety. GABA enhances immunity, evaluated by measuring IgA levels, during stressful conditions [24].

Consumption of GABA either from fermented products or supplements can have a beneficial effect at certain doses for rats and humans. However, clinical trials on the effects of the consumption of GABA-containing fermented foods and beverages on human health are still needed.

6. Opportunity and challenges

GABA-enriched fermented foods and beverages can potentially become a trend as functional foods. The processing of GABA by microorganisms in fermented foods and beverages is simple and does not require high production costs during the purification process. Thus, both the industry and the customer can receive benefits.

Although studies have been carried out to identify microbiological sources of GABA and maximize production through fermentation, there is not enough information available on the production of GABA in fermented foods and beverages at industrial scale. Therefore, the process of scale-up needs to be completed. It may present a new challenge, such as the need for microorganisms which produce higher GABA in the pilot or mini-scale for the subsequent mass production.

7. Concluding remarks

γ-aminobutyric acid is a bioactive agent found in plants, animals and microorganisms that has potential functional effects as an antihypertensive, antidiabetic, anticarcinogenic, antidepressant and immune enhancer. GABA production is performed by fermentation using selected microorganisms. LAB, such as *Lactobacillus plantarum*, *L. brevis* and *Streptococcus thermophilus* are used as starters in fermented foods and beverages to produce GABA. Temperature, pH, substrate, culture time and L-glutamate content during the fermentation process affected GABA synthesis. So those factors need to be watched. GABA-enriched fermented foods and beverages can be potentially developed as functional foods. However, optimisation and scale-up are needed to ensure that production at a large scale is optimal.

Extensive details, in particular on aspects of clinical and pre-clinical studies on the application of GABA from fermented foods and beverages, should also be of concern. Given the long-term effects of fermented products consumption, and their role in improving the health of those who eat them.

Declarations

Author contribution statement

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Data included in article/supplementary material/referenced in article.

Declaration of interests statement

The authors declare no conflict of interest.

Additional information

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