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Changes of Ginsenoside Compositions in Cultivated Wild Ginseng with Different Steaming Temperatures and Time

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ABSTRACT

This study was conducted to investigate changes in the ginsenoside compositions of cultivated wild ginseng caused by steaming at different temperatures (95, 117, 126, and 132℃) and times (10, 30, 50, 70, 90, 110, and 130 min). On increasing steaming temperatures from 95 to 132℃, levels of protopanaxadiol (PPD) ginsenosides Rg3, Rk1, and Rg5 increased from 0.69, 1.11, and 1.79 mg/g to 4.08, 5.16, and 8.98 mg/g, respectively, whereas levels of protopanaxatriol (PPT) ginsenosides Re, Rf, Rg6, F4, Rk3, and Rh4 increased from 2.04, 0.79, 0.53, 0.77, 0.53, and 0.52 mg/g to 2.44, 2.50, 1.83, 2.74, 1.39, and 1.72 mg/g, respectively. Furthermore, amounts of total PPD ginsenosides and total ginsenosides increased on increasing temperature, and total PPT ginsenoside amounts peaked at 126℃. In addition, when the steaming time was increased from 10 to 70 min, amounts of PPD ginsenosides Rg3, Rk1, and Rg5 increased 2.06, 1.90, and 1.89-fold, respectively, and amounts of PPT ginsenosides Rf, Rg6, F4, Rk3, and Rh4 increased 1.22, 1.44, 1.66, 1.61, and 1.95-fold, respectively. However, levels of total PPT ginsenosides and total ginsenosides peaked at a steaming time of 10 min.

Key words: cultivated wild ginseng, ginsenosides, steaming temperature, steaming time

INTRODUCTION

Panax ginseng C.A. Meyer (Araliaceae) is commonly known as Korean ginseng. It is one of the most widely used tonic to enhance immune response and consequently improve health and longevity for over 2000 years in Oriental countries (Patel S & Rauf A 2017). Mountain wild ginseng is found in the natural environment of mountainous regions, whereas cultivated wild ginseng is grown in forests and mountains to mimic mountain wild ginseng. However, mountain wild ginseng is considered superior to regular cultivated ginseng as it contains higher amounts of certain ginsenosides. Furthermore, ginsenoside levels have been found to be consistently lower in more intensively cultivated crops, although their growth is consistently higher (Lim W *et al* 2005). Generally, cultivated ginseng is systematically cultivated on land and harvested after 4−6 years of cultivation, whereas cultivated wild ginseng grows in the wild or deep in mountains, making it difficult to harvest. Their different growth environments can lead to differences in several functional compounds and pharmacological effects (Yu GJ *et al* 2015). It has been reported that cultivated wild ginseng is more effective than cultivated ginseng in terms of efficacy. Its ginsenoside content is also higher than that of cultivated ginseng. Cultivated wild ginseng is also known to be effective against cancer, hypotension, oxidants, hepatotoxicity, and lipid weakening (Kim YJ & Son DY 2012). To date, nearly two hundred ginsenosides have been isolated and identified from various tissues of ginseng plants (Chen W *et al* 2019). Based on chemical structures of aglycones moieties, ginsenosides are mainly divided into protopanaxadiol (PPD) type ginsenosides (such as Rb1, Rb2, Rc, Rd, Rg3, and so on) and protopanaxatriol (PPT) type ginsenosides (such as Rg1, Re, Rg2, Rh1, and so on).

Heat treatment is the most widely used method for preserving and extending the shelf-life of food products and nutritional supplements. This treatment can improve biological activity and ginsenoside content of ginseng. However, some naturally occurring nutrients can be lost during thermal processing because most bioactive compounds are relatively unstable to heat (Banga JR *et al* 2003; Awuah GB *et al* 2007). Thermally processed foods, especially fruits and vegetables, show increased biological activities compared with fresh foods owing to the chemical changes that occur during heat treatment (Ryley J & Kajda P 1994). Especially, steaming is known to induce a structural change in ginsenoside and enhance biological activities of ginseng (Yang SJ *et al* 2006; Kim KY *et al* 2007). These steaming procedures can transform major

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ginsenosides including Rb1, Rb2, Rc, Rd, Re, and Rg1 into minor ginsenosides including Rg3, Rk1, Rg5, and F2. Characteristic compounds in red and black ginseng have potential biological activities including anticancer, antidiabetic, neuroprotective, and anti-inflammatory activities (Chen J *et al* 2008; Kang KS *et al* 2008; Sun BS *et al* 2009; Yayeh T *et al* 2012; Kim JH *et al* 2016). Therefore, the objective of this study was to investigate changes in ginsenoside compositions of cultivated wild ginseng induced by steaming processing at different steaming temperatures and time.

MATERIALS AND METHODS

1. Materials

Five-year-old cultivated wild ginseng roots was collected on August 5, 2019 in the experimental field of Jinsaengbio Farm Association Co., Hamyang-gun, Gyeongnam, South Korea. Standards of ginsenosides Rb1, Rg1, Re, Rf, Rh1, Rc, Rb2, Rd, Rg6, F4, Rk3, Rh4, Rg3, Rk1, and Rg5 were purchased from Ambo Institute (Daejeon, Korea). Acetonitrile and high-performance liquid chromatography (HPLC) grade water were purchased from J.T. Baker (Phillipsburg, NJ, USA). A solid-phase extraction (SPE) column (Agilent, Bond Elut Plexa Cartridge 6 mL/200 mg, CA, USA) was used to purify and concentrate samples. All other chemicals used were of analytical grade.

2. Sample Preparation

Main roots of cultivated wild ginseng were washed with tap water to remove soil and other debris. Raw cultivated wild ginseng was then dried at 40℃ in a forced convection oven (LID-1904S, L'equip Co., Korea) or 6 hrs until the final moisture content was less than 30%. Dried cultivated wild ginseng was then steamed at 95℃ for 1.5 h using an autoclave (HK-AC60, Hankuk S&I Co., Korea). After cooling to room temperature, the autoclaved cultivated wild ginseng was dried again at 60℃ for 3 hrs in a forced convection drying oven. After secondary drying, autoclaved cultivated wild ginseng was steamed for 30 minutes at 95℃ (0 kfg/cm^2), 117℃ (1.0 kfg/cm^2), 126℃ (1.5 kfg/cm^2), or 132℃ (2.0 kfg/cm^2) using an autoclave and then dried at 60℃ for 3 hours to prepare cultivated wild ginseng samples with different steaming temperatures. To prepare cultivated wild ginseng samples with different steaming time, cultivated wild ginseng was first dried in the same way and then steamed for 10 to 130 minutes under the condition of 132℃ using an autoclave and then dried at 60℃ for 3 hrs.

3. Analysis of Ginsenosides

1) Extraction

Steamed cultivated wild ginseng was dried at 50℃. Dried cultivated wild ginseng was ground to 20−30 mesh and refluxed with 10 volumes (v/w) of hot water at 80℃ for 3 h. After reflux, the extract was filtered twice and concentrated at 55℃. The concentrate was then freeze-dried and stored at −75℃ until used.

2) SPE Column Purification

SPE was performed using a Varian Vac Elute SPS 24 vacuum manifold (Varian Inc., Walnut Grove, CA, USA). The SPE cartridge (Agilent, Bond Elut Plexa Cartridge 6 mL/200 mg, CA, USA) was conditioned with 6 mL of methanol and 6 mL of water before introducing sample solution. A 1.0 mL aliquot of the sample solution was introduced into the SPE cartridge at a flow rate of 0.1 mL/min. A washing step was then performed with 1.0 mL of ultra-pure water at the same flow rate. Retained analytes were eluted with 1.0 mL of methanol at a flow rate of 0.08 mL/min. The eluate solution was filtered through a 0.22 μm filter prior to analysis.

3) Determination of Ginsenosides by HPLC

Ginsenosides were determined using the method described by Dong H *et al* (2011) with slight modifications. Analyses were performed using an Agilent 1260 liquid chromatograph (Hewlett Packard, Wilmington, NC, USA) equipped with a quaternary gradient pump and multiple wavelength detector operating at 203 nm. Samples were separated on a Zorbax Eclipse XDB-C18 column (4.6 mm × 150 mm, 5 μm; Agilent Technologies, Inc. CA, USA) at 35℃ with a sample injection volume of 10 μL. The mobile phase consisted of a gradient of water (A) and acetonitrile (B). The following gradient was used: 20% B (0 min), 20% (0−10 min), 32% (10−40 min), 50% (40−55 min), 65% (55−70 min), 90% (70−82 min), and 80% (82−90 min). Data analysis was performed using a Chemstation software (Hewlett Packard). The flow rate of the mobile phase was set at 0.9 mL/min. Stock solutions of ginsenosides Rb1, Rg1, Re, Rf, Rh1, Rc, Rb2, Rd, Rg6, F4,

Rk3, Rh4, Rg3, Rk1, and Rg5 were prepared in methanol. A series of standard operating solutions of different concentrations were obtained by diluting standard stock solutions.

4. Statistical Analysis

Experimental data were subjected to analysis of variance (ANOVA). Significant differences between mean values as determined from measurements carried out in five replicate tests (i.e., $p<0.05$) were obtained by Duncan's multiple-range test using statistical analysis software (SPSS 20.0, IBM Inc., NY, USA).

RESULTS AND DISCUSSION

1. Changes of Ginsenosides in Cultivated Wild Ginseng Induced by Steaming Processing at Different Steaming Temperatures

Changes in ginsenoside compositions of cultivated wild ginseng induced by steaming processing at different steaming temperatures are shown in Table 1. Ginsenoside compositions varied significantly with steaming temperature. With increasing temperature, levels of PPD ginsenosides Rc, Rb2, and Rd decreased from 3.88, 4.10, and 3.12 mg/g to 1.78, 1.57, and 2.63 mg/g, respectively. In contrast, levels of ginsenosides Rg3, Rk1, and Rg5 increased from 0.69, 1.11, and 1.79 mg/g to 4.08, 5.16, and 8.98 mg/g, respectively, with increasing temperature. However, ginsenoside Rb1 was not detected at any steaming temperature. The level of ginsenoside Rg5 was the highest at 8.98 mg/g when the steaming temperature was 132℃. It increased with increasing steaming temperature. On the other hand, levels of PPT ginsenosides Rg1 and Rh1 only decreased from 4.01 and 7.39 mg/g to 1.28 and 5.86 mg/g, respectively, with increasing temperature. In contrast, levels of ginsenosides Re, Rf, Rg6, F4, Rk3, and Rh4 increased from 2.04, 0.79, 0.53, 0.77, 0.53, and 0.52 mg/g to 2.44, 2.50, 1.83, 2.74, 1.39, and 1.72 mg/g, respectively, with increasing temperature. Although ginsenoside Rh1 was decreased with increasing temperature, among PPT ginsenosides, ginsenoside Rh1 showed the highest content at 5.86 mg/g when the steaming temperature was 132℃. Moreover, amounts of total PPD ginsenosides and total ginsenosides were increased with increasing temperature. Levels of total PPD ginsenosides and total ginsenosides were 24.20 and 43.94 mg/g at 132℃, respectively. However, the amount of total PPT ginsenosides was the highest with a content of 21.30 mg/g at 126℃. This result was consistent with results of Wang D *et al* (2012) & Xiong Y *et al* (2019). Changes of chemical composition and content can be extrapolated from chemical structure. Under a steaming condition, the sugar chain at C-20 of ginsenosides Rb1 and Rd could be easily and selectively eliminated to produce ginsenoside 20(*S*)/(*R*)-Rg3 and ginsenoside Rg3 at C-20 could be dehydrated to yield ginsenosides Rg5 and Rk1 (Huang X *et al* 2019). Ginsenosides Rg1 and Re are likely to first lose a glycosyl moiety at C-20 and subsequently its terminal sugar unit at C-6 to form ginsenosides Rg2 and/or Rh1. Ginsenoside Rh1 is further converted to Rk3 and Rh4 through dehydration at C-20 (Sun S *et al* 2011). Additionally, Kim WY *et al* (2000) have reported the structural change in ginsenosides during red ginseng manufacturing with decreased levels of ginsenosides Rb1, Rb2, Rc, Rd, and Rg1 but increased levels of ginsenosides Rf, Rg3, and Rg5 after steaming.

2. Changes of Ginsenosides in Cultivated Wild Ginseng Induced by Steaming Processing with Different Steaming Time

Changes in ginsenoside compositions of cultivated wild ginseng induced by steaming processing at different steaming time are shown in Table 2. Among PPD ginsenosides, ginsenoside Rb1 was not detected with any steaming time. Levels of ginsenosides Rc, Rb2, and RD were decreased when the steaming time was increased. Ginsenosides Rc and Rb2 were not detected after 50 min of steaming. Ginsenoside Rd was not detected after 90 min of steaming. In contrast, levels of ginsenosides Rg3, Rk1, and Rg5 were increased until steaming time of 70 min. They were then decreased thereafter. At 70 min of steaming time, levels of ginsenosides Rg3, Rk1, and Rg5 were 6.22, 7.81, and 14.12 mg/g, respectively. In particular, levels of ginsenosides Rg3, Rk1, and Rg5 were increased by 2.06, 1.90, and 1.89 folds, respectively, after 70 min of steaming compared to those after 10 min of steaming. For PPT ginsenosides, levels of ginsenosides Rg1 and Re were decreased when steaming time was increased, whereas Rh1 level was decreased, increased, and then decreased again. In contrast, levels of ginsenosides Rf, Rg6, F4, Rk3, and Rh4 were increased until the steaming time was 70 min. They were then decreased thereafter. After 70 min of steaming, levels of ginsenosides Rf, Rg6, F4, Rk3, and Rh4 were 2.66, 2.41, 3.92, 2.05, and 2.97 mg/g, respectively. The level of

Table 1. Contents of ginsenosides in cultivated wild ginseng induced by steaming processing at different steaming temperatures

Ginsenosides (mg/g)	Steaming temperature and pressure, ℃ (kfg/cm^2)			
	95 (0)	117 (1)	126 (1.5)	132 (2)
20(S)-protopanaxadiol (PPD) groups				
Rb1	-[1)]	-	-	-
Rc	3.88±0.31^b	6.09±0.30^a	3.16±0.04^c	1.78±0.07^d
Rb2	4.10±0.51^a	2.71±0.06^b	2.66±0.06^b	1.57±0.08^c
Rd	3.12±0.04^a	2.93±0.25^{ab}	2.77±0.16^{bc}	2.63±0.17^c
Rg3	0.69±0.05^d	1.80±0.04^c	3.08±0.04^b	4.08±0.13^a
Rk1	1.11±0.17^d	2.52±0.07^c	3.80±0.12^b	5.16±0.09^a
Rg5	1.79±0.07^d	4.52±0.24^c	6.85±0.36^b	8.98±0.18^a
20(S)-protopanaxatriol (PPT) groups				
Rg1	4.01±0.14^a	3.98±0.02^a	2.19±0.05^b	1.28±0.07^c
Re	2.04±0.06^b	2.58±0.08^a	2.50±0.03^a	2.44±0.18^a
Rf	0.79±0.02^d	1.05±0.03^c	2.26±0.04^b	2.50±0.07^a
Rh1	7.39±0.29^b	8.71±0.49^a	7.82±0.12^b	5.86±0.33^c
Rg6	0.53±0.29^d	1.20±0.01^c	1.48±0.01^b	1.83±0.04^a
F4	0.77±0.10^d	1.72±0.02^c	2.22±0.03^b	2.74±0.03^a
Rk3	0.53±0.02^d	0.84±0.01^c	1.26±0.01^b	1.39±0.02^a
Rh4	0.52±0.03^d	0.93±0.01^c	1.57±0.02^b	1.72±0.03^a
Total PPD	14.70±0.85^d	20.57±0.69^c	22.32±0.59^b	24.20±0.49^a
Total PPT	16.55±0.19^c	21.03±0.50^a	21.30±0.27^a	19.74±0.63^b
Total content	31.25±0.94^c	41.60±1.17^b	43.62±0.82^a	43.94±0.93^a
PPD/PPT ratio	0.89±0.05^d	0.98±0.01^c	1.05±0.02^b	1.23±0.04^a

Values are presented as mean±S.D. (n=5).
[a−d] Different superscripts within a row indicate significant differences at $p<0.05$.
[1)] Not detected (limit of detection: 0.1 mg/g).

total PPD ginsenosides was 29.01 mg/g after 70 min of steaming, while levels of total PPT ginsenosides and total ginsenosides were 25.68 and 53.19 mg/g after 10 min of steaming. Moreover, levels of ginsenosides Rf, Rg6, F4, Rk3, and Rh4 were increased by 1.22, 1.44, 1.66, 1.61, and 1.95 folds, respectively, after 70 min of steaming compared to those after 10 min of steaming. Results of this study are consistent with those of Wang CZ *et al* (2004). They reported that levels of ginsenosides Rg1, Re, Rb1, Rc, Rb2, Rb3, and Rd appeared to decrease after steaming, whereas those of ginsenosides Rg3 were increased after steaming. An increase in saponin content of steamed ginseng might be explained by pyrolysis of malonyl ginsenoside, producing aglycones of diol-series saponins (Ryu GH 2007). In addition, Park IH *et al* (2002) have isolated three new dammarane glycosides (ginsenosides Rk1, Rk2, and Rk3) from heat-processed ginseng. Chen W *et al* (2020) have investigated ginsenoside changes in black ginseng leaf products and suggested that polar PPD-type ginsenosides (Rb1, Rb2, Rc, Rd, etc.) are more likely to be converted to ginsenosides Rk1 and Rg5 by dehydration from Rg3 and to ginsenosides Rk2 and Rh3 through losing an H_2O from Rh2 than to be completely degraded to aglycones PPD

Table 2. Contents of ginsenosides in cultivated wild ginseng induced by steaming processing after different steaming time

Ginsenosides (mg/g)	Steaming time (min) at 132℃ (2.0 kfg/cm^2)						
	10	30	50	70	90	110	130
20(S)-protopanaxadiol (PPD) groups							
Rb1	-[1)]	-	-	-	-	-	-
Rc	5.47±0.11^a	2.03±0.07^b	0.81±0.06^c	-	-	-	-
Rb2	4.03±0.16^a	1.11±0.05^b	0.74±0.09^c	-	-	-	-
Rd	3.39±0.14^a	1.81±0.11^b	1.43±0.15^c	0.86±0.05^d	0.70±0.06^e	-	-
Rg3	3.02±0.04^e	4.86±0.09^c	5.36±0.11^b	6.22±0.32^a	4.83±0.40^c	3.99±0.05^d	4.58±0.04^c
Rk1	4.12±0.04^g	5.89±0.09^e	6.92±0.12^b	7.81±0.09^a	6.68±0.05^c	5.76±0.06^f	6.38±0.04^d
Rg5	7.48±0.07^e	10.59±0.18^d	12.43±0.22^b	14.12±0.19^a	12.32±0.11^{bc}	10.65±0.10^d	12.13±0.10^c
20(S)-protopanaxatriol (PPT) groups							
Rg1	3.53±0.05^a	1.44±0.06^c	-	1.80±0.08^b	1.03±0.05^d	0.93±0.06^e	0.87±0.02^e
Re	3.09±0.03^a	2.60±0.15^b	1.97±0.08^c	1.97±0.04^c	1.48±0.02^d	1.20±0.06^e	1.19±0.06^e
Rf	2.18±0.05^b	1.78±0.14^c	1.20±0.04^e	2.66±0.09^a	1.82±0.06^c	1.39±0.07^d	1.29±0.06^{de}
Rh1	10.06±0.23^a	4.11±0.18^b	0.80±0.04^f	3.22±0.12^c	2.86±0.14^d	2.34±0.20^e	2.71±0.12^d
Rg6	1.67±0.02^d	2.17±0.03^b	2.40±0.04^a	2.41±0.03^a	1.97±0.02^c	1.61±0.01^e	1.53±0.01^f
F4	2.36±0.04^f	3.42±0.05^c	3.72±0.06^b	3.92±0.05^a	3.01±0.02^d	2.57±0.01^e	2.37±0.01^f
Rk3	1.27±0.01^f	1.42±0.02^e	1.55±0.02^d	2.05±0.03^a	1.82±0.01^b	1.41±0.01^e	1.70±0.01^c
Rh4	1.52±0.01^f	1.76±0.02^e	2.06±0.03^d	2.97±0.03^a	2.84±0.02^b	2.12±0.02^c	2.87±0.02^b
Total PPD	27.51±0.18^b	26.29±0.44^c	27.69±0.52^b	29.01±0.57^a	24.53±0.54^d	20.40±0.19^f	23.08±0.17^e
Total PPT	25.68±0.32^a	18.69±0.21^c	13.69±0.18^f	21.00±0.21^b	16.83±0.26^d	13.55±0.30^f	14.51±0.21^e
Total content	53.19±0.47^a	44.98±0.38^c	41.38±0.69^d	50.01±0.59^b	41.36±0.80^d	33.95±0.40^f	37.59±0.26^e
PPD/PPT ratio	1.07±0.01^f	1.40±0.03^e	2.02±0.02^a	1.38±0.03^e	1.46±0.01^d	1.51±0.03^c	1.59±0.03^b

Values are presented as mean±S.D.(n=5).
[a-g] Different superscripts within a row indicate significant differences at $p<0.05$.
[1)] Not detected (limit of detection: 0.1 mg/g).

during a heat process. Furthermore, the levels of total PPD ginsenosides and total PPT ginsenosides were decreased after 90 min of steaming. Xie YY *et al* (2012) reported that the concentration of polar ginsenosides such as Rb1, Rb2, Rb3, Rd, Re, Rg1, and Rf decreases, while that of non-polar ginsenosides such as ginsenosides Rg3, Rh2, compound K, Rh3, Rh4, Rk1, Rk2, Rk3, and Rg5 increases during steaming. Therefore, the reduction in PPD and PPT ginsenoside content after a heating time of 90 minutes may be attributed to the conversion of polar ginsenosides to non-polar ginsenosides and transformation to unmeasured ginsenosides occurred.

SUMMARY AND CONCLUSIONS

In conclusion, results of this study indicated that steaming process had a positive influence on changes of ginsenoside compositions in cultivated wild ginseng. With increases of steaming temperature and steaming time, levels of PPD ginsenosides (Rg3, Rk1, and Rg5), PPT ginsenosides (Re, Rf, Rg6, F4, Rk3, and Rh4), total PPD ginsenosides, and total ginsenosides were increased until a heating time of 70 minutes. Amounts of PPD ginsenosides (Rg3, Rk1, and Rg5), PPT ginsenosides (Rf, Rg6, F4, Rk3, and Rh4), and total PPD ginsenosides were the higher after 70 min of steaming than

those after 10 min of steaming. However, levels of total PPT ginsenosides and total ginsenosides were higher after 10 min of steaming. As a result, it was concluded that the most effective steaming temperature and time for cultivated wild ginseng is a heating temperature of 132℃ (2.0 kfg/cm^2) for 70 minutes, during which the highest ginsenoside content was achieved. Results of the present study suggest that the steaming process could be used to develop value-added cultivated wild ginseng products and red ginseng.

REFERENCES

Awuah GB, Ramaswamy HS, Economides A (2007) Thermal processing and quality: Principles and overview. Chem Eng Process 46(6): 584-602.

Banga JR, Balsa-Canto E, Moles CG, Alonso AA (2003) Improving food processing using modern optimization methods. Trends Food Sci Technol 14(4): 131-144.

Chen J, Peng H, Ou-Yang X, He X (2008) Research on the antitumor effect of ginsenoside Rg3 in B16 melanoma cells. Melanoma Res 18(5): 322-329.

Chen W, Balan P, Popovich DG (2019) Comparison of the ginsenoside composition of Asian ginseng (*Panax ginseng*) and American ginseng (*Panax quinquefolius* L.) and their transformation pathways. Stud Nat Prod Chem 63: 161-195.

Chen W, Balan P, Popovich DG (2020) Changes of ginsenoside composition in the creation of black ginseng leaf. Molecules 25(12): 2809.

Dong H, Bai LP, Wong VKW, Zhou H, Wang JR, Liu Y, Jiang ZH, Liu L (2011) The *in vitro* structure-related anti-cancer activity of ginsenosides and their derivatives. Molecules 16(12): 10619-10630.

Huang X, Liu Y, Zhang Y, Li SP, Yue H, Chen CB, Liu SY (2019) Multicomponent assessment and ginsenoside conversions of *Panax quinquefolium* L. roots before and after steaming by HPLC-MS^n. J Ginseng Res 43(1): 27-37.

Kang KS, Yamabe N, Kim HY, Park JH, Yokozawa T (2008) Therapeutic potential of 20(S)-ginsenoside Rg3 against streptozotocin-induced diabetic renal damage in rats. Eur J Pharmacol 591(1-3): 266-272.

Kim JH, Pan JH, Cho HT, Kim YJ (2016) Black ginseng extract counteracts streptozotocin-induced diabetes in mice. PLoS ONE 11(1): e0146843.

Kim KY, Shin JK, Lee SW, Yoon SR, Chung HS, Jeong YJ, Choi MS, Lee CM Moon KD, Kwon JH (2007) Quality and functional properties of red ginseng prepared with different steaming time and drying method. Korean J Food Sci Technol 39(5): 494-499.

Kim WY, Kim JM, Han SB, Lee SK, Kim ND, Park MK, Kim CK, Park JH (2000) Steaming of ginseng at high temperature enhances biological activity. J Nat Prod 63(12): 1702-1704.

Kim YJ, Son DY (2012) Antioxidant and inhibitory effects of Korean panax ginseng extract on pro-inflammatory mediators in LPS-stimulated RAW264.7 Macrophages. J Korean Soc Food Sci Nutr 41(10): 1371-1377.

Lim W, Mudge KW, Vermeylen F (2005) Effects of population, age, and cultivation methods on ginsenoside content of wild American ginseng (*Panax quinquefolium*). J Agric Food Chem 53(22): 8498-8505.

Park IH, Kim NY, Han SB, Kim JM, Kwon SW, Kim HJ, Park MK, Park JH (2002) Three new dammarane glycosides from heat processed ginseng. Arch Pharm Res 25(4): 428-432.

Patel S, Rauf A (2017) Adaptogenic herb ginseng (*Panax*) as medical food: Status quo and future prospects. Biomed Pharmacother 85: 120-127.

Ryley J, Kajda P (1994) Vitamins in thermal processing. Food Chem 49(2): 119-129.

Ryu GH (2007) Recent trend in red ginseng manufacturing process and characteristics of extruded red ginseng. Food Eng Prog 11(1): 1-10.

Sun BS, Gu LJ, Fang ZM, Wang CY, Wang Z, Lee MR, Li Z, Li JJ, Sung CK (2009) Simultaneous quantification of 19 ginsenosides in black ginseng developed from *Panax ginseng* by HPLC-ELSD. J Pharm Biomed Anal 50(1): 15-22.

Sun S, Qi LW, Du GJ, Mehendale SR, Wang CZ, Yuan CS (2011) Red notoginseng: Higher ginsenoside content and stronger anticancer potential than Asian and American ginseng. Food Chem 125(4): 1299-1305.

Wang CZ, Aung HH, Ni M, Wu JA, Tong R, Wicks S, He TC, Yuan CS (2004) Red American ginseng: Constituents and antiproliferative activities of heat-processed *Panax quinquefolius* roots. Planta Med 73(7): 669-674.

Wang D, Liao PY, Zhu HT, Chen KK, Xu M, Zhang YJ, Yang CR (2012) The processing of *Panax notoginseng* and the transformation of its saponin components. Food Chem

132(4): 1808-1813.

Xie YY, Luo D, Cheng YJ, Ma JF, Wang YM, Liang QL, Luo GA (2012) Steaming-induced chemical transformations and holistic quality assessment of red ginseng derived from Panax ginseng by means of HPLC-ESI-MS/MS(n)-based multicomponent quantification fingerprint. J Agric Food Chem 60(33): 8213-8224.

Xiong Y, Chen L, Man J, Hu Y, Cui X (2019) Chemical and bioactive comparison of *Panax notoginseng* root and rhizome in raw and steamed forms. J Ginseng Res 43(3): 385-393.

Yang SJ, Woo KS, Yoo JS, Kang TS, Noh YH, Lee JS, Jeong HS (2006) Change of Korean ginseng components with high temperature and pressure treatment. Korean J Food Sci Technol 38(4): 521-525.

Yayeh T, Jung KH, Jeong HY, Park JH, Song YB, Kwak YS, Kang HS, Cho JY, Oh JW, Kim SK, Rhee MH (2012) Korean red ginseng saponin fraction downregulates proinflammatory mediators in LPS stimulated RAW264.7 cells and protects mice against endotoxic shock. J Ginseng Res 36(3): 263-269.

Yu GJ, Choi IW, Kim GY, Kim BW, Park C, Hong SH, Moon SK, Cha HJ, Chang YC, Paek KY, Kim WJ, Choi YH (2015) Anti-inflammatory potential of saponins derived from cultured wild ginseng roots in lipopolysaccharide-stimulated RAW 264.7 Macrophages. Int J Mol Med 35(6): 1690-1698.

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