Bioconversion, health benefits, and application of ginseng and red ginseng in dairy products

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Abstract Ginseng and red ginseng are popular as functional foods in Asian countries such as Korea, Japan, and China. They possess various pharmacologic effects, including antioxidant, anti-inflammatory, anti-cancer, anti-obesity, and anti-viral activities. Ginsenosides are a class of pharmacologically active components in ginseng and red ginseng. Major ginsenosides are converted to minor ginsenosides, which have better bioavailability and cellular uptake, by microorganisms and enzymes. Studies have shown that ginseng and red ginseng can affect the physicochemical and sensory properties, ginsenosides content, and functional properties of dairy products. In addition, lactic acid bacteria in dairy products can convert into minor ginsenosides and ginseng and red ginseng improve functionality of products. This review will discuss the characteristics of ginseng and red ginseng, and their bioconversion, functionality, and application in dairy products.

Keywords Ginseng · Red ginseng · Ginsenoside · Bioconversion · Dairy product

Introduction

The consumption of healthy foods has risen following an increase in average income and many consumers purchase various functional products including vitamins, probiotics, and ginseng-related products [1]. Ginseng and red ginseng are popular functional foods in Korea. Especially, sales of red ginseng have risen steadily [1].

In Korea, ginseng is commercially distributed as four types, namely; fresh ginseng, white ginseng, *Taekuksam*, and red ginseng, and these are manufactured using different methods [2]. Fresh ginseng has high water content and coexists with soil microorganisms [3]. White ginseng is produced by sun-drying fresh ginseng [4]. *Taekuksam* is produced by blanching in water and drying [2]. Red ginseng is produced by repeatedly steaming and air-drying fresh ginseng [5]. Four types of ginseng were manufactured to use ginseng root. White ginseng was referred to as ginseng in oriental medicine books and red ginseng has a long history of production development and export to other countries [6]. Ginseng and red ginseng are delivered in diverse forms including natural root, powder, tablet, tea, extract, and beverage [7, 8]. The major companies that manufacture red ginseng products have emphasized functionality and manufacture fermented red ginseng for the satisfaction of consumer needs and the expansion of ginseng sales in the domestic and foreign functional food markets [9, 10].

According to a report by the Ministry of Agriculture, Food and Rural Affairs, the production of milk has remained steady in recent years, while the production and consumption of milk powder, fermented milk, and soy milk have increased and the domestic milk powder were exported to China [11]. Dairy companies have produced diverse functional dairy products including organic,

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reduced fat, and artificial-additives-free, reduced sodium and sugar, lactose-free, probiotics-supplemented, and nutrient-, calcium-, or protein-fortified products [11, 12]. This review aims to introduce the characteristics of ginseng and red ginseng and explore their potential applications in dairy products for Korean consumers.

Ginseng and red ginseng

Characteristics

The term ginseng refers to the dried root of several plant species in the genus *Panax* (family Araliaceae) that have a history of medicinal use spanning over 5000 years [13]. The ginseng species are *Panax ginseng*, *Panax quinquefolius*, *Panax notoginseng*, and *Panax japonicus* [13]. *P. ginseng*, commonly called Korean ginseng, is an important herb in East Asia. This species has a short root and possesses antioxidant, anticarcinogenic, antidiabetic, and anti-stress effects [14]. *P. quinquefolius*, commonly called American ginseng, is used in North America and is resistant to spoilage. It has antioxidative, antiulceric, and neuroprotective effects [14]. *P. notoginseng*, commonly called Chinese ginseng, is valuable in Japan and southern areas of China, and may prevent rheumatoid arthritis and decrease cholesterol [14]. *P. japonicus* is a traditional medicinal herb in the southwest region of China, and its use was recorded in a book of traditional Chinese medicine published in 1765. *P. japonicus* may help to prevent a decrease in haematopoietic activity and inhibit tumor growth [15]. The chemical constituents of ginseng are carbohydrates, amino acids, minerals, lipids, proteins, and bioactive components such as ginsenosides, acidic polysaccharides, and polyacetylenes [14]. Polyacetylenes are unsaturated triple-bonded polyalcohols that represent the main nonpolar active constituents of ginseng [16]. Polyacetylenes have lipophilic properties and include panaxynol, panaxydol, panaxydiol, panaxytriol, panaxacol, panaxyne epoxide, and ginsenyne A-K [16]. They have anticancer and antioxidant effects that are attributed panaxydol, panaxynol, and panaxytriol [17]. The acidic polysaccharides of ginseng comprise of galacturonic acid, glucuronic acid and manuronic acid, which have molecular weights over 15,000 Da [18, 19]. Acidic polysaccharides have pharmaceutical activities including anticoagulating and anticancer effects [19, 20].

Red ginseng was reported in the Annals of King Jeongjo, and the method for processing red ginseng was introduced in Goryeo Dogyeong [21]. An overview of the process is as follows; fresh ginseng is selected, the dirt is removed, and the root is washed with clean water. The washed ginseng is steamed for 1–3 h at 90–98 °C. Then it

is dried with hot air and laid in the sun until its moisture content drops to between 15 and 18% [21]. The production process, which includes significant heating, increases the amounts of total sugar, reducing sugar, and polyphenols in red ginseng [22]. The amounts of arginine-fructose-glucose and arginine-fructose increase during the steaming and drying processes. In addition, the color and maltol content of red ginseng are changed by the steaming process [23]. The bioactive components such as ginsenosides, acidic polysaccharides, and polyacetylenes changed during the production process of red ginseng. The amount of acidic polysaccharides in red ginseng is three times higher than that in white ginseng because of the degradation of sugar components [21]. The ginsenoside content in red ginseng was increased during the production process especially, that of ginsenosides Rh₁, Rg₂, Rg₃, Rk₃, Rh₄, Rk₁, and Rg₅ because of deglycosylation at the C-20 position [23].

Health functionality

Previous studies have indicated that ginseng and red ginseng may contribute to the prevention of diseases through diverse mechanisms such as antiobesity, antioxidative, anti-inflammatory, anti-stress, antiviral, and anticancer effects.

Ginseng increased the plasma adiponectin level and inhibited fat accumulation and adipogenesis in 3T3-L1 cells [24]. Ginseng exhibited electron-donating activity and inhibited nitric oxide production and NF-κB activity [25]. Ginseng alleviated the degradation of immune organs in the rat because it reduced the secretion of corticosterone [26]. Ginseng increased the antioxidant enzyme superoxide dismutase in the skin and liver, and reduced acanthosis and tumor nets [27].

Red ginseng inhibited the growth of lung carcinoma cells, reduced the activities of rennin and angiotensin-converting enzyme, decreased the angiotensin II levels, activated nitric oxide production, and caused a reduction of arterial blood pressure [28, 29]. Red ginseng inhibited the synthesis of cholesterol and HMG-CoA reductase activity [30]. It reduced behavioral impairment, protected dopaminergic neurons, prevented oxidative stress-induced apoptosis, and inhibited apoptosis via the upregulation of PI3 K/Akt signals in brain cells under oxidative stress [31, 32]. Red ginseng ameliorated the decline of learning potential and memory retention in aged mice by showing that red ginseng extract improved the activities of the antioxidant enzyme Nrf2 and HO-1 [33]. Red ginseng was effective against diverse virus types including influenza virus and norovirus [5]. Red ginseng also acted as a mucosal adjuvant against influenza virus A/PR8 during viral infection and improved H1N1 vaccine efficacy by increasing anti-influenza virus A-specific IgG titers and

survival rates [5]. Pretreatment with red ginseng and ginsenosides induced antiviral protein in feline calicivirus-infected Crandell-Reese feline kidney [5]. Red ginseng inhibited obesity, adipocyte hypertrophy, and adipose inflammation in high fat diet-fed ovariectomized mice [34]. It has been demonstrated that the pharmaceutical effects of ginseng and red ginseng can be attributed to their ginsenoside content.

Ginsenosides

Analysis and classification

Ginsenosides are characteristic components of ginseng that have been reported to show pharmaceutical effect, and more than 50 ginsenosides have been identified using methods including thin layer chromatography (TLC), high performance liquid chromatography (HPLC), gas chromatography (GC), capillary electrophoresis, near infrared spectroscopy, and enzyme immunoassay [21, 35]. TLC is a simple and easy-to-operate analytical technique, and HPLC is the most common analytical method, so TLC and HPLC are usually used to together identify ginsenosides [36, 37].

Ginsenosides are categorized based upon the positions of their hydroxyl groups and/or double bonds [38]. Ginsenosides are classified into two major types, dammarane and oleanane. The dammarane-type ginsenosides are divided into three groups: protopanaxadiol (PPD), protopanaxatriol (PPT), and ocotillol types. The oleanane group contains oleanolic acid type [39]. The PPD type consists of an aglycone with a dammarane skeleton and sugar moieties attached to the β -OH at C-3 and/or C-20 and includes ginsenosides Ra₁, Ra₂, Ra₃, Rb₁, Rb₂, Rb₃, Rc, Rd, Rg₃, Rh₂, F₂, and compound K [39]. The PPT type consists of an aglycone with a dammarane skeleton and sugar moieties attached to the α -OH at C-6 and/or β -OH at C-20 and includes ginsenoside Re, Rf, Rg₁, Rg₂, Rh₁, and F₁ [39]. The ocotillol type has an epoxy ring at C-20 and includes majonoside R₂ and pseudoginsenoside F₁₁. The oleanane group consists of a pentacyclic structure with aglycone oleanolic acid and includes only ginsenoside R_O [39].

Bioconversion using enzymes and microorganisms

Minor ginsenosides have more pharmaceutical activity than major ginsenosides because of their smaller size, higher bioavailability, and better permeability across cell membranes [40]. Therefore, several research groups have studied the deglycosylation of ginsenosides. The methods for converting major ginsenosides to minor ginsenosides

are mild acid or alkali hydrolysis, heating, microbial, and enzymatic action [40–42]. Several studies have reported that major ginsenosides can be deglycosylated by digestive enzymes or microorganisms (Table 1). Such biotransformation processes have the advantages of high specificity and selectivity, and a low environmental impact [40].

Enzymatic bioconversion

Enzymatic transformation is one of the various methods used for converting major ginsenosides into minor ginsenosides. β -Glucosidase, β -glycosidase, pectinase, cellulase, and naringinase are used commercially for this purpose [42–45]. β -Glucosidase and β -glycosidase converted ginsenoside Rb₁ to ginsenoside compound K, and pectinase reacted with ginseng to produce ginsenoside compound K [42, 43]. Cellulase generated ginsenoside Rg₃ in white ginseng extract, and cellulase mixed with naringinase transformed ginsenosides Re and Rg₁ into ginsenoside F₁ [44, 45].

Microbial bioconversion

Microorganisms produce various enzymes including β -glucosidase, β -glycosidase, and β -galactosidase for the transformation of ginsenosides [42, 43]. Lactic acid bacteria including *Bifidobacterium bifidum*, *B. longum*, *Bifidobacterium* sp., *Leuconostoc paramesenteroides*, *Leu. mesenteroides* subsp. *mesenteroides*, *Lactobacillus delbrueckii*, *L. plantarum*, *L. delbrueckii* subsp. *bulgaricus*, *L. fermentum*, *L. delbrueckii* subsp. *lactis*, *L. rhamnosus*, and *Lactococcus lactis* participated in biotransformation and produced β -glucosidase [46–51]. Lactic acid bacteria convert major ginsenosides Rb₁ or Rd into minor ginsenosides Rg₃, F₂, Rh₂, and compound K (Fig. 1). Fungi also produced β -glucosidase and transformed major ginsenosides into minor ginsenosides [52–57]. *Aspergillus* sp. hydrolyzed PPD type-ginsenosides, especially, *A. usarii*, *A. niger*, and *A. oryzae* and produced ginsenosides Rg₃, compound K, and small sized ginsenosides [52–57]. *Paecilomyces bainier* produced β -glucosidase and hydrolyzed ginsenoside Rb₁ into ginsenosides Rd, F₂, and compound K [58–60].

Improved health functionality through bioconversion

Ginsenosides are the main bioactive constituents in ginseng and have diverse pharmaceutical effects (Table 2). Ginsenoside Rb₁, of the PPD type, has been found to exert anti-apoptotic effect via the stimulation of estrogen receptor, appeared to cause the downregulation of pro-inflammatory cytokines, and had a protective effect against

Table 1 The pathway of ginsenosides by enzymatic and microbial bioconversion

Materials	Pathway of bioconversion (References)	Materials	Pathway of bioconversion (References)
<i>Enzyme</i>			
β -Glucosidase	Rb ₁ → Rd → compound K [42]	Cellulase 12T	Rb ₁ → Rd → Rg ₃ [44]
β -Glycosidase	Rb ₁ or Rb ₂ → Rd → F ₂ → compound K [43]	Cellulase KN	Re → Rg ₁ → F ₁ [45]
	Rc → compound Mc → compound K [43]		
<i>Microorganism</i>			
<i>Bifidobacterium</i> sp. Int57	Rb ₂ , Rc → Rd [46]	<i>A. usamii</i> KCTC 6954	Rb ₁ → Rd → F ₂ → compound K [53]
<i>Bifidobacterium</i> sp. SH5	Rb ₁ , Rb ₂ , Rc → Rd [46]	<i>A. niger</i> KCCM 11239	Rb ₁ → Rd → Rg ₃ [54, 55]
<i>Leu. paramesenteroides</i> ^a	Rb ₁ → Rd → F ₂ → Rh ₂ [46]	<i>A. niger</i> g.848	Rb ₁ → Rd → F ₂ → compound K [56]
<i>L. plantarum</i>	Rb ₁ → Rd → Rg ₃ [47]	<i>P. bainier</i>	Rb ₁ → Rd → F ₂ → compound K [58]
<i>Leu. mesenteroides</i> DC102	Rb ₁ → gypenoside XVII/ Rd → F ₂ → compound K [49]	<i>P. bainier</i> sp. 229	Rb ₁ → gypenoside XYII/ Rd → F ₂ → compound K [59]
<i>L. rhamnosus</i> GG	Rb ₁ → Rd [50]		Rb ₁ → Rd → Rg ₃ → Rh ₂ [59]
<i>Lc. lactis</i>	Rb ₁ → Rd → F ₂ [51]	<i>P. bainier</i> 229-7	Rb ₁ → Rd [60]

^a *L.*, *Lactobacillus*; *Lc.*, *Lactococcus*; *Leu.*, *Leuconostoc*; *A.*, *Aspergillus*; *P.*, *Paecilomyces*

Fig. 1 The bioconversion pathway of ginsenosides by starter cultures in dairy products [40, 46, 49–51]. 1 *Bifidobacterium* sp.; 2 *Leuconostoc mesenteroides*; 3 *Lactobacillus rhamnosus*; 4 *Lactococcus lactis*

Table 2 The main functionalities of ginsenosides

Ginsenoside	Functionality	Reference
Protopanaxadiol (PPD)-type	Rb ₁	Anti-apoptotic effect, anti-inflammatory effect, antioxidant effect [61]
	Rb ₂	Anti-osteoporosis effect [62]
	Rb ₃	Effect against myocardial injury and heart function impairment [63]
	Rc	Anti-inflammatory effect [64]
	Rd	Neuroprotective effect, anti-inflammatory effect [65, 66]
	Rg ₃	Anti-cancer effect, anti-melanogenic effect [67–69]
	Rh ₂	Anti-obesity effect, anti-inflammatory effect, anti-cancer effect, anti-viral effect [70–73]
	F ₂	Anti-cancer effect, anti-obesity effect, inhibition effect of skin inflammation [74–76]
	Compound K	Anti-allergic effect, anti-diabetic effect, anti-aging effect [42]
Protopanaxatriol (PPT)-type	Re	Anti-arrhythmic effect, reduction of insulin resistance [77, 78]
	Rf	Inhibition of tolerance to analgesia [79]
	Rg ₁	Anti-depressant effect, anti-inflammatory effect, neuroprotective effect, protection against sepsis-associated encephalopathy [80–83]
	Rg ₂	Neuroprotective effect, anti-apoptosis effect, protective effect against UV-B [84–86]
	Rh ₁	Inhibitory effect of atopic dermatitis, anti-metastatic effect [87, 88]
	F ₁	Protective effect against UV-B [89]
Ocotillol type	Pseudoginsenoside F ₁₁	Protective effect against neurotoxicity, anti-amnesic effect, anti-neuroinflammatory effect [90–92]
Oleanolic acid type	R _o	anti-inflammatory effect, anti-apoptosis effect [93, 94]

oxidative stress induced by tetra-butylhydroperoxide [61]. Ginsenoside Rb₂ has an anti-osteoporosis effect as shown by its ability to protect osteoblastic MC3T3-E1 cells against cytotoxicity and osteoblast dysfunction induced by H₂O₂ [62]. Ginsenoside Rb₃ inhibited the isoproterenol-induced increase in malondialdehyde levels, increased the activities of creatine kinase and lactate dehydrogenase, and attenuated myocardial ischemia injury induced by isoproterenol and impaired heart function [63]. Ginsenoside Rc reduced the inflammatory response by suppressing the TBK1/IRF-3 and p38/ATF-2 pathways [64]. Ginsenoside Rd exhibited a neuroprotective effect and a protective effect against from lipid peroxidation, and increased the activities of antioxidant enzymes [65, 66]. Ginsenoside Rg₃ inhibited the growth of colon cancer and breast cancer cell, and suppressed melanin synthesis and tyrosinase activity [67–69]. Ginsenoside Rh₂ had anti-obesity, anti-inflammatory, anticancer, and antiviral activities [70–73]. Ginsenoside F₂ induced the apoptosis in breast cancer stem cells, inhibited adipogenesis process, and suppressed IL-17A production [74–76]. Ginsenoside compound K inhibited histamine release, enhanced insulin secretion, increased the level of type I procollagen and decreased MMP-1 activity [42].

Ginsenoside Re of the PPT type exhibited an antiarrhythmic effect and insulin sensitivity, and promoted the uptake and disposal of glucose in 3T3-L1 adipocytes

[77, 78]. Ginsenoside Rf enhanced U50-induced analgesia and inhibited tolerance to analgesia [79]. Ginsenoside Rg₁ ameliorated depression-like behavior, showed neuroprotective action, alleviated hepatic histological abnormality in mice with CCl₄-induced liver injury, and reduced inflammatory mediators. It also protected dopaminergic neurons from 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine-induced toxicity and brain damage from sepsis by inhibiting cerebral inflammation and neuron loss in the hippocampus [80–83]. Ginsenoside Rg₂ had a protective effect against glutamate-induced neuronal injury and the formation of Aβ in PC12 cells, protected memory functions against impairment induced by cerebral ischemia–reperfusion and the neuronal apoptosis, and attenuated the UV-B-induced promatrix metalloproteinase-2 gelatinolytic activity and protein level [84–86]. Ginsenoside Rh₁ inhibited the infiltration of inflammatory cells into skin lesions and MMP-1 transcriptional activity and decreased the concentrations of IgE and IL-6 in serum, expression and stability of Ap-1 dimer, c-Fos, and c-Jun by inhibiting the activation of JNK and ERK 1/2 in HepG2 cells [87, 88]. Ginsenoside F₁ had a protective effect against UVB-induced apoptosis in HaCaT cells [89].

Pseudoginsenoside F₁₁, an ocotillol type-ginsenosides, antagonized methamphetamine-induced neurotoxicity in mice and shortened the prolonged latency induced by methamphetamine [90]. Pseudoginsenoside F₁₁ rescued the

cognitive impairment in mice treated with $\text{A}\beta_{1-42}$, and inhibited the neuroinflammation induced by lipopolysaccharides (LPS) in N9 microglia via inhibition of TLR4-mediated TAK1/IKK/NF- κ B, MAPK, and PI3 K/Akt pathways [91, 92].

Ginsenoside Ro, the oleanolic acid type, downregulated inflammatory cytokines including nitric oxide synthase and cyclooxygenase-2 that are induced by LPS, inhibited caspase 3 activity, and alleviated IL-1 β -induced inflammation and matrix degradation [93, 94].

Application in dairy products

Milk fortified with ginseng and red ginseng

Milk of cows, buffaloes, goats, and sheep is used for human consumption directly and as various dairy products [95]. Milk consists of water, lactose, proteins, lipids, organic acids, minerals, vitamins, salts (Ca, Mg, K, and Na), and enzymes (lysozyme, oxidoreductase, phosphatase, lipolytic enzyme, and proteinase) [95, 96]. Raw milk is processed via several steps including storage, cleaning, homogenization, fat standardization, heat treatment, cooling, and filling/packing [96].

Milk products fortified with ginseng or red ginseng have been developed and information about them is available through published research, conference abstracts, and patent applications. A method for extracting saponin from ginseng-supplemented milk has been optimized as a quantitative method of indicating the presence of ginseng in milk [97]. The optimized temperature, time, and cooling temperature were 86 °C, 2 h 50 min, and 4 °C, respectively, for the extraction of total saponin from ginseng milk [97]. A milk beverage fortified with 0.1% American ginseng extract was evaluated for its ginsenoside content using HPLC and sensory tests including a quantitative descriptive analysis and a consumer study [98]. Ginsenosides Rb₁, Rb₂, Rc, Rd, Re, and Rg₁ were detected in the American ginseng-supplemented milk beverage [98]. Sensory tests demonstrated that the American ginseng affected flavor attributes, increased the bitterness and metallic taste of the product, and changed its color [98]. Those findings demonstrated that the dairy industry could potentially develop ginseng milk, using sensory tests to achieve consumer satisfaction.

Red ginseng-supplemented milk products have been made with red ginseng alone or red ginseng mixed with lactoferrin, cyclodextrin, and black garlic [99–102]. Bae et al. [99] demonstrated the possibility of red ginseng milk through color, stability, and consumer acceptability. Park et al. [100] developed milk fortified with red ginseng extract (0.3–1.5%) and cyclodextrin (α , β , and γ).

Cyclodextrin, a banana extract, and a flavoring agent were used to reduce the bitterness of red ginseng in accordance with the preferences the children, the elderly, and the infirm [100]. Chung et al. [101] made a red ginseng milk beverage fortified with black garlic extract. They added black garlic extract (0.1–20%), red ginseng extract (0.001–10%), and gintonin (0.001–10%), and conducted a sensory evaluation with consumers. Jung et al. [102] made red ginseng milk and determined its physicochemical properties and antioxidant capacity. The physicochemical properties of red ginseng milk (0.5–2%) were measured including pH, titratable acidity, color, general composition, and sensory properties. Antioxidant activities were measured using a DPPH radical scavenging activity assay, β -carotene bleaching assay, and ferric thiocyanate assay. Red ginseng in milk had the following effects: the lactose content, titratable acidity, a value (green–red), b value (blue–yellow), and antioxidant effects were increased, whereas the pH and L values (white–black) were decreased [102]. Oligosaccharide and cyclodextrin were mixed with red ginseng milk to improve the taste, and these two additives resulted in stronger sweetness and weaker bitterness [102].

Ginseng and red ginseng milk are manufactured as functional dairy products and their compositions and physicochemical properties have been analyzed by diverse methods. The presence of ginsenosides in ginseng milk was confirmed by HPLC analysis, and it can be expected that they will provide health benefits. The addition of cyclodextrin, banana, and vanilla should reduce bitterness and increase sweetness in red ginseng milk.

Yogurt fortified with ginseng and red ginseng

Yogurt is produced the fermentation of lactose to lactic acid to lower the pH of milk proteins to near their isoelectric points. Starter bacteria are used, including *S. thermophilus*, *L. bulgaricus*, *L. acidophilus*, *L. casei*, and *Bifidobacterium* sp. [103, 104]. Yogurt types are classified as set, stirred, drinking sweet, fruit, frozen, and dried [103]. Plain yogurt is made by cup incubation of vat incubation, and yogurt is sold as full-fat, low-fat, and non-fat [105]. Plain/stirred yogurt is manufactured through several steps; milk storage, standardization, pre-heating, homogenization, heat/cooling, inoculation, sugar or flavor preparation, filler, cooling, and cold storage [105].

Several research groups have manufactured yogurts fortified with ginseng and red ginseng (Tables 3, 4; Fig. 2). Ginseng yogurt was evaluated for its physicochemical, microbial, and sensory properties and functional effects [106–116]. Mice that administered 2% ginseng yogurt using starter cultures of *L. acidophilus* L 54, *S. thermophilus* CHR 16–18, and *B. bifidum* ATCC

Table 3 Microbial strains and conditions for manufacture of yogurt fortified with ginseng

Type	Starter culture ^a	Fermentation conditions	References
Yogurt	<i>L. acidophilus</i> L. 54, <i>S. thermophilus</i> CHR 16–18, <i>B. bifidum</i> ATCC 11863	Ginseng extract (2%); inoculation volume, 2%; incubation temperature, 37 °C	[106]
	<i>S. thermophilus</i> 018812, <i>L. bulgaricus</i> 011711	Ginseng extract (39 mg/g saponin); additives, 8% sugar; inoculation volume, 2%; incubation temperature, 42 °C	[107, 108]
	<i>L. bulgaricus</i> KCTC 3188, <i>S. thermophilus</i> KCTC 3658	Ginseng extract (0.5, 1, 1.5, and 2%); inoculation volume, 2%; incubation temperature, 37 °C	[109]
	<i>B. minimum</i> KK-1, <i>B. cholerium</i> KK-2	Ginseng extract (1, 2, and 3%); additives, 7% sugar; inoculation volume, 3%; incubation temperature, 37 °C	[110]
	<i>Bifidobacterium</i> sp. KK-1, KK-2, K-103, K-506, <i>L. bulgaricus</i> , <i>S. thermophilus</i>	Ginseng powder (1%); additives, 0.1% vit. C; inoculation volume, 1% (each culture); incubation temperature, 37 °C	[111]
	Kefir starter (<i>S. lactis</i> , <i>S. cremoris</i> , <i>S. diacetylactis</i> , <i>L. casei</i> var. <i>rhamnosus</i> , <i>L. acidophilus</i>)	Ginseng (0.5, 1, 1.5, and 2%); incubation temperature, 23 °C	[112]
	<i>B. longum</i> H 1 (KCCM 10493)	Ginseng extract concentration; 10 brix	[113]
	<i>L. rhamnosus</i> GR-1	Alcoholic and aqueous ginseng extract (150 or 500 µg/mL milk); inoculation volume, 1%; incubation temperature, 37 °C	[114]
	Starter culture (<i>L. bulgaricus</i> , <i>L. delbrueckii</i> , <i>S. thermophilus</i>), Probiotic mother culture (<i>L. rhamnosus</i> GR-1)	Ginseng extract (0.5, 1, and 2%); inoculation volume, 2% starter culture and 4% probiotic mother culture; incubation temperature, 37.5 °C	[115]
	Chr. Hansen (<i>L. bulgaricus</i> , <i>S. thermophilus</i> , <i>B. bifidum</i>)	Nanopowdered ginseng (0.1, 0.3, 0.5, and 0.7%); inoculation volume, 0.02%; incubation temperature, 43 °C	[116]

^a *L.*, *Lactobacillus*; *S.*, *Streptococcus*; *B.*, *Bifidobacterium*

Table 4 Microbial strains and conditions for manufacture of yogurt fortified with red ginseng

Type	Starter culture ^a	Fermentation conditions	References
Yogurt	<i>L. acidophilus</i> KCTC 3150, <i>L. salivarius</i> subsp. <i>salivarius</i> CNU 27	Red ginseng extract (0.1, 0.2, 0.4, and 1%); inoculation volume, 2% (each culture); incubation temperature, 37 °C	[117]
	Yomix 321 (<i>S. thermophilus</i> , <i>L. bulgaricus</i>)	Red ginseng extract (0.25, 0.5, and 1%); additives, 1.5% glucose; incubation temperature, 42 °C	[118]
	Yo-MIX 401 (<i>L. delbrueckii</i> subsp. <i>bulgaricus</i> , <i>S. thermophilus</i>)	Red ginseng extract (0.1–0.3%); incubation temperature, 43 °C	[119]
	<i>L. acidophilus</i> , <i>S. thermophilus</i>	Red ginseng extract (0.5, 1, 1.5, and 2%); inoculation volume, 0.02%; incubation temperature, 40 °C	[120]

^a *L.*, *Lactobacillus*; *S.*, *Streptococcus*

11863 for 3 weeks, showed an increase of HDL cholesterol content, and a decrease of blood glucose level, total cholesterol content, LDL-cholesterol content, and cholesterol ester content [106]. Kim [107, 108] made a yogurt fortified with ginseng extract, white ginseng extract, and tail ginseng extract using *S. thermophilus* 018812 and *L. bulgaricus* 011711. Ginseng, white ginseng, and tail ginseng affected the pH, titratable acidity, viscosity, and viable cell counts of the product. Sensory evaluations showed that ginseng and tail ginseng had potential as dairy product components [107, 108]. Lee et al. [109] made yogurts with diverse concentration (0.5–2%) of ginseng that were incubated using *L.*

bulgaricus KCTC 3188 and *S. thermophilus* KCTC 3658. The addition of ginseng affected the pH value, titratable acidity, lactic acid bacteria counts, viscosity, amino acid content, and organic acids content, because ginseng promoted acid formation by lactic acid bacteria [109]. In addition, yogurt products with different concentrations of ginseng were tested by sensory evaluation [109]. In another study, a yogurt containing 1–3% ginseng was fermented with *B. minimum* KK-1 and *B. cholerium* KK-2 [110]. This ginseng yogurt did not score highly in assessment by consumers, however, an increase in the concentration of ginseng enabled an increase of viable bacterial cell counts [110]. Hekmat et al. [114]

Fig. 2 Manufacturing process of yogurt fortified with ginseng and red ginseng [106–120, 122]. The addition of ginseng or red ginseng before incubation could improve the pharmaceutical effect because of

bioconversion [1, 2]. The addition of ginseng or red ginseng after incubation did not affect the growth of lactic acid bacteria [3, 4]

investigated a yogurt supplemented with ginseng extracts produced by the alcohol and water. The yogurt was inoculated with *L. rhamnosus* GR-1 and stored for 28 days. The viable cells of *L. rhamnosus* GR-1 remained in the ginseng-supplemented yogurt during storage and this results indicated that *L. rhamnosus* GR-1 was stable in ginseng [114]. Cimo et al. [115] made yogurt containing *P. quinquefolius* (American ginseng roots) and inoculated *L. rhamnosus* GR-1 as the mother culture and *L. bulgaricus*, *L. delbrueckii*, and *S. thermophilus* as starter culture. This study indicated that American ginseng improved the viability of *L. rhamnosus* GR-1 and the mother culture enhanced quantity of ginsenosides Rg₁, Re, Rb₁, and Rb₂ in American ginseng [115]. Yogurt was made by inoculating *L. bulgaricus*, *S. thermophilus*, and *B. bifidum* and adding nanopowderd and powdered ginseng (concentrations of 0.1, 0.3, 0.5, and 0.7%) [116]. This study showed that nanopowdered and powdered ginseng improved viable bacterial cell number, physico-chemical properties, DPPH radical scavenging activity, and sensory evaluation results and changed the color of the yogurts during storage [116]. Especially, the nanopowdered ginseng showed remarkable results than the powdered ginseng on lower concentration [116]. Addition of ginseng affected physicochemical properties and improved functionalities of product.

Red ginseng yogurt was evaluated for its physico-chemical, microbial, taste, and functional properties

[117–120]. Red ginseng yogurt was made by mixing skim milk, soy milk, and red ginseng (0.1–1.0%) and inoculating *L. acidophilus* KCTC 3150 and *L. salivarius* subsp. *salivarius* CNU 27 as starter cultures [117]. The pH, titratable acidity, viable cell counts, viscosity, carbohydrate content, organic acid content, and sensory properties were examined. Red ginseng promoted the growth of lactic acid bacteria through bioactive components [117]. In addition, red ginseng improved the yield of enzymes that hydrolyze carbohydrates, resulting in a change in lactose content [117]. In another study, a yogurt containing 0.25–1% red ginseng extract was analyzed to determine its physico-chemical and antioxidant properties [118]. The red ginseng content of the yogurt was decided according to the effect on its sensory properties, especially, bitterness and astringent taste of red ginseng [118]. Red ginseng yogurt had a higher antioxidant capacity because of the phenols and flavonoids in red ginseng [118]. Choi et al. [119] made a red ginseng yogurt that contained 0.1–0.3% red ginseng, and used *L. delbrueckii* subsp. *bulgaricus* and *S. thermophilus* as starter cultures. Red ginseng yogurt was assessed by its contents of protein, fat, moisture, salt, and total solids, as well as its pH value, and the concentration of red ginseng was decided according to the results of sensory evaluations [119]. Jung et al. [120] developed a red ginseng yogurt by adding 0.5–2% red ginseng extract and inoculating the culture with *L. acidophilus* and *S. thermophilus*. This red ginseng yogurt was assessed for its

physicochemical and microbial properties, and antioxidant effects. The addition of red ginseng extract affected the composition, color, incubation time, and antioxidant capacity of the yogurt. Red ginseng promoted the growth of lactic acid bacteria, which reduced the fermentation time, and the fat content of the yogurt was also lower [120]. The potential use of ginseng and red ginseng as additives in dairy products was assessed through physicochemical analysis, sensory test, and functional evaluation. The inclusion of ginseng or red ginseng in yogurt can potentially be adjusted to meet the preferences of consumers while providing functionalities such as antioxidant and anti-tumor effects.

Cheese fortified with ginseng and red ginseng

Cheese is produced in more than 2000 varieties worldwide, which are divided into three major types: rennet or natural, fresh or non-ripened, and processed [96]. Cheese consists of fat, cholesterol, protein, lactose, vitamins, and minerals. Starter cultures for cheese include *Lactococcus* sp. (*Lc. lactis* subsp. *cremoris* and *Lc. lactis* subsp. *lactis*), *Leuconostoc* sp., *S. thermophilus*, and *Lactobacillus* sp. (*L. delbrueckii* subsp. *bulgaricus*, *L. delbrueckii* subsp. *lactis*, and *L. helveticus*) [121]. Cheese is made via several steps, including preripening, curding, moulding, pressing, salting, drying, ripening, and packing [122].

Several research teams have manufactured diverse cheeses fortified with additives including red ginseng (Table 5; Fig. 3). Red ginseng cheese has been evaluated

for its physicochemical properties and taste [123–126]. Further, other components such as black garlic and *Rubus coreanus* have been included in red ginseng cheese [127, 128]. Park et al. [123] made fresh cheese containing fermented red ginseng (1, 3, and 5%) by *L. acidophilus*. During the storage period, the number of viable cells of lactic acid bacteria in the red ginseng cheese increased, because lactic acid bacteria used red ginseng as a nutrient. The acceptability of the cheese to consumers was decreased in proportion to the concentration of red ginseng because of red ginseng flavor [123]. Nam et al. [124] made red ginseng cheese with the addition of the amino acid-fermented red ginseng condensate to reduce the bitterness added by red ginseng. In other studies, asiago cheese was fortified with red ginseng extracts, red ginseng hydrolyzates, nanopowdered red ginseng, and powdered red ginseng [125, 126]. The red ginseng additives affected the physicochemical properties, numbers of viable cells of lactic acid bacteria, components, and sensory aspects of the asiago cheese during ripening. Previous studies demonstrated that a low concentration of red ginseng extract, red ginseng hydrolysate, nanopowdered red ginseng, and powdered red ginseng was acceptable for utilization in dairy products [125, 126]. Chung et al. [127] made three types of cheese, namely mozzarella, cheddar, and appenzeller, which were fortified with red ginseng and black garlic extract. Chung et al. [128] made appenzeller cheese fortified with fermented red ginseng and *Rubus coreanus* using *L. acidophilus*. These fortified cheeses were evaluated as having excellent tastes. In Korea, cheeses fortified with nutrients

Table 5 Microbial strains and conditions for manufacture of cheese fortified with red ginseng

Type	Starter culture ^a	Fermentation conditions	References
Cheese	LYO50 (<i>Lc. lactis</i> subsp. <i>lactis</i> , <i>Lc. lactis</i> subsp. <i>cremoris</i> , <i>Lc. lactis</i> subsp. <i>lactis</i> biovar. <i>diacetylactis</i>)	Fermented red ginseng (1, 3, and 5%); inoculation volume, 0.003%; incubation temperature, 30–32 °C	[123]
	ABT-5 (<i>L. acidophilus</i> , <i>Bifidobacterium</i> sp., <i>S. thermophilus</i>)	Inoculation volume, 0.004%	[124]
	Flora Danica (<i>Lc. lactis</i> subsp. <i>lactis</i> , <i>Lc. lactis</i> subsp. <i>cremoris</i> , <i>Lc. lactis</i> subsp. <i>lactis</i> biovar. <i>diacetylactis</i> , <i>Leu. mesenteroides</i> subsp. <i>cremoris</i>)	Red ginseng extract and red ginseng hydrolyzates (0.1, 0.3, and 0.5%); inoculation volume, 1%	[125]
	Flora Danica (<i>Lc. lactis</i> subsp. <i>lactis</i> , <i>Lc. lactis</i> subsp. <i>cremoris</i> , <i>Lc. lactis</i> subsp. <i>lactis</i> biovar. <i>diacetylactis</i> , <i>Leu. mesenteroides</i> subsp. <i>cremoris</i>)	Nanopowdered red ginseng and powdered red ginseng (0.1, 0.3, and 0.5%); inoculation volume, 1%	[126]
	Mozzarella: <i>L. bulgaricus</i> , <i>S. thermophilus</i> , Cheddar and appenzeller: ALP-DIP D (CHOOZIT Alp D; <i>Lc. lactis</i> subsp. <i>lactis</i> , <i>Lc. lactis</i> subsp. <i>cremoris</i> , <i>Lc. lactis</i> subsp. <i>lactis</i> biovar. <i>diacetylactis</i> , <i>S. salvarius</i> subsp. <i>thermophilus</i> , <i>L. helveticus</i> , <i>L. lactis</i>)	Red ginseng extract (0.001–10%); additives, 0.1–20% black garlic extract; inoculation volume, 1.5%	[127]
	FLORA-DANICA (<i>Lc. lactis</i> subsp. <i>cremoris</i> , <i>Lc. lactis</i> subsp. <i>diacetylactis</i> , <i>Lc. lactis</i> subsp. <i>lactis</i> , <i>Leu. mesenteroides</i> subsp. <i>cremoris</i>)	Fermented red ginseng and <i>Rubus coreanus</i> (0.5, 1, 1.5, 2, and 2.5%); inoculation volume, 0.003%	[128]

^a *L.*, *Lactobacillus*; *S.*, *Streptococcus*; *B.*, *Bifidobacterium*; *Lc.*, *Lactococcus*; *Leu.*, *Leuconostoc*

Fig. 3 Manufacturing process of cheese fortified with ginseng and red ginseng [122–128]. Cheese was fortified with ginseng or red ginseng fermented product, powder, and solution [1]

and flavors have sold, but research has been lacking about the physicochemical and microbial properties, functionality, and appeal of red ginseng cheese. There is a potential for the dairy industry to conduct research with the aim of reducing the flavor and bitterness imparted by red ginseng and improve the taste while adding the functionality.

In conclusion, ginseng and red ginseng are being developed, prepared, and sold in various forms, such as concentrate, tablet, tea, and powder, to enhance consumer acceptance. The diverse functionalities of ginseng and red ginseng can be attributed to ginsenosides, which are their main pharmacologically active components. To enhance their functionalities, microorganisms and enzymes are being used to convert ginsenosides into smaller minor ginsenoside molecules, although studies on the functionalities of ginsenosides, and the microorganisms and enzymes used for the conversion, are ongoing. Dairy products are known worldwide as highly nutritious foods, with milk, yogurt, and cheese being the most common examples. Recent studies have examined approaches for increasing the nutritional value of dairy products by adding ginseng or red ginseng. These materials have an impact on the physicochemical properties of dairy products. Other studies are being conducted to identify approaches for enhancing the consumer acceptability of dairy products by adding various materials such as cyclodextrin, black garlic, and Korean

black raspberry, in addition to ginseng or red ginseng. Although anti-cholesterol and antioxidant effects have been identified as functionalities of dairy products containing ginseng or red ginseng, experiments on other functionalities are still lacking. Moving forward, additional functionality testing on dairy products containing ginseng or red ginseng should be conducted to provide a foundation of basic data required for their use as functional food ingredients.

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Compliance with ethical standards

Conflict of interest The authors declare no conflict of interest.

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