Biogenic Amine in Kimchi Products

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Biogenic amines produced during fermentation may be harmful when ingested in high concentrations. As current regulations remain insufficient to ensure the safety of fermented vegetable products, the current study determined the risks associated with the consumption of kimchi by evaluating the biogenic amine concentrations reported by various studies.

kimchi Jeotgal Aekjeot Myeolchi-jeot Myeolchi-aekjeot biogenic amines recommended limits occurrence reduction starter cultures

1. Introduction

Kimchi refers to a group of traditional Korean fermented vegetable products consumed worldwide [1]. Dating back to the 12th century during the Three Kingdoms period of ancient Korea, salted and fermented vegetable products represent the earliest form of kimchi, however, the addition of several ingredients such as the introduction of red peppers in the 16th century was eventually adopted for kimchi production [2]. The availability of local ingredients across different provinces in Korea led to the development of many regional kimchi varieties [3] (Figure 1). Currently, there are over 200 varieties of kimchi with over 100 different ingredients used for kimchi production [4]. Each kimchi variety is categorized according to the ingredients selected for production [5]. Kimchi in its current form has been recognized globally through international standardization as well [6]. Kimchi is prepared by trimming Napa cabbage, followed by salting, rinsing, and then draining excess water. The seasoning ingredients include red pepper powder, garlic, ginger, radish, glutinous rice paste, sugar, *Jeotgal*, and *Aekjeot*. The salted Napa cabbage is then mixed with the seasoning and stored at low temperatures (typically 0–10 °C in Korea [5]) to ferment until ripened [6]. While the production method described by the Codex only describes *Baechu* kimchi (Napa cabbage kimchi), slight variations are used to produce other kimchi varieties.

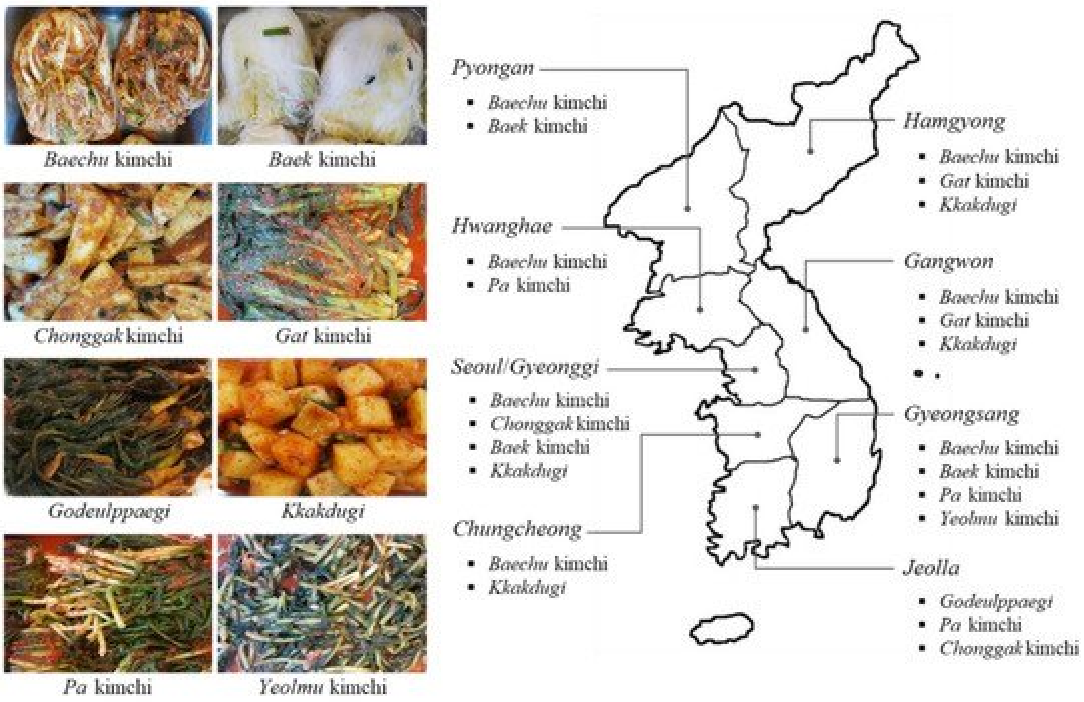

Figure 1. Kimchi varieties available across different provinces in Korea. *Baechu* kimchi: Napa cabbage kimchi; *Baek* kimchi: Napa cabbage kimchi prepared without red pepper powder; *Chonggak* kimchi: ponytail radish kimchi; *Gat* kimchi: mustard leaf kimchi; *Godeulppaegi*: Korean lettuce kimchi; *Kkakdugi*: diced radish kimchi; *Pa* kimchi: green onion kimchi; *Yeolmu* kimchi: young radish kimchi.

Nonetheless, nearly every kimchi variety benefits from preliminary brining, which inhibits the growth of pathogenic bacteria while selecting for lactic acid bacteria (LAB) known for promoting beneficial effects such as gastrointestinal regulation and prevention of colon cancer [7][8]. The LAB such as *Leuconostoc*, *Lactobacillus*, and *Weissella* species as well as the enzymes present in the ingredients are responsible for kimchi fermentation [9][10]. Consumption of kimchi is reported to provide numerous health benefits such as anti-oxidative, anti-carcinogenic, anti-mutagenic, and anti-aging effects [8][11][12].

Despite the numerous beneficial functional qualities, fermented foods such as kimchi may contain potentially harmful substances known as biogenic amines (BA). The nitrogenous compounds are mostly produced by microorganisms during fermentation through enzymatic decarboxylation of amino acids, as well as transamination of ketones and aldehydes [13]. BA are often categorized as aliphatic: putrescine, cadaverine, spermidine, spermine; aromatic: β-phenylethylamine, tyramine; heterocyclic: tryptamine, histamine [14][15]. The intake of BA at high concentrations as well as amine oxidase inhibition and deficiency may lead to toxic effects [16]. Recently, histamine, tyramine, putrescine, cadaverine, spermidine, and spermine were found to be cytotoxic toward human intestinal cells [17][18][19]. Furthermore, BA may also be converted to potentially carcinogenic N-nitrosamines in the presence of nitrites [20][21]. Excessive intake of foods containing high concentrations of histamine may potentially induce “scombroid poisoning” with symptoms such as headaches, hives, diarrhea, dyspnea, and hypotension [22]. Similarly, ingestion of foods with excessive tyramine content may cause a “cheese crisis” with symptoms that include severe headaches, hemorrhages, hypertensive effects or even heart failure [23]. As a result, many countries have implemented regulations on the production of histamine-rich seafood products, however many other food products are not currently regulated [24]. Several studies have suggested limits for BA content in food products of 100 mg/kg for histamine, 100–800 mg/kg for tyramine, 30 mg/kg for *β*-phenylethylamine, and 1000 mg/kg for total BA content [14][15]. The concentrations of BA in many fermented food products such as fermented meats and cheese have been widely reported to exceed limits for safe consumption. Similarly, BA have been detected in kimchi products, the most widely consumed traditional Korean food. High concentrations of BA have also been detected in kimchi ingredients *Jeotgal* (Korean fermented seafood) and *Aekjeot* (Korean fermented fish sauce), which contribute to the overall BA content in kimchi [25]. In addition, microorganisms isolated from kimchi as well as the fermented seafood products *Jeotgal* and *Aekjeot* have been reported to produce BA. Current regulations remain insufficient to address the potential health risks associated with the consumption of kimchi with high concentrations of BA. Therefore, the current article evaluated the risks associated with the BA content of kimchi products according to intake limits for *β*-phenylethylamine (30 mg/kg), histamine (100 mg/kg), and tyramine (100 mg/kg) as recommended by Ten Brink et al. [15], and reviewed potential sources of BA, and methods for reducing BA content.

2. Biogenic Amine Content in Kimchi Products

Table 1 displays the BA content of kimchi products as reported by various studies. The BA content of *Baechu* kimchi (Napa cabbage kimchi), the most popular kimchi variety consumed worldwide, has been reported by several studies. Cho et al. [25] reported histamine and tyramine concentrations in *Baechu* kimchi that exceeded recommended limits. Another study also showed that tyramine content in *Baechu* kimchi exceeded the recommended limit [26]. Tsai et al. [27] notably reported the highest histamine content which exceeded the recommended limit by a factor of 53. Tsai et al. [27] suggested that the high concentration of histamine in kimchi might be due to ingredients such as fish sauce or shrimp paste used in the kimchi production process. Shin et al. [28] reported *β*-phenylethylamine, histamine, and tyramine content at safe concentrations below 30 mg/kg. Similarly, Mah et al. [29] reported both histamine and tyramine content at safe concentrations below 30 mg/kg. In ripened *Baechu* kimchi, Kang et al. [26] reported tyramine content at concentrations that nearly reached the recommended limit.

Table 1. Biogenic amine content of Korean fermented vegetable products.

Korean Fermented Vegetable Products	N [1]	Biogenic Amines (mg/kg) [2]								Ref.
		TRP	PHE	PUT	CAD	HIS	TYR	SPD	SPM	
Baechu kimchi (Napa cabbage kimchi)	3	NT [3]	NT	11.2–89.0 [4]	ND [5]-151.8	ND-5.1	ND-28.2	ND	ND	[29]

Korean Fermented Vegetable Products	N [1]	Biogenic Amines (mg/kg) [2]								Ref.
		TRP	PHE	PUT	CAD	HIS	TYR	SPD	SPM	
	20	2.3–22.6	ND-6.8	15.1–240.4	3.6–44.9	0.6–142.3	9.7–118.2	7.7–16.5	ND-3.7	[25]
	37	ND-114	ND	ND-73	ND-1550	ND-5350	ND-42	ND-88	ND-121	[27]
	18	ND-43.9	NT	ND-245.9	ND-63.3	NT	ND-103.6	ND-74.8	NT	[26]
	20	ND-74.8	ND-2.0	2.3–148.6	0.9–39.8	ND-21.8	1.1–27.9	ND-6.7	ND-5.1	[28]
Baek kimchi (Napa cabbage kimchi prepared without red pepper powder)	3	NT	NT	ND-54.7	ND-94.8	ND	ND	ND	ND	[29]
	3	tr [6]	NT	1.9–39.6	11.5–25.6	NT	7.8–64.9	ND-1.7	NT	[26]
Chonggak kimchi (ponytail radish kimchi)	3	NT	NT	ND-11.2	ND-70.7	ND	ND	ND	ND	[29]
	3	2.3–15.2	NT	ND-20.3	ND-85.7	NT	20.2–58.1	ND	NT	[26]
	5	ND-23.70	ND-2.80	3.89–853.70	2.00–148.50	8.24–131.20	0.79–18.70	6.10–14.00	ND-20.74	[30]
Gat kimchi (mustard leaf kimchi)	3	NT	NT	ND-10.4	ND-11.6	ND	ND	ND	ND	[29]

Korean Fermented Vegetable Products	N [1]	Biogenic Amines (mg/kg) [2]								Ref.
		TRP	PHE	PUT	CAD	HIS	TYR	SPD	SPM	
	13	ND-26.74	ND-15.75	1.89–720.82	2.12–52.43	3.30–232.10	1.28–149.77	12.26–32.62	ND-61.94	[31]
Godeulppaegi (Korean lettuce kimchi)	3	NT	NT	ND-6.4	ND-26.7	ND	ND	ND	ND	[29]
Kkakdugi (diced radish kimchi)	3	NT	NT	ND-15.4	ND-55.1	ND	ND-9.0	ND	ND	[29]
	5	5.5–18.6	NT	ND-51.6	ND-56.2	NT	ND-10.8	ND-21.8	NT	[26]
	5	ND	ND-15.24	10.85–982.32	ND-124.60	18.75–127.78	2.97–76.95	ND-16.76	ND-3.10	[30]
Pa kimchi (green onion kimchi)	3	NT	NT	ND-7.8	ND-15.9	ND-21.7	ND	ND	ND	[29]
	13	ND-15.95	ND-5.97	ND-254.47	ND-123.29	8.67–386.03	ND-181.10	2.32–18.74	ND-33.84	[31]
Yeolmu kimchi (young radish kimchi)	3	NT	NT	ND	ND	ND	ND	ND	ND	[29]

which exceeded the recommended limit by a factor of 2, while tyramine content slightly exceeded the limit. In contrast, Mah et al. [29] reported that *Gat* kimchi did not contain histamine and tyramine at detectable levels. *Kkakdugi* (diced radish kimchi) as reported by Jin et al. [30] contained tyramine at safe concentrations below the recommended limit, however, histamine concentrations exceeded the recommended limit. In contrast, Mah et al. [29] reported that histamine was not detected in *Kkakdugi*, and tyramine content was at safe concentrations below recommended limits. Similarly, Kang et al. [26] also reported tyramine concentrations in *Kkakdugi* below the recommended limit. As for *Pa* kimchi (green onion kimchi), Lee et al. [31] reported histamine and tyramine concentrations exceeded recommended limits by a factor of 4 and 2, respectively. In contrast, Mah et al. [29]

reported histamine and tyramine in *Pa* kimchi at safe concentrations as tyramine content was not detected while histamine content remained below 30 mg/kg. Other kimchi varieties such as *Baek* kimchi (Napa cabbage kimchi prepared without red pepper powder), *Godeulppaegi* (Korean lettuce kimchi), and *Yeolmu* kimchi (young radish kimchi) were reported to contain histamine and tyramine at safe concentrations below 100 mg/kg [29].

Nonetheless, as the vast majority of studies are primarily focused upon *Baechu* kimchi, further research on the BA content of other kimchi varieties remains necessary. Currently, the severity of the risks associated with the BA content of kimchi remains difficult to thoroughly assess as limited research has been conducted. Though various BA have been detected in kimchi products, several studies have reported histamine and tyramine content at concentrations that exceeded the recommended intake limits of 100 mg/kg. Furthermore, the risk of nitrosamine formation entails the need for continuous monitoring of BA content during fermentation, especially as putrescine and cadaverine were detected at particularly high concentrations. Due to the toxicological risks associated with the consumption of BA, the content in kimchi necessitates regulation and control to ensure its safety.

3. Biogenic Amine Content of Other Vegetable Products

Research has also been conducted on the BA content of vegetable products originating from other countries (Table S1). The popular fermented food sauerkraut is produced through lactic acid fermentation of white cabbage [32][33]. Among European fermented food products, sauerkraut most closely resembles Korean kimchi [34]. Despite its popularity, Taylor et al. [35] reported that sauerkraut contained histamine concentrations that exceeded recommended limits. Ten Brink et al. [15] also reported that histamine and tyramine in sauerkraut exceeded recommended limits by a factor of 1 and 2, respectively. Many varieties of Japanese *Tsukemono* are preserved vegetables produced utilizing methods such as fermentation, salting, and pickling [36]. *Tsukemono* are differentiated based on ingredients, pickling method, and microorganisms responsible for fermentation [5]. Handa et al. [37] reported that histamine and tyramine in *Tsukemono* exceeded recommended limits by a factor of 3 and 4, respectively. As an important part of the Taiwanese diet, mustard pickle is prepared using mustard greens submerged in 14% NaCl brine for 4 months [38]. Kung et al. [38] reported that mustard pickles contained histamine and tyramine at safe concentrations below 100 mg/kg. Though fermented vegetable products are consumed worldwide, limited research has been conducted on the BA content of vegetable-based fermented foods. The few studies available had reported a wide range of BA content, including concentrations that exceeded recommended limits. Therefore, as the risks associated with the consumption of fermented vegetables remains largely undetermined, additional research is necessary to ensure the safe consumption of fermented foods.

4. Strategies to Reduce Biogenic Amine Content in Kimchi Products

Despite the risks associated with BA accumulation, limited research has been conducted on reducing the BA content of kimchi products. Instead of directly reducing BA content in kimchi, several studies have reported various methods to reduce BA concentrations in the kimchi ingredients *Jeotgal* and *Aekjeot*. Kim et al. [39] reported that kimchi produced using fermented seafood products contained BA at significantly higher concentrations. Lee et al. [40] suggested that the BA concentration of kimchi products may be reduced by limiting the quantity of the fermented seafood products used during kimchi production. For example, Kang [41] reported the histamine content of kimchi without *Myeolchi-aekjeot* at safe levels, however, the addition of *Myeolchi-aekjeot* raised histamine content to unsafe concentrations above the recommended limit by a factor of approximately 6. The study also described the effect of heat treatment of *Myeolchi-aekjeot* on the histamine content of kimchi. Histamine concentrations in kimchi produced using heat-treated *Myeolchi-aekjeot* were reported at 546.14 ± 1.33 mg/kg, while non-treated kimchi contained 592.78 ± 3.43 mg/kg. The reported results indicate that microorganisms from *Myeolchi-aekjeot* contributed towards the production of histamine during kimchi fermentation. Also, as research shows that histamine is heat-stable [42], the lower BA content in kimchi produced using the heat-treated *Myeolchi-aekjeot* may be due to the sterilization of histamine-producing microorganisms [41]. In addition to the contribution of BA content in kimchi by *Myeolchi-aekjeot*, Lee et al. [31] suggested that microorganisms from *Myeolchi-aekjeot* may produce BA during kimchi fermentation. Utilizing substitute ingredients in lieu of *Myeolchi-aekjeot* and *Kkanari-aekjeot* may also be effective in reducing BA content in kimchi. As other *Jeotgal* products including *Ojingeo-jeot* (salted and fermented sliced squid), *Toha-jeot* (salted and fermented *toha* shrimp), *Jogae-jeot* (salted and fermented clam), *Baendaengi-jeot* (salted and fermented big-eyed herring), and *Eorigul-jeot* (salted and fermented oysters) have been found to contain individual BA content below 100 mg/kg [43], utilization of the fermented seafood products with low BA content for kimchi production is expected to reduce the overall BA content of kimchi products [29].

Research on using additives to reduce the BA content of fermented seafood products has also been reported. Mah et al. [44] conducted research to reduce BA production by microorganisms isolated from *Myeolchi-jeot*, introducing additives into assay media and *Myeolchi-jeot*. The results confirmed that compared to the control, garlic extract was the most effective inhibitor of bacterial growth and BA production by yielding lower in vitro production of putrescine, cadaverine, histamine, tyramine, and spermidine by 11.2%, 18.4%, 11.7%, 30.9%, and 17.4%, respectively. Further results revealed that compared to *Myeolchi-jeot* samples treated with ethanol (control), the addition of 5% garlic extract to *Myeolchi-jeot* (treatment) inhibited bacterial growth and consequently reduced overall BA production by up to 8.7%. In another study by Mah and Hwang [45], other additives were also used for the reduction of BA production by *Myeolchi-jeot* microorganisms in assay media and *Myeolchi-jeot*. Among the additives tested in assay media, glycine most effectively inhibited in vitro BA production by bacterial strains. In comparison to the control without additives, the addition of 10% glycine in assay media resulted in reductions in putrescine, cadaverine, histamine, tyramine, and spermidine production by 32.6%, 78.4%, 93.2%, 100.0%, and 100.0%, respectively. Compared to the *Myeolchi-jeot* samples salted at 20% NaCl, additional supplementation of 5% glycine reportedly reduced overall BA content by 73.4%. The results suggest that the addition of glycine as well as salt may improve the safety of fermented seafood products. It is noteworthy that despite the results showing effective BA reduction, the use of garlic extract or glycine may affect the flavor of the final product.

Aside from additives, other studies have utilized starter cultures to reduce BA content in *Jeotgal*. In a study by Mah and Hwang [46], some bacterial strains isolated from *Myeolchi-jeot* were found to reduce BA content in *Myeolchi-jeot*. The reported results showed that, of the 7 starter candidate strains, *S. xylosus* exhibited the highest histamine degradation capability as well as the ability to slightly degrade tyramine in assay media. In comparison to the uninoculated *Myeolchi-jeot* control, the addition of the starter culture reduced the production of putrescine, cadaverine, histamine, tyramine, and spermidine by 16.5%, 10.8%, 18.0%, 38.9%, and 45.6%, respectively. Jeong et al. [47] isolated strains from *Jeotgal* for use as potential starters and found that *S. equorum* strain KS1039 did not produce putrescine, cadaverine, histamine, and tyramine in vitro.

A limited number of studies have even attempted to directly reduce the BA content of kimchi through the inoculation of bacterial strains. Kim et al. [48] reported reductions in tryptamine, putrescine, cadaverine, histamine, and tyramine levels in *Baechu* kimchi fortified with *Leu. carnosum*, *Leu. mesenteroides*, *Lb. plantarum*, and *Lb. sakei* strains. Similarly, Jin et al. [30] reported that *Kkakdugi* and *Chonggak* kimchi inoculated with *Lb. plantarum* strains incapable of producing BA contained lower level of tyramine (but not the other BA) than the uninoculated control. Therefore, utilizing LAB strains unable to produce (and/or able to degrade) BA as kimchi starter cultures may likely reduce the total BA content during kimchi fermentation.

Although the aforementioned studies have shown both direct and indirect methods of reducing BA content in kimchi, current commercial kimchi production processes do not appear to utilize the BA reduction techniques. This might be due to the application of BA reduction methods such as the use of additives, starter cultures, and adjusting the quantity of fermented seafood products have been reported to affect the flavor of kimchi products [45][49][50]. Consequently, inconsistent product quality is reflected in the wide range of BA content of kimchi products, including concentrations that exceed recommended limits for safe consumption. The high BA content reported for various kimchi products indicates that modern production methods require further preventative measures to ensure the safety of the fermented vegetable products, including practical application of research-based BA reduction techniques described above. Commercial kimchi production may greatly benefit from utilizing the aforementioned and novel strategies including control of fermentation conditions, utilizing starter cultures, alternative ingredients, and/or ingredients with low BA content. Furthermore, the establishment and expansion of regulations limiting BA content in fermented foods remain necessary to safeguard consumers against the potential BA intoxication.

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