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Review

A Review of the Health Benefits of Kimchi Functional Compounds and Metabolites

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Kimchi is a traditional Korean dish made with salted fermented vegetables and contains various nutrients and functional substances with potential health benefits. The fermentation process used to make kimchi creates chemical changes in the food, developing nutrients and functional substances that are more easily absorbed and enhanced by the body. Recent studies have shown that several lactic acid bacteria strains isolated from kimchi exhibit probiotic properties and have several health benefiting properties such as such as anticancer, anti-obesity, and anti-constipation; they also promote colon health and cholesterol reduction in in vitro and in vivo experiments, as well as in epidemiological cohort studies. Kimchi contains prebiotics, non-digestible fibers that nourish beneficial gut bacteria; therefore, its intake effectively provides both probiotics and prebiotics for improved gut health and a fortified gut-derived immune system. Furthermore, fermentation of kimchi produces a variety of metabolites that enhance its functionality. These metabolites include organic acids, enzymes, vitamins, bioactive compounds, bacteriocins, exopolysaccharides, and γ-aminobutyric acid. These diverse health-promoting metabolites are not readily obtainable from single food sources, positioning kimchi as a valuable dietary option for acquiring these essential components. In this review, the health functionalities of kimchi ingredients, lactic acid bacteria strains, and health-promoting metabolites from kimchi are discussed for their properties and roles in kimchi fermentation. In conclusion, consuming kimchi can be beneficial for health. We highlight the benefits of kimchi consumption and establish a rationale for including kimchi in a balanced, healthy diet.

Keywords: Kimchi, health benefits, functional compounds, lactic acid bacteria, metabolites

Introduction

November 22 is designated “Kimchi Day” and was established in 2020 to promote the growth of the kimchi (Korean traditional fermented food) industry, preserve and advance kimchi culture, and raise awareness of kimchi’s nutritional value and importance. This date was chosen because it is considered the most suitable time of the year for making kimchi. Additionally, this date symbolizes the fact that kimchi, made with each ingredient one by one, exhibits 22 different health benefits. Furthermore, kimchi is the only food with a designated legal commemorative day.

Kimchi is the most popular fermented food in Korea, embodying the wisdom and ingenuity of the Korean people as a traditional fermented food. It is a fermented vegetable dish made primarily from ingredients such as kimchi cabbage and radish, which are first salted and mixed with various additional ingredients such as garlic, ginger, red pepper powder, and fish sauce, and then fermented with lactic acid bacteria (LAB). Various types of LAB are involved in kimchi fermentation, and kimchi

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types can differ depending on factors such as its ingredients, fermentation temperature, and salt concentration. The dominant bacteria driving kimchi fermentation belong to the genera *Leuconostoc*, *Lactobacillus*, and *Weissella* [1]. *Leuconostoc* predominates in the initial stages of fermentation, producing various metabolites such as lactic and acetic acids (providing a sour taste), carbon dioxide (providing a refreshing taste), mannitol (providing a cool sweetness), and acetoin (providing a unique fermentation aroma), together resulting in a refreshingly sweet and tangy taste as well as a crisp texture [2]. As fermentation progresses, *Lactobacillus* and *Weissella* increase in abundance, enhancing the nutritional value and giving rise to the rich and savory taste of mature kimchi. Kimchi has become an iconic food that represents Korea and sometimes appears as a symbol of Korean culture. Kimchi is remarkable because it is an exceptional way of preserving vitamin C-rich vegetables throughout cold winters, which was especially important before the invention of refrigerators. This preservation method allowed the ancestors of Korean people to consume vitamin C during cold winters. Kimchi is known not only for its unique taste and flavor but also for providing new nutrients that are not present in its original ingredients, along with a multitude of beneficial lactic acid bacteria (LAB). With a history spanning thousands of years, kimchi is now recognized worldwide as a high-quality, healthy food, contributing to the spread of Korean culture and making it a representative of Korean (K)-food.

Kimchi's adoption into international standards by the CODEX Alimentarius Commission in 2001 signified its global recognition as the only fermented food with acknowledged hygiene, safety, and quality among vegetable mixes. In 2006, kimchi was selected as one of the world’s top five health foods by the American health magazine “Health” [3]. This recognition has garnered attention in Korea as well as worldwide. Kimchi fermentation and ripening enhance the absorption of many bioactive substances. In addition to vitamins, minerals, and dietary fiber, kimchi contains a variety of functional substances, and their contents are further increased through fermentation, thus providing various health benefits [4].

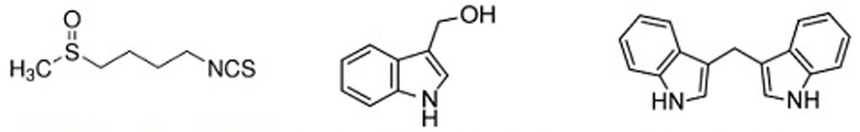
Research on the health benefits of kimchi has been conducted from various perspectives. In particular, differences in functionality depending on the kimchi ingredients, LAB, and metabolites have been demonstrated. The health benefits of kimchi are well known worldwide. During the 2002 SARS outbreak, a claim attributed the low infection rate in Korea to kimchi consumption. Recently, a French research group analyzed the dietary differences among different countries and concluded that kimchi consumption was the reason for the relatively low coronavirus disease 2019 (COVID-19) mortality rate in Korea [5, 6]. The scientifically demonstrated antiviral effects of kimchi and identification of kimchi ingredients with strong virus-suppressing abilities support this claim. In recent years, Korean kimchi has been exported to more than 90 countries, allowing people worldwide to experience its flavors. The present study elucidates the diverse health functionalities of kimchi in the era of the “healthy 100-year lifespan”. Furthermore, it emphasizes the benefits of kimchi as a healthy food.

Health Benefits of Kimchi Ingredients

The variety of ingredients used for preparing kimchi determines its characteristics, functionality, and microbial composition [1]. In this section, health benefits of the main ingredients of kimchi, namely kimchi cabbage, red pepper, garlic, and ginger, are discussed, with a focus on the mechanistic studies on active compounds.

Kimchi Cabbage

Kimchi cabbage (*Brassica rapa*) is the main ingredient in many fermented vegetable mixes, including sauerkraut in Europe and kimchi in East Asia. The main active compounds of cruciferous plants, including kimchi cabbage, are sulforaphane (SFN), indole-3-carbinol (I3C), 3,3’-diindolylmethane (DIM), allyl isothiocyanate, phenyl isothiocyanate, and benzyl isothiocyanate (Fig. 1) [7, 8], and their many health benefits have been reported in basic and clinical studies [9]. Kimchi has recently been recognized as an ideal food because of its nutritional value and health benefits. High consumption of cabbage and fermented vegetables has been associated with low death rates due to COVID-19 in Eastern Asia, Central Europe, and the Middle East. Kimchi cabbage contains precursors of SFN, the most active natural activator of nuclear erythroid 2-related factor 2 (Nrf2), a



DL-Sulforaphane (SFN) **Indole-3-carbinol (I3C)** **3,3'-diindolylmethane (DIM)**

Fig. 1. Main compounds of kimchi cabbage.

transcription factor that regulates the expression of genes involved in antioxidant and detoxification systems [10]. The disruption of Nrf2 results in lipid accumulation, mitochondrial dysfunction, inflammation, insulin resistance, and oxidative stress in cells and animal models [11, 12]. Nrf2-activating factors, including berberine, curcumin, EGCG, genistein, quercetin, resveratrol, SFN, *Lactobacillus*, and kimchi, mitigate COVID-19 mortality by downregulating the angiotensin converting enzyme (ACE)-angiotensin-II-AT1R axis pathway [10, 13, 14]. Potassium is the most abundant nutrient element in the leaves of kimchi cabbage [15], and it may compensate for the sodium content in kimchi, resulting in a hypotensive effect; however, further studies are needed to reveal the mechanisms behind this.

SFN [1-isothiocyanato-4-(methylsulfinyl) butane] is an isothiocyanate that occurs in stored forms, such as glucoraphanin and others, in cruciferous vegetables and fermented cabbage. Fermented vegetables contain glucoraphanin, which is converted to SFN by the gut microbiome or by myrosinase in plants. In addition, SFN generation by bacterial microflora in the colon has been observed in mice [16]. Many studies have shown that SFN has broad health benefits, including anticancer effects [17, 18] and provides protection against COVID-19 [6, 14] as well as cardiovascular [19, 20], inflammatory bowel [21], and fatty liver diseases [22–25]. Nonalcoholic fatty liver disease (NAFLD) pathogenesis is associated with the dysregulation of glucose and lipid metabolism, excess inflammation, oxidative stress, and the dysregulation of the gut microbiota [26]. SFN attenuates weight gain and hepatic inflammation and improves intestinal barrier integrity and intestinal dysbiosis [22]. In addition, bisphenol A-induced liver damage was reversed using SFN by inhibiting the expression of genes involved in hepatic ER stress and lipogenesis [23]. Epidemiological studies [27, 28] and clinical trials have shown that SFN intervention is inversely correlated with cancer prevalence [18].

I3C, a naturally occurring plant product found in numerous cruciferous vegetables, is converted to DIM by the condensation of two I3C molecules in the acidic conditions of the stomach [29]. I3C can prevent colitis-associated microbial dysbiosis by increasing the secretion of n-butyric acid and IL-22 [30]. Moreover, as a natural dietary agonist of the aryl hydrocarbon receptor, I3C alleviates ulcerative colitis by downregulating the transcription of genes involved in necroptosis and inflammation [31]. Several studies have reported that I3C and DIM have anti-obesity effects associated with improved glucose intolerance, adipogenesis, thermogenesis, and inflammation in mice fed a high-fat diet [32–34]. I3C and DIM have been extensively studied as chemopreventive agents for cancer through cellular and molecular mechanisms including apoptosis, cell cycle arrest, senescence, angiogenesis, and metastasis [29]. The treatment of cancer cells with I3C and DIM activates apoptosis, as evidenced by the upregulation of ER stress-mediated mitochondrial apoptosis and the downregulation of the PI3K/Akt signaling pathway [35, 36]. Moreover, cardiac hypertrophy, fibrosis, and dysfunction were reversed by I3C in AMPK-α2 knockout mice [37].

Red Pepper

Red pepper (*Capsicum annuum*) is one of the most popular vegetable species and was first cultivated more than 7 000 years ago. Its fruits contain many phytochemicals, such as capsaicinoids, flavonoids, phenolic acids, saponins, anthocyanins, and vitamins C, E, and A, as well as volatile compounds [38]. The most predominant and active compound of *C. annuum* is capsaicin, which has many health benefits, including antioxidant, anti-obesity, anticancer, anti-inflammatory, anti-diabetic, antiviral, immunomodulatory, and cardioprotective effects. Here, we discuss and highlight its health benefits, focusing on the anticancer [39–41], cardioprotective

[42–45], and anti-obesity effects [46–50]. Capsaicin binds to the TPPV1 receptor and induces apoptosis signaling, cytochrome c release, mitochondrial calcium overload, and cell cycle arrest in carcinoma cells [39, 40]. Additionally, it exerts antiangiogenic effects by inhibiting vascular endothelial growth factor-induced cell proliferation, thus blocking new blood vessel formation in cancer cells [41]. Increasing evidence has suggested that capsaicin protects against cardiovascular diseases, mainly by regulating oxidative stress, inflammation, endothelial dysfunction, cholesterol metabolism, and gut microbiota dysbiosis [42, 43]. Capsaicin administration prevents atherosclerosis by modulating gut microbiota and cecal metabolites, indicating that capsaicin alleviates intestinal inflammation and intestinal mucosal barrier dysfunction [43]. Capsaicin contributes to the activation of the TRPV1 pain receptor, which has been shown to provide cardiovascular protection to cells, animals, and humans in clinical trials [42, 44, 45]. It is an effective medicinal compound used for the prevention and treatment of obesity. Many studies have reported that its anti-obesity mechanism involves alterations in the gut microbiota, reduction in intestinal permeability, and regulation of the microbiome-gut-brain axis pathway [46]. Increases in the abundances of *Bacteroides*, *Coprococcus*, *Prevotella*, *Akkermansia*, and metabolites in capsaicin-treated mice were accompanied by a decrease in body weight, stimulation of intestinal mucus secretion, and improvement of intestinal barrier function compared to those in mice fed a high-fat diet [47, 48]. Red pepper powder used during kimchi fermentation plays a key role in the growth of *Weissella* species, which have strong arginine deiminase activities, resulting in high levels of ornithine in kimchi and associated anti-obesity effects [51–53].

Garlic

Garlic (*Allium sativum*) contains several bioactive compounds, including organosulfur compounds, saponins, phenolic compounds, and polysaccharides, which contribute to its many health benefits and pharmacological activities [54, 55]. Sulfur-containing compounds such as allicin, diallyl sulfide, diallyl disulfide, diallyl trisulfide, alliin, S-allylcysteine, and S-allylmercaptocysteine have been reported to have anticancer effects (Fig. 2) [56–62]. Accumulating evidence has demonstrated that garlic has the potential to protect against cardiovascular diseases, hypertension, hyperlipidemia, atherosclerosis, and heart disease via anti-inflammatory, antioxidant, hypolipidemic, and anti-apoptotic mechanisms, regulating the gut microbiota and increasing Na^+/K^+-ATPase levels [63–67]. Furthermore, diallyl disulfide has been shown to exert a hypocholesterolemic effect by inhibiting ER stress in apolipoprotein E-deficient mice [68]. In the experimental group subcutaneously injected with extracts of common cabbage kimchi (0.05–1.25 mg/mouse), 14% inhibition of tumor metastasis was observed. At all tested concentrations, kimchi extracts with high contents of garlic and red pepper powder exhibited inhibitory effects on tumor metastasis, and the highest inhibitory effect at 49% was found in the group injected with 1.25 mg/mouse of the kimchi extract [69]. Recently, high levels of organosulfur compounds in garlic were reported to interact strongly with the amino acids of the

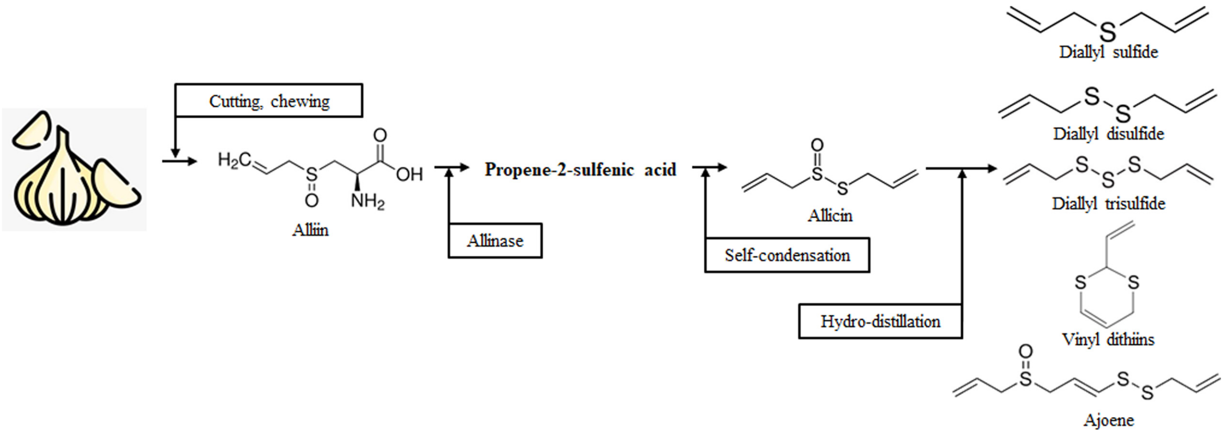


Fig. 2. Conversion of allicin into the main components of garlic essential oil [54].

Table 1. Functionalities of compounds in kimchi ingredients.

Ingredients	Compound	Effects	Mechanisms	References
Kimchi cabbage	Sulforaphane (SFN)	Anti-COVID-19	SFN mitigates COVID-19 mortality by downregulating the ACE-angiotensin-II-AT1R axis pathway.	[6, 10, 13, 14]
		Anticancer	SFN restrains cell proliferation and induces apoptosis by HDAC inhibition.	[17, 18]
		Anti-cardiovascular diseases	SFN improves dyslipidemia and inhibits atherosclerotic plaque formation by activating Nrf2 expression.	[19, 20]
		Intestinal inflammation management	SFN regulates inflammation and modified microbial communities.	[21]
		Liver/hepatic health improvement	SFN improves intestinal barrier integrity and hepatic lipogenesis.	[22-26]
	Indole-3-carbinol (I3C) 3,3′-diindolylmethane (DIM)	Anti-colitis	I3C prevents colitis-associated microbial dysbiosis by increasing the secretion of n-butyric acid and IL-22.	[30]
		Anti-obesity	I3C and DIM have anti-obesity effects, improving glucose intolerance, adipogenesis, thermogenesis, and inflammation in mice fed a high-fat diet.	[32-34]
		Anticancer	I3C and DIM activates apoptosis in cancer cells.	[35-37]
Red pepper	Capsaicin	Anticancer	Capsaicin exhibits anticancer effects by inducing the apoptosis signaling pathway.	[39-41]
		Anti-cardiovascular diseases	Capsaicin prevents atherosclerosis by modulating gut microbiota and cecal metabolites in atherosclerotic apoE$^{-/-}$ mice.	[42-45]
		Anti-obesity	Capsaicin has anti-obesity effects by alternating the gut microbiota, reducing intestinal permeability, and regulating the microbiome–gut–brain axis pathway.	[46-48]
Garlic	Organosulfur compounds	Hypocholesterolemic	Diallyl disulfide exerts a hypocholesterolemic effect by inhibiting ER stress in apoE$^{-/-}$ mice.	[68]
		Anticancer	Kimchi extracts with high contents of garlic exhibits an inhibitory effect on tumor metastasis.	[69]
		Anti-COVID-19	High organosulfur compounds in garlic prevent COVID-19 by interacting with the amino acids of the ACE2 protein.	[70, 71]
Ginger	Shogaol	Antioxidant and anti-inflammatory	6-shogaol had the greatest antioxidant effect because of α,β-unsaturated ketone moiety.	[75]
	Gingerol	Antioxidant and anti-inflammatory	6-gingerol reduces inflammation and pyroptosis by activating the Nrf2 pathway in sepsis-induced liver injury.	[76]
		Anti-colitis	Gingerol attenuates colitic symptoms by decreasing inflammation and oxidative stress and increasing antioxidant activities.	[79]
		Anti-COVID-19	Ginger results in a shorter hospitalization time in people with COVID-19.	[81]
		Anti-SARS-CoV-2	Ginger is a potential inhibitor of the SARS-CoV-2 protease and spike receptor.	[82, 83]
		Anti-diabetic	6-gingerol ameliorates diabetes mellitus by inhibiting hyperglycemia, inflammation, and oxidative stress.	[84, 85]

ACE2 protein and prevent COVID-19 [70, 71].

Ginger

Ginger (*Zingiber officinale*) is rich in various chemical constituents such as phenolic compounds, terpenes, polysaccharides, lipids, organic acids, and fiber [72–74]. Among its main phenolic compounds, gingerols and shogaols are the most important physiologically active ingredients and have been reported to have antioxidant [75–78], anti-inflammatory [79], analgesic [80], antitumor, and anti-COVID-19 effects [81]. The antioxidant and anti-inflammatory effects of 6-, 8-, 10-gingerol and 6-shogaol, as evidenced by the reduction in nitric oxide and PGE2 release, increased in a dose-dependent manner in RAW264.7 cells; among the tested compounds, 6-shogaol had the greatest antioxidant effect, which can be attributed to the presence of an α,β-unsaturated ketone moiety [75]. One study showed that 6-gingerol can reduce inflammation and pyroptosis by activating the Nrf2 pathway in sepsis-induced liver injury [76]. Additionally, gingerol was shown to attenuate colitis symptoms such as serious colon damage and imbalance of antioxidant systems by decreasing inflammation and oxidative stress and increasing antioxidant activities [79]. Recently, spices such as onion, garlic, ginger, turmeric, red chili, fenugreek, cumin, and peppermint, which are used as traditional medicinal foods, have been recognized as potential inhibitors of the SARS-CoV-2 protease and spike receptor [82, 83]. In addition, in people with COVID-19, ginger supplementation resulted in a shorter hospitalization time [81]. Furthermore, 6-gingerol was found to ameliorate diabetes mellitus by inhibiting hyperglycemia, inflammation, and oxidative stress [84, 85].

Role of LAB in Kimchi Fermentation

Kimchi is a traditional Korean fermented food that preserves food safely and imparts taste and nutritional value through the fermentation process involving various naturally occurring microorganisms present in the raw ingredients and brining process, with LAB being the main species. Owing to variations in raw ingredients and fermentation conditions, the dominant strains of LAB and their fermentation metabolites can differ, making the microbial community of kimchi a crucial factor in its fermentation. Kimchi contains 8–10 log/g of LAB depending on the fermentation stage. The key bacteria involved in kimchi fermentation include species from the genera *Leuconostoc*, *Lactobacillus*, and *Weissella*. Kimchi has been recognized as a source of various functional LAB, and research on its potential for health promotion has been actively pursued. Therefore, in this section, we review the functional properties of kimchi-associated LAB and their health-promoting effects.

Lactobacillus

Throughout kimchi fermentation, *Lactobacillus* species play an ongoing role by steadily transforming the sugars found in vegetables into lactic acid. This not only inhibits the proliferation of detrimental microorganisms, such as spoilage bacteria and pathogens, but also facilitates the production of a diverse range of flavor compounds. In addition, a multitude of research findings have underscored the beneficial effects of the *Lactobacillus* species originating from kimchi on crucial physiological processes, including metabolism, immunity, and musculoskeletal regulation.

Numerous reports have highlighted the efficacy of LAB in enhancing liver function and alleviating metabolic diseases such as obesity and diabetes. Supplementation with *Lactococcus lactis* has demonstrated remarkable effectiveness in restoring various markers associated with NAFLD. Administration of *Lc. lactis* resulted in the recovery of critical metabolites, including short-chain fatty acids, bile acids, and tryptophan metabolites. By modulating the metagenomic and metabolic environment within the gut, especially the tryptophan pathway in the gut-liver axis, *Lc. lactis* showed the potential to counteract the progression of NAFLD [86]. Additionally, the consumption of LAB derived from kimchi, such as *Lactiplantibacillus plantarum* DSR J266, *Levilactobacillus brevis* DSR J301 (AL group), and *Lacticaseibacillus rhamnosus* GG (AG group), mitigates inflammation, liver damage, gut dysbiosis, and abnormal intestinal nutrient metabolism caused by alcohol consumption [87]. Hypercholesterolemia was alleviated by *Lb. plantarum* NR74 from Korean kimchi. This strain modulates cholesterol absorption by downregulating Niemann-Pick C1-like 1 expression in Caco-2 enterocytes [88]. *Lb. sakei* WIKIM31 treatment was associated with reduced body weight gain, decreased adipose tissue mass, lowered blood triglyceride and total cholesterol levels, and suppressed lipogenesis-related gene expression in obese mice. Importantly, the treatment improved gut barrier function and mitigated inflammatory responses [89]. Similarly, *Lb. sakei* OK67 effectively ameliorated high-fat-diet-induced hyperglycemia and obesity by reducing inflammation and enhancing the expression of colon tight junction proteins [90]. *Lb. plantarum* strains DSR M2 and DSR 920 exhibited anti-obesity effects including the suppression of obesity-related markers, alteration of gut microbial composition, and modulation of immune cell responses [91]. Furthermore, *Lb. amylovorus* KU4 demonstrated the potential to counteract diet-induced obesity by enhancing mitochondrial levels and function, promoting the thermogenic gene program, and partly elevating lactate levels [92]. Clinical study demonstrated that *Lb. sakei* CJLS03 is a

Table 2. Functionalities of LAB in kimchi fermentation.

Genus	Species	Effects	Mechanisms	References
Lactobacillus	*L. lactis*	Liver/hepatic health	*L. lactis* interrupted the progression of NAFLD by modulating the metagenomic and metabolic environment within the gut.	[86]
	L. plantarum DSR J266, *L. rhamnosus* GG		These strains alleviated inflammation, liver damage, gut dysbiosis, and abnormal intestinal nutrient metabolism.	[87]
	L. plantarum NR74	Anti-hyperlipidemic	*L. plantarum* NR74 modulated cholesterol absorption by downregulating NPC1L1 expression in Caco-2 enterocytes.	[88]
	L. sakei WIKIM31	Anti-hyperglycemia, anti-obesity	*L. sakei* WIKIM31 improved the gut barrier function and mitigated inflammatory responses of obese mice.	[89]
	L. sakei OK67	Anti-obesity effects	*L. sakei* OK67 reduced inflammation and enhanced the expression of colon tight junction proteins.	[90]
	L. plantarum DSR M2, *L. plantarum* DSR 920		These strains suppressed obesity-related markers, altered gut microbial composition, and modulated immune cell responses.	[91]
	L. amylovorus KU4		*L. amylovorus* KU4 counteracts obesity by enhancing mitochondrial function, and promoting the thermogenic gene program.	[92]
	L. sakei CJLS03		*L. sakei* CJLS03 can reduce body fat without causing significant adverse effects.	[93]
	L. plantarum HAC01		*L. plantarum* HAC01 improved the symptoms of glycemic control in T2D mice.	[94]
	L. brevis KCCM 12203P, *L. plantarum* 200655	Immunomodulatory	These strains activated RAW 264.7 macrophage cells, inducing immune-enhancing effects without cytotoxicity.	[95]
	L. plantarum HY7712		*L. plantarum* HY7712 exhibited immunostimulatory effects in irradiated and immunosuppressed mice, enhancing their NK and Tc cell responses.	[96, 97]
	L. plantarum LB5		*L. plantarum* LB5 was regulated the expression of pro- and anti-inflammatory cytokines in LPS-stimulated Caco-2 cells.	[99]
	L. plantarum IDCC 3501	Anti-inflammatory	*L. paracasei* KB28 induced the expression of certain cytokines in mouse macrophages and activated major MAPKs.	[98]
	L. paracasei KB28		*L. plantarum* IDCC 3501 reduced the mRNA expression of inflammatory markers.	[100]
	L. gasseri NK109	Neurodegenerative disorders	*L. gasseri* NK109 alleviated cognitive impairment and depression in mice induced by *E. coli* K1 by reducing IL-1β expression.	[101, 102]
	L. sakei WIKIM30	Atopic dermatitis management	*L. sakei* WIKIM30 inhibited atopic dermatitis by promoting the differentiation of Treg cells and influencing the gut microbiota composition.	[104]
	L. sakei Probio65		*L. sakei* Probio65 reduced IgE levels in the bloodstream and decreased IL-4 secretion.	[105]
	L. plantarum WiKim83, *L. plantarum* WiKim87	Antimicrobial and antioxidant	These strains exhibited antimicrobial, β-galactosidase, and antioxidant activities.	[106]
	L. plantarum KU200656	Antimicrobial	*L. plantarum* KU200656 has an antipathogenic effect against *Staphylococcus aureus*, *Listeria monocytogenes*, *E. coli*, and *Salmonella typhimurium*.	[107]
	L. plantarum AF1	Antifungal	*L. plantarum* AF1 prevented fungal growth in a specific food model system.	[108]
	L. curvatus BYB3	Anti-colitis	*L. curvatus* BYB3 decreased the disease activity index, colon length, and weight loss in a mouse model of DSS-induced colitis.	[110]
	L. curvatus WiKim38		*L. curvatus* WiKim38 increased the survival rate of mice with DSS-induced colitis.	[111]
	L. paracasei LS2		*L. paracasei* LS2 ameliorates inflammation and DSS-induced colitis.	[112]
	L. plantarum CJLP243		*L. plantarum* CJLP243 administration improves in some subscales of bowel function in clinical trials.	[113]
	L. plantarum MD35	Joint/bone health	*L. plantarum* MD35 improved the trabecular bone loss through regulation of osteoclast-related molecular mechanisms in an animal model.	[114]
	L. rhamnosus JY02		*L. rhamnosus* JY02 alleviated sarcopenia by reducing the abundance of pro-inflammatory cytokines and increasing of anti-inflammatory cytokines.	[115]
	L. plantarum HY7715		*L. plantarum* HY7715 increased the physical performance and skeletal muscle mass.	[116]
	L. fermentum JNU532	Improved skin health	*L. fermentum* JNU532-derived CFS inhibited melanogenesis by suppressing the expression of transcription factor MITF-mediated tyrosinase.	[117]
	L. plantarum K8		*L. plantarum* K8 lysate reduced horny layer formation and epidermal thickening in a clinical study.	[118]

Table 2. Continued.

Genus	Species	Effects	Mechanisms	References
Leuconostoc	*Leu. mesenteroides* WiKim0121, *Leu. mesenteroides* WiKim33, *Leu. mesenteroides* WiKim32	Intestinal inflammation management	These strains increased intestinal permeability by increasing the expression of tight junction-related proteins in an LPS-induced Caco-2 cell line.	[119]
	Leu. mesenteroides DRC1506	Intestinal inflammation management	*Leu. mesenteroides* DRC1506 decreased the inflammatory responses and increased tight junction factors in a DSS-induced inflammatory.	[120]
	Leu. lactis EJ-1	Anti-colitis	*Leu. lactis* EJ-1 inhibited NF-κB signaling and promoted a transition from M1 to M2 macrophages.	[121]
	Leu. mesenteroides H40	Neuroprotective	*Leu. mesenteroides* H40 enhanced BDNF expression and reduced the Bax/Bcl-2 ratio.	[122]
	Leu. mesenteroides YML003	Antiviral	*Leu. mesenteroides* YML003 showed antiviral activity against avian influenza virus infection.	[123]
	Leu. mesenteroides KDK411	Anti-hyperlipidemic	*Leu. mesenteroides* KDK411 administration increased the excretion of cholesterol.	[124]
	Leu. kimchii GJ2	Anti-hyperlipidemic	*Leu. kimchii* GJ2 can produce functional kimchi with consistent quality and cholesterol-lowering effects as a starter.	[125]
Weissella	*W. cibaria* JW15	Anti-inflammatory, immunomodulatory	*W. cibaria* JW15 suppressed the production of pro-inflammatory factors through the suppression of NF-κB via the MAPK signaling pathway. Also, this strain exhibited immunostimulatory activity in vitro and improved immune function in aged mice.	[126, 127]
	W. cibaria WIKIM28	Atopic dermatitis management	*W. cibaria* WIKIM28 increased the proportion of Treg cells and IL-10 production and improved dermatitis symptoms by reducing Th2-related allergic responses.	[128]
	W. koreensis OK1-6	Anti-obesity	*W. koreensis* OK1-6 showed anti-obesity properties by modulating the lipid metabolism.	[129]

promising treatment for reducing the body fat of individuals with obesity (BMI ≥ 25 kg/m^2) without causing significant adverse effects [93]. In a clinical study involving 40 subjects with impaired glucose tolerance, *Lb. plantarum* HAC01 significantly regulated the metabolic parameters, leading to a notable reduction in 2 h postprandial glucose and hemoglobin A1c levels compared to those in the placebo group [94].

In this context, we focused on the immunomodulatory properties of *Lactobacillus* species isolated from kimchi. In vitro studies revealed that *L. brevis* KCCM 12203P and *Lb. plantarum* 200655 activated RAW264.7 macrophage cells, inducing immune-enhancing effects without cytotoxicity [95]. *Lb. plantarum* HY7712 exhibited immunostimulatory effects in irradiated and immunosuppressed mice, enhancing their NK and Tc cell responses [96, 97]. Furthermore, *Lb. paracasei* KB28, which produces extracellular polymeric substances, was found to induce cytokine expression and activate major mitogen-activated protein kinases (MAPKs) in mouse macrophages [98]. Meanwhile, *Lb. plantarum* LB5 was shown to regulate the expression of pro- and anti-inflammatory cytokines in lipopolysaccharide (LPS)-stimulated Caco-2 cells [99]. *Lb. plantarum* IDCC 3501 cell-free supernatant (CFS) significantly reduced the mRNA expression of inflammatory markers in LPS-induced RAW264.7 macrophages [100]. *Lb. gasseri* strain NK109 alleviated cognitive impairment and depression by reducing neuroinflammation and the abundance of co-expressed NF-κB/Iba1/IL-1R cells, along with an increase in BDNF/NeuN-expressing cells within the hippocampus [101].

Numerous studies have documented the immunomodulatory effects of functional LAB in diseases related to immune imbalances, such as allergies and autoimmune diseases. Allergic rhinitis (AR) is a hypersensitive condition driven by a dominant T helper (Th) 2 response, which becomes more prevalent than the Th1 response upon re-exposure to a specific allergen. Oral administration of *Lb. plantarum* NR16 mitigated AR symptoms by inducing a Th1 immune response, thereby rebalancing the Th2/Th1 ratio by increasing the production of interferon-γ (IFN-γ) and interleukin-12 (IL-12) while reducing IL-4 secretion in mucosal lesions [102]. *Lb. plantarum* IM76 suppresses the transformation of splenic T cells into Th2 cells and promotes regulatory T cells in vitro, thereby alleviating AR and mitigating gut microbiota disturbances [103]. In a murine model, *Lb. sakei* WIKIM30 inhibited atopic dermatitis by promoting the differentiation of regulatory T cells and influencing the gut microbiota composition [104]. Additionally, the consumption of *Lb. sakei* Probio65 led to a reduction in IgE levels in the bloodstream and a decrease in IL-4 secretion by spleen cells in mice with induced atopic symptoms [105]. Moreover, numerous reports have documented the antibacterial, antifungal, and antiviral properties attributed to the *Lactobacillus* species isolated from kimchi. The strains *Lb. plantarum* WiKim83 and *Lb. plantarum* WiKim87 exhibited antimicrobial, β-galactosidase, and antioxidant activities, making them suitable as starter cultures in various fermented foods [106]. *Lb. plantarum* KU200656 exhibits an antipathogenic effect against *Staphylococcus aureus*, *Listeria monocytogenes*, *Escherichia coli*, and *Salmonella typhimurium* [107]. The antifungal compounds of *Lb. plantarum* AF1 effectively prevented fungal growth in a specific food model system [108]. *Lb. plantarum*, a common lactic acid bacterium found in kimchi, was found to protect against influenza. The oral intake of heat-killed *Lb. plantarum* delayed the time to death in a mouse model challenged with influenza A (H1N1 and H3N2 subtypes) and B viruses (Yamagata lineage) [109]. According to recent reports, kimchi contains lactobacilli that are potent Nrf2 activators capable of enhancing Nrf-2 associated antioxidant effects, which may be helpful in mitigating COVID-19 [6]. In a mouse model of 14-day dextran sulfate sodium (DSS)-induced colitis, treatment with *Lb. curvatus* BYB3 significantly reduced the disease activity index, colon length, and weight loss [110]. Oral administration of *Lb. curvatus* WiKim38 also increased the survival rate of mice with DSS-induced colitis, improving the clinical signs and histopathological severity in their colon tissues [111]. *Lb. paracasei* LS2 inhibited the development of DSS-induced experimental colitis, reducing the Th1 (IFN-γ) population while increasing the abundance of CD4(+) FOXP3(+) regulatory T (Treg) cells responsible for IL-10 production. Simultaneously, LS2 administration reduced the number of macrophages [CD11b (+) F4/80(+)] and neutrophils [CD11b(+) Gr-1(+)] in lamina propria lymphocytes, indicating its anti-inflammatory effects and amelioration of DSS-induced colitis [112]. A pilot randomized double-blind placebo-controlled trial of *Lb. plantarum* CJLP243 administration indicated potential improvements in some subscales of bowel function measures, warranting further study [113].

Recently, significant findings regarding probiotics showed that they enhance the functionality of the musculoskeletal system and skin. In an animal model, oral administration of *Lb. plantarum* MD35 notably improved the trabecular bone loss induced by ovariectomy and alleviated femoral plate growth disruption through the regulation of osteoclast-related molecular mechanisms [114]. Sarcopenia, characterized by muscle mass and strength loss due to aging, may be improved through the gut-muscle axis, indicating a potential link between gut health and muscle phenotypes following LAB treatment. *Lactobacillus rhamnosus* JY02 alleviated sarcopenia by reducing the abundance of pro-inflammatory cytokines (IL-6, IFN-γ) and increasing that of anti-inflammatory cytokines (IL-10) in DEX-treated mice [115]. *Lb. plantarum* HY7715 increased the physical performance and skeletal muscle mass of 80-week-old male aged BALB/c mice by inducing myoblast differentiation and mitochondrial biogenesis and inhibiting the sarcopenic process in skeletal muscle while recovering the microbiome composition [116]. *Lb. fermentum* JNU532-derived CFS inhibited melanogenesis in B16F10 cells by suppressing the expression of transcription factor MITF-mediated tyrosinases (TYR, TRP-1, and TRP-2) [117]. *Lb. plantarum* K8 lysate effectively reduced horny layer formation and epidermal thickening in DNCB-treated SKH-1 hairless mouse skin. A clinical study involving healthy volunteers further corroborated these findings, demonstrating improvements in skin barrier repair and function when individuals consumed candy containing *Lb. plantarum* K8 lysate [118].

Leuconostoc

The treatment of intestinal inflammation with microbes from kimchi has been well studied. In an in vitro model of the intestinal epithelium, LAB strains *Leu. mesenteroides* WiKim0121, *Leu. mesenteroides* WiKim33, and *Leu. mesenteroides* WiKim32, which are used as kimchi fermentation starters, increased intestinal permeability by increasing the expression of tight junction-related proteins in an LPS-induced Caco-2 cell line [119]. Oral administration of *Leu. mesenteroides* DRC1506 downregulated the inflammatory responses and upregulated tight junction factors in a DSS-induced inflammatory bowel disease model [120]. *Leu. lactis* EJ-1 effectively alleviated 2,4,6-trinitrobenzene sulfonic acid-induced colitis by attenuating various inflammatory responses. Oral administration of *Leu. lactis* EJ-1 also modulated immune-related factors, inhibited pro-inflammatory markers, induced anti-inflammatory IL-10 expression, and elevated M2 macrophage markers. This strain inhibits NF-κB signaling and promotes a transition from M1 to M2 macrophages, thus contributing to colitis improvement. The extracellular vesicles produced by *Leu. mesenteroides* prevented the production of NO and pro-inflammatory cytokines (IL-1β, IL-6, and TNF-α) in LPS-stimulated microglial cells by suppressing the downstream Erk/p38 signaling pathways [121]. *Leu. mesenteroides* H40 isolated from kimchi showed neuroprotective effects by enhancing brain-derived neurotrophic factor expression and reducing the Bax:Bcl-2 ratio in oxidative stress-induced SH-SY5Y cells [122]. *Leu. mesenteroides* YML003 showed antiviral activity against avian influenza virus infection both in vitro in an MDCK cell line and in vivo in specified pathogen-free chickens [123]. Previous studies have reported that LAB and kimchi reduce cholesterol levels. Oral administration of *Leu. mesenteroides* KDK411 improved hypercholesterolemia in rats by increasing the excretion of cholesterol into their feces [124]. In addition, using *Leu. kimchii* GJ2 as a fermentation starter can produce functional kimchi with consistent quality and cholesterol-lowering effects [125].

Weissella

Weissella cibaria JW15 (JW15) is known for its probiotic and antioxidant properties. Heat-killed *W. cibaria* JW15 treatment suppressed the production of pro-inflammatory factors through the suppression of NF-κB via the MAPK signaling pathway in LPS-stimulated RAW264.7 cells [126]. Furthermore, when administered orally, this strain showed immunostimulatory activity in vitro and improved immune function in aged mice. The levels of white and red blood cells, splenocytes, and cytokines such as IFN-g and IL-6 increased in JW15-treated mice compared to those in the old control mice [127]. In a murine atopic dermatitis model induced by TNBS, *W. cibaria* WIKIM28 administration increased the proportion of Treg cells and the production of IL-10, improving dermatitis symptoms by reducing Th2-related allergic responses and promoting Treg responses [128]. Kimchi fermented using the *W. koreensis* OK1-6 starter has been reported to exhibit anti-obesity properties by modulating the lipid metabolism both in vitro and in vivo [53, 129].

In summary, extensive research on various *Lactobacillus* strains and other LAB has revealed their diverse and promising health benefits for different medical conditions. These findings highlight the multifaceted potential of LAB as therapeutic and preventive agents, ranging from allergy management to gastrointestinal health, metabolic regulation, and skin care. As research in this field continues to advance, LAB are becoming increasingly recognized for their role in improving overall well-being and health maintenance.

Products Synthesized during Kimchi Fermentation

Organic Acids

A clear difference between kimchi before and after fermentation is the production of organic acids, mainly lactic acid, by LAB during fermentation. Organic acids are produced by enzymes in vegetables or microorganisms involved in fermentation. Hence, their contents vary according to the major and minor ingredients of kimchi, fermentation temperature, salt concentration, and fermentation time [130]. The non-volatile organic acids produced in cabbage kimchi include malic, fumaric, lactic, succinic, malonic, oxalic, glycolic, citric, and tartaric acids, among which lactic and succinic acids are the main compounds [131]. The lactic and succinic acid contents are higher during fermentation at high temperatures (22℃) than that at low temperatures (6℃) [1]. The volatile organic acids in kimchi include formic, acetic, propionic, butyric, valeric, caproic, and heptanoic acids, among which acetic and propionic acids are the main

Table 3. Functionalities of products synthesized during kimchi fermentation.

Products	Substances	Effects	References
Organic acids	Lactic, acetic, malic, fumaric, succinic, malonic, oxalic, glycolic, citric, tartaric, formic, acetic, propionic, butyric, valeric, caproic and heptanoic acids	Prevention of constipation	[130-132]
Prebiotic dietary fibers	Cellulose, hemicellulose, lignin and water-insoluble pectin, oligosaccharides	Anti-obesity effect Anticancer effect Lowers blood cholesterol and triglyceride levels Anti-arteriosclerosis and cardiovascular diseases	[133, 134]
Bioactive compounds	Suppression of β-glucosidase, β-glucuronidase, nitroreductase, 7-α-dehydrogenase, azoreductase Vitamin C, vitamin B, β-carotene, phenolic compounds, chlorophyll, β-sitosterol, polyunsaturated fatty acid derivatives, glucosinolates, isothiocyanates, indoles, allyls	Antioxidant Anti-aging Antimutagenic effects	[138-141]
Bacteriocins	Antimicrobial peptides, nisin, lantibiotics	Antibacterial activity	[142]
Exopolysaccharides (EPSs)	Levan	Anticancer effects Immune-enhancing Antiulcer Cholesterol-lowering effects	[157, 158]
γ-aminobutyric acid	GABA	Reduction of blood pressure, suppression of blood cholesterol and triglyceride levels, improvement of blood flow in the brain, pain alleviation, antioxidant effects, diuretic effects, tranquilizing effects	[160, 177]

compounds. Organic acids are key metabolites in kimchi, and their by-product CO_2 is the primary component responsible for the taste of kimchi. Acetic acid and CO_2 contents were found to be higher in kimchi fermented at a low temperature with a low salt concentration than in kimchi fermented at a high temperature with a high salt concentration. The taste of kimchi is enhanced by low-temperature fermentation, as these compounds are produced in abundance by the main fermentation species *Leu. mesenteroides*. Together with dietary fibers, organic acids produced by LAB facilitate peristalsis and increase the volume of intestinal contents, which plays an important role in preventing constipation as potential laxative agents [132].

Prebiotic dietary fibers

Dietary fibers in foods are carbohydrates that are not digested by enzymes for absorption in the body. Most dietary fibers remain almost fully undigested as they pass through the gastric and small intestinal tracts to reach the large intestine, where they are partially decomposed for absorption by intestinal microorganisms. The dietary fibers obtained from kimchi include cellulose, hemicellulose, lignin, and water-insoluble pectin [133]. The well-known functions of dietary fibers include waste removal from the body, intestinal peristalsis facilitation to prevent constipation, and appetite reduction based on high water content, thus exhibiting an anti-obesity effect. In the large intestine, the dietary fibers in kimchi undergo fermentation by LAB to produce short-chain fatty acids, which are known to induce apoptosis, a cell death mechanism related to anticancer effects. Additionally, dietary fibers can absorb lipids to lower blood cholesterol through the excretion of bile acid in stool, and they play a significant role in preventing cardiovascular diseases [134].

Bioactive compounds

LAB suppress the synthesis of enzymes with harmful effects in the intestines, such as β-glucosidase, β-glucuronidase, nitroreductase, 7-α-dehydrogenase, and azoreductase. The activities of harmful enzymes that convert procarcinogens into carcinogens in the intestine are significantly reduced by kimchi, and the intestinal pH is lowered (as the pH of feces decreases), which plays an important role in the prevention of colorectal cancer. C3H/10T1/2 cells are mouse embryonic cells that form foci upon exposure to carcinogens. These foci develop into types II and III, which are known to cause 50% and 80% of tumorigenesis in C3H mice, respectively. Carcinogenesis in C3H mice was remarkably suppressed by kimchi methanol extract, which significantly reduced the numbers of both types II and III foci (92% inhibition when 200 μg was used). In vivo, a wing hair spot test using *Drosophila melanogaster* showed that kimchi extracts inhibited somatic mutations [135]. In a micronucleus test using mouse peripheral blood, kimchi extracts were also shown to have anticancer effects, such as the inhibition of micronucleus induction in immature reticulocytes in the presence of carcinogens [136]. Kimchi extracts inhibited the proliferation of human cancer cells such as gastric cancer cell line AGS, colon cancer cell line HT-29, osteosarcoma cell line MG63, hematoma cell line HL-60, and hepatoma cell line Hep 3B. Kimchi fractions also inhibited DNA synthesis in cancer cells. Furthermore, they are thought to increase the activity of NK cells and lead to their anticancer effects. In a study investigating the mechanisms underlying the anticancer effects of kimchi, the dichloromethane fraction of cabbage kimchi was able to induce apoptosis of hematoma HL-60 cells, thus reducing the number of cancer cells [137].

Vegetables in kimchi are sources of vitamin C and carotene, whereas different types of vitamin B are abundant in seafood, such as salted fish. Notably, red pepper powder is a key source of vitamin C and carotene, and oyster is the main source of vitamin B. In an experiment using a senescence-accelerated mouse model, kimchi intake led to reduced blood lipid levels, with lower HMG-CoA reductase activity compared to that in the control, exerting an anti-aging effect by lowering lipid levels and promoting the antioxidant defense system [138]. Kimchi has a neutralizing effect on H_2O_2 toxicity in keratinocytes, the main epidermal cells, following exposure to H_2O_2, which artificially induces oxidative stimulus. An inhibitory effect against oxidative stress was detected after long-term administration of kimchi. These effects were more prominent with adequately fermented kimchi. When oxidative stress was induced in hypodermal fibroblasts, which are hypodermal cells, kimchi showed an outstanding effect in alleviating skin aging [139].

Anticancer effects of kimchi can be attributed to its contents of β-sitosterol, polyunsaturated fatty acid derivatives, glucosinolates, isothiocyanates, indoles, allyls, and LAB. In vitro, the Ames test and SOS chromotest revealed that kimchi has an inhibitory effect on mutagenesis mediated by carcinogens [140]. The LAB produced during kimchi fermentation also demonstrated antimutagenic effects; among them, the strongest effect was exhibited by *L. mesenteroides*. A higher antimutagenic effect of LAB was found in the cell wall fractions than in the cytosolic fractions, which is thought to be related to the glycopeptides in the cell wall fractions [141].

Bacteriocins

LAB exert antibacterial effects on various putrefactive and pathogenic bacteria owing to the several characteristic metabolites of LAB, including lactic acid and acetic acid, and compounds such as hydrogen peroxide and diacetyl [142]. In addition, the bacteriocins produced by LAB, which are characteristic proteins or protein-based compounds, exhibit bactericidal activity against morphologically and phylogenetically similar strains [143, 144]. They puncture the cell membranes of pathogenic bacteria, leading to cell death. They use a mechanism distinct from that of conventional antibiotics for bacterial growth inhibition, rendering them a potential candidate for next-generation antibiotics. Additionally, LAB-bacteriocins hold high commercial value as natural preservatives applicable across all sectors of the food production industry.

The fermentation of kimchi involves several LAB species, with *Leu. mesenteroides* as the dominant species in the early stage, creating an anaerobic condition as CO_2 production increases, whereas in the mid-stage, *W. cibaria* or *W. koreensis* becomes dominant, gradually lowering the pH. Species of the genus *Lactobacillus* exert their antibacterial effects as the pH falls below 4.0 at the end of fermentation. *Lb. plantarum, Lb. sakei*, and *Lb. brevis* are the predominant LAB species in kimchi, and the bacteriocins produced by them have been identified in previous studies. *Lb. sakei* P3-1 exhibited antibacterial activity against *Lb. plantarum* and *L. monocytogenes*. Researchers named the compound responsible for this antibacterial activity “bacteriocin” because it loses its activity after the culture supernatant is treated with the proteinase K enzyme [145]. *Lb. sakei* B16 produces bacteriocin with antibacterial activity against several gram-positive bacteria and, surprisingly, against gram-negative bacteria such as *S. typhimurium* and *E. coli* KCTC 1467 as well. The bacteriocin gene cluster was amplified using polymerase chain reaction (PCR) to investigate the similarity between this bacteriocin and sakacin P, and the results showed that their gene clusters were identical [146]. Bacteriocin produced by *Lb. paraplantarum* C7 was purified through diethylaminoethyl-sephacel column chromatography and C18 reverse-phase high-performance liquid chromatography to determine a 28-amino acid sequence. Based on this amino acid sequence, degenerate PCR primers were prepared to study the structural genes of this bacteriocin, which was identified as a novel type of class II bacteriocin with a Gly-Gly motif. The gene cluster responsible for producing this bacteriocin was shown to be located in chromosomal DNA and not in the plasmid [147].

Leuconostoc sp. J2 exhibited antibacterial activity against *S. aureus*. The molecular weight of the bacteriocin produced by this strain was analyzed using tricine–SDS-PAGE and ranged from 2.5 to 3.5 kDa [148]. The bacteriocin produced by *Leu. mesenteroides* B7 exhibited antibacterial activity against *Lb. plantarum* and had a uniquely high pH and thermal stability, retaining its antibacterial activity even at pH levels of 2.5–9.5 and under heat treatment ranging from 4–120℃. The molecular weight was approximately 3.5 kDa. Notably, the production of this bacteriocin increased when the strain was co-cultured with *Lb. plantarum* KFRI 464, the indicator strain for bacteriocin, and the factor that induced bacteriocin production was reported to be present within the susceptible strain [149]. Similarly, kimchicin GJ7, a bacteriocin produced by the strain *Leu. citreum* GJ7, also isolated from kimchi, displayed facilitated production in the presence of *Lb. plantarum* KFRI 464 [150]. *Pediococcus pentosaceus* K23-2 exhibited antibacterial activity against *L. monocytogenes* and *S. aureus*, and the associated bacteriocin (pediocin K23-2) was characterized. This bacteriocin remained active under different pH levels, heat treatments, and exposure to organic solvents. The purified bacteriocin belonged to class IIa with a molecular weight of approximately 5.0 kDa [151]. Among the isolated bacteriocins, only paraplantaricin C7, produced by *Lb. paraplantarum* C7, was reported as a novel class of bacteriocin, whereas most others were similar or identical to nisin, pediocin, or sakacin. Together, these findings indicate the presence of various bacteriocin-producing strains in kimchi and the potential for the identification new strains of bacteriocin-producing LAB.

Exopolysaccharides

Exopolysaccharides (EPSs) are polysaccharides constituting the cell walls of microorganisms, forming capsules around the walls or accumulating as mucilage on the wall exterior during fermentation [152]. Being abundantly produced by microorganisms, EPSs can be readily collected and thus have high industrial potential [153]. Two broad types of EPSs are produced by LAB: homopolysaccharides and heteropolysaccharides.

Homopolysaccharides consist of a single form of saccharide, including dextran from *Leu. mesenteroides* subsp. *mesenteroides* and subsp. *dextranicum* and alternan from *Leu. mesenteroides* [154, 155]. Heteropolysaccharides consist of two or more monosaccharides in varying proportions and have lower productivity than homopolysaccharides. They are primarily produced by *Lc. lactis* subsp. *lactis*, *Lb. casei*, and *Lb. sakei*. Although they protect microorganisms from external conditions, such as dehydration, osmotic stress, antibiotics, and toxic chemicals, they are not utilized as an energy source [156]. EPSs have been recently highlighted as bioactive materials with industrial potential rather than simple functional materials. *Lactobacillus*-derived EPSs have been shown to exhibit anticancer, immune-enhancing, antiulcer, and cholesterol-lowering effects [157]. Further, the EPSs produced by kimchi-isolated LAB were found to be useful as functional materials acting as self-defense molecules against extreme conditions [158].

γ-aminobutyric acid

γ-aminobutyric acid (GABA) is a ubiquitous non-protein amino acid and a critical component of the central nervous system, including the brain and spinal fluid; it is also the main inhibitory neurotransmitter [159]. In the human body, GABA improves blood flow, and thereby the oxygen supply, to the brain. Therefore, GABA is often referred to as a “brain food” that enhances brain metabolism, and GABA deficiency can lead to dementia. It also plays various bioactive roles, including the reduction of blood pressure, suppression of blood cholesterol and triglyceride levels, improvement of blood flow in the brain, pain alleviation, antioxidant effects, diuretic effects, and tranquilizing effects in insomnia, depression, and anxiety [160]. GABA is produced via the irreversible decarboxylation of glutamic acid by L-glutamic acid decarboxylase (GAD) [161]. The

GAD in the cytosol of plant cells can rapidly produce GABA in response to external stress [162]. GABA-producing LAB strains have been isolated, identified, and characterized [163], and the characteristics of these strains have been modified to enhance GABA production in kimchi [164]. A study measuring GABA content in cabbage kimchi reported the highest GABA content after 14 d of storage and fermentation. During this period, the initial GABA content of approximately 7.7 mg/100 g of cabbage kimchi increased to nearly 20.4 mg [165]. Another study analyzing the GABA content in cabbage kimchi based on storage time and examining the correlation between L-glutamic acid and GABA reported that the initial GABA content after kimchi production was 72.43 μM/100 g fresh weight (fw), which increased to 229.06 μM/100 g fw toward the end of fermentation. This finding indicates an upward trend with an increase in the fermentation period, with the rapid production of GABA in the initial stage attributed to the activity of GAD and L-glutamic acid [166]. LAB represent a key group of microorganisms that produce GABA, owing to the GAD system in the members of the genus *Lactobacillus* [167–170]. GABA-producing LAB have been isolated from various fermented foods, and their use in the development of functional fermented foods have investigated in various studies. Strains of LAB with high GABA productivity were isolated from aged kimchi for use in the fermentation of kimchi, and GABA-containing functional foods have been produced using GABA-producing LAB as a starter [167, 171, 172]. Recently, animal and clinical studies have reported anti-depression and antianxiety effects in addition to stress relief effects of GABA-producing kimchi LAB. As the association between LAB and GABA is further established, an increasing number of studies are examining correlations between LAB and GABA in terms of brain function [173]. A culture extract of GABA-producing LAB isolated from kimchi had a neuroprotective effect against neurotoxin-induced apoptosis. The association between gut microflora and brain functions has long been explored [174]. Naseribafrouei *et al.* studied the correlation between clinical depression and the human fecal microbiome. They reported the similarity between GABA and valeric acid, the final metabolite of an *Oscillibacter* strain expressed in low levels in the feces of patients with depression, predicting a significant correlation with depression [175]. Janik *et al.* reported that the levels of various neurotransmitters, including GABA, glutamate, and glutamine, increased during *Lb. rhamnosus* JB-1 treatment in mice, and the levels of glutamate and glutamine continued to increase after treatment discontinuation. This finding suggests the role of neurotransmitters produced by LAB in the activity and functions of specific brain areas associated with anxiety and depression [176]. Kochalska *et al.* monitored the brain response in rats exposed to stress and reported that the post-stress levels of neurotransmitters, including GABA, glutamate, and glutamine, returned to pre-stress levels after *Lb. rhamnosus* JB-1 treatment [177].

Conclusion and Future Directions

Kimchi is a well-known ethnic food generally recognized as a healthy food worldwide and an important iconic food in Korean culture. The variety of ingredients, fermentation time, and salt concentration used for kimchi determine its characteristics, functionality, and microbial communities.

A systemic analysis of recently published research articles showed that it has a considerable role in cancer and obesity protection as an anti-mutagenic or anti-obesity agent. Other important functional activities include antimicrobial, antioxidant, immunomodulatory, cardiovascular, anti-hyperlipidemic, anti-inflammatory, colitis preventing, and others. In addition, Randomized controlled trials (RCTs) on kimchi have reported health functional effects such as blood lipid improvement, gut health, and anti-obesity effects [178–180]. As a result of clinical trials involving the consumption of kimchi, the health benefits of kimchi were confirmed through literatures showing functional properties.

The chemical investigation of kimchi revealed that phytochemicals, *Lactobacillus*, and metabolites are the predominant principal actors and are responsible for various health benefits. In particular, phytochemicals from ingredients and LAB from the fermentation of kimchi, which are Nrf2 interacting factors, alleviate COVID-19 mortality by downregulating the ACE–angiotensin-II–AT1R axis pathway.

Future studies are necessary to evaluate the possible health-promoting activity of novel LAB or active compounds used for the treatment or prevention of various diseases using advanced bioinformatics and epidemiologic techniques. Studies focusing on the safety or undesirable effects of kimchi consumption are especially warranted. Thus, further pre-clinical and clinical studies are necessary to explore the potential health benefits of kimchi.

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Conflict of Interest

The authors have no financial conflicts of interest to declare.

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