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Microwave Heating Rapidly Alters Ginsenoside Composition of Fresh Ginseng (*Panax ginseng* CA Meyer)

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Abstract Heating and drying is an important process to improve the preservation of herbs and its bioactive constituents. Ginseng is most popular medical herbs worldwide. Red ginseng is one of the products, which is prepared by heating and drying fresh ginseng. Red ginseng have ginsensides Rg3, Rg3, and Rk1 which is known for beneficial effect on inflammation, cancer, and obesity compared with other types of ginseng product. However, it is required to spend for long time to produce red ginseng with traditional preparation method. Thus, we aimed to develop a convenient ginseng process method that increases the unique form of bioactive ginsenoside in fresh ginseng. Microwave heating was used as a source of heating energy to dry and heating of fresh ginseng. Our result showed that fresh ginseng treated with microwave heating for 40 min efficiently increased the both of protopanaxadiol (PPD) and protopanaxatriol (PPT) in ginseng. In particular, red ginseng specific-detected ginsenosides Rg3, Rg5, and Rk1 were found in ginseng treated with microwave heating for 40 min compared with other periods of microwave heating condition. In addition, the appearance quality of ginseng after heating and drying affect the market value of ginseng. We observed that fresh ginseng treated with microwave heating for 40 min increased the composition of ginsenoside with proper color change of ginseng. Thus, microwave heating not only can alter the composition of ginsenosides in the short time, but also can improve the appearance of ginseng after heating and drying the processes. Moreover, our method might bring a benefit to produce high quantity of bioactive ginsenoside with a convenient process in ginseng-associated food industry.

Keywords: *mircowave heating, ginseng, red ginseng, prosapogenin, protopanaxadiol, protopanaxatriol, Rg_3, Rg_5*

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1. Introduction

Ginseng (*Panax ginseng*) has been used a valuable traditional medicine to maintain the health condition over the past thousands year [1]. Ginseng has a number of medical applications, which is known to prevent cardiovascular disease, chronic obstructive pulmonary disease, obesity, and environmental heat stress [2,3,4,5].

Therapeutic effects of ginseng primarily due to their ginsenoside constituents [6,7]. The majority of ginsenoside is divided into two different types of saponin such as protopanaxadiol (PPD) and protopanaxatriol (PPT) depend on sugar moieties binding sites [8,9,10]. PPD type of ginsenoside, has sugar moieties binding at C-3 or C-20 position of the structure, is well known to include Rb1, Rb2, Rb3, Rc, Rd, Rg3, Rh2, and Rs1 [11], while PPT (Rg1, Rg2, Rh1, Re, and Rf) type of ginsenoside possess a hydroxyl group at C-3 and sugar moieties at C-6 or C-20 position of the structure.

PPD and PPT is mainly converted from fresh ginseng derived ginsenoside after food processing such as steam, dry, high pressure, fermentation, and ultrasonic stimuli [12,13,14,15,16]. In previous, several studies have been shown steaming and drying procedure produce a unique form of flavonoid and bioactive compound [17,18,19]. Fresh ginseng usually contain approximately 75% of moisture [20,21], and the levels of moisture is requited to be reduced to less than approximately 15% for their preservation [22,23]. On the other hand, the appearance of ginseng after streaming and drying process is also one of the most important factor for justifying of their commercial values. Hence, streaming and drying procedure are a crucial process to modify the constituents of ginseng and to improve its market value in ginseng industry.

Korean red ginseng, is one of the famous ginseng products, refers to a food process of steaming and then drying of fresh ginseng at least nine times. Traditional preparation procedure of red ginseng enhances the

composition of bioactive ginsenoside contents including Rg3 and Rh2 [24,25,26]. Several mechanisms of Rg3 and Rh2 have been suggested for their role in prevention of non-communicable diseases [27,28]. Thus, red ginseng has been being raised higher market values than other type of ginseng products in worldwide. However, long-term preparation is required to produce Rg3 and Rh2-enriched red ginseng with a traditional method.

In this study, we aimed to develop a convenient, highly cost effective, and safety method of ginseng process which can improve the component of bioactive ginsenoside compared with fresh ginseng.

2. Materials and Methods

2.1. Materials

The 6-years fresh ginseng for experiment was purchased at Eumsong in South Korea on June 20, 2011. These specimens were stored at the oriental medical food research laboratory of Semyung University. Dry oven was purchased from Jeio Tech (FO-600M, Korea). Microwave oven was purchased from Samsung Electronics (RE-C20DB, Seoul, South Korea). All other reagents purchased were analytical grade and obtained from Sigma-Aldrich (St. Louis, MO, USA).

2.2. Preparation of Crude Saponin from Ginseng

The exact amount (1g) of each samples extracted with ethyl ether three times by sonicator (Kodo Co. Ltd., 4020P, South Korea), followed by removal of lipid soluble materials with ethylether phase. And then residue was treated with water saturated-n-butanol three times again. n-Butanol fraction was obtained in sonicator, and then it was filtered and concentrated by vacuum evaporator. All process was performed quantitatively, and the amount of concentrate was equivalent to that of crude extracts.

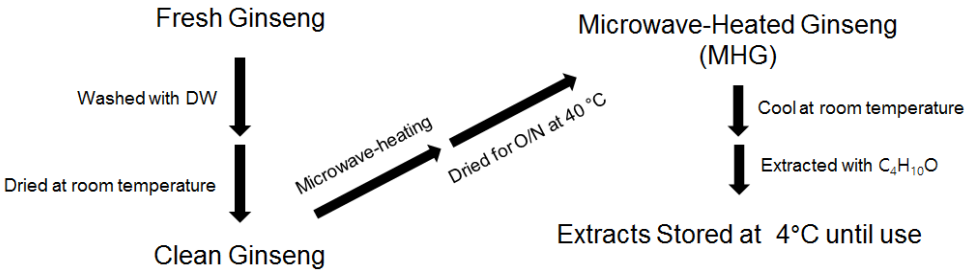

Figure 1. Procedure for preparation of microwave heated ginseng

2.3. HPLC Analysis of Ginsenoside Composition in Ginseng

Ginsenoside composition of the concentrate was analyzed by HPLC according to the method of Ko et al [29]. The total ginsenoside content and ginsenoside composition of each sample were analyzed three times. The pure ginsenoside standards (99% purity) used in this experiment were purchased from Chromadex (St. Santa Ana, CA, USA) and Ambo Institute (Seoul, South Korea). The HPLC instrument was Waters 1525 binary HPLC system (Boston, MA, USA), and the column was Eurospher 100-5 C18 (Knauer, 250 x 3mm, Germany). Mobile phase was the mixture of acetonitrile and distilled water (J.T. Baker, NJ, and USA).

The content of acetonitrile was sequentially increased from 17 % to 25 % (25 min), 24 % to 40 % (50 min), 40 % to 60 % (105 min), 60 % to 100 %(110 min), 100 % to 100 % (120 min) and adjusted from 100 % to 17 % (125 min, stay for 10 min) again in the last. Operating temperature was set to room temperature, and the flow rate was 0.8 mL/min. The elution profile on chromatogram was obtained by using a UV/VIS detector at 203 nm (Boston, MA, USA).

2.4. Statistical Analysis

Values are represented as mean ± standard deviation (SD) of triplicate. Statistical differences were determined by one-way analysis of variance (ANOVA) followed by Duncan's multiple range test. Values with different letters are significantly different, $p<0.05$.

3. Result

3.1. Preparation of Microwave-heated Ginseng

To reach the aims of this study, microwave oven has been used to heat rapidly and dry fresh ginseng. In general, ginseng is harvested at 6 year to perform the manufacturing process of red ginseng [5,30]. Thus, 6 years of age ginseng is used in all experiments. Prior to perform the experiment, fresh ginseng was washed with distilled water and dried at room temperature (Figure 1).

Fresh ginseng was treated for 10, 15, 30, 40 or 60 min in a microwave (700 W) and dried overnight in a dry oven at 40°C. Microwave-heated ginseng (MHG) was then allowed to cool to room temperature. Fresh ginseng and MHG were extracted as described in Materials and Methods. All of crude extracts were stored at 4 °C until use.

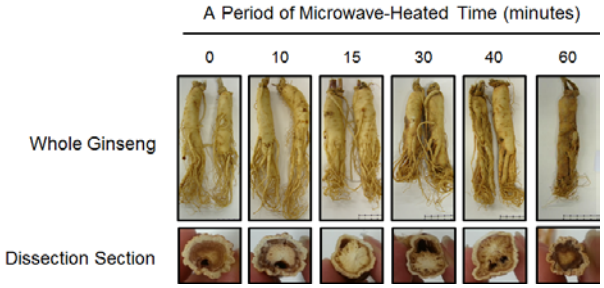

Figure 2. Change of appearance of fresh ginseng by microwave heating.

3.2. Phenotype Analysis of Microwave-heated Ginseng

The high temperature-induced browning of ginseng has been shown to contain a large number of bioactive ginsenoside [31,32]. As shown in Figure 2, fresh ginseng has a yellow color, while microwave heating altered the ginseng color turn into brown color in microwave heating time dependent manner. Moreover, the dissection section of ginseng revealed that inside color of ginseng was started the color change to browning at microwave heating for 30 min. After longer exposure (60 min) of microwave heating, inside of ginseng was significantly elevated into dark brown color compared to fresh ginseng.

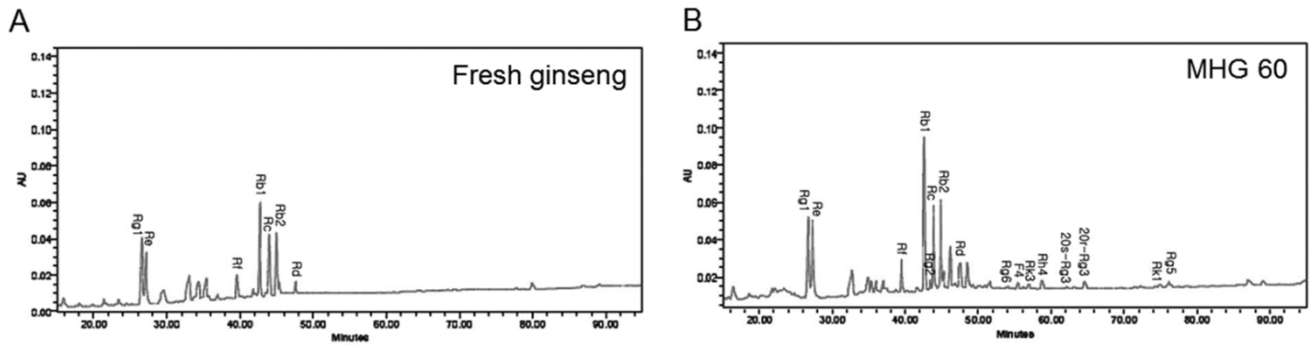

Figure 3. Change of ginsenoside composition after microwave heating. Typical ginsenoside chromatogram of fresh ginseng (A) and MHG 60 (B). FG: Fresh ginseng; MHG 60: fresh ginseng treated with microwave-heated for 60 minutes

3.3. Analysis of Ginsenoside Composition in Microwave-heated Ginseng

To investigate whether microwave heating-induced browning of ginseng affect the composition of ginsenoside in ginseng, we analyzed the ginsenoside contents by using HPLC in fresh ginseng and MHG. We found that fresh ginseng have ginsenosides Rg1, Re, Rf, Rb1, Rc, Rb2, and Rd [33], while MHG also include other member of ginsenoside such as Rg2, Rg6, F3, Rk3, Rh4, 20s-Rg3, 20f-Rg3, Rk1, and Rg5 as shown in Figure 3.

In particular, total amount of PPD were dramatically increased after microwave heating for 40 min. Ginsenosides Rb1, Rb2 and Rc were increased almost two fold in 40 min MHG compared to fresh ginseng (Table 1). In addition, ginsenosides 20S-Rg3 and 20R-Rg3 were observed after microwave heating for 15 min and then were subsequently raised up to two fold at 40 and 60 min incubation with microwave heating.

Table 1. The composition of protopanaxadiol (PPD) ginsenoside in fresh ginseng and microwaved-heated ginseng

	Protopanaxadiol (PPD)					
	Microwave processed drying raw ginseng (%,w/w)					
	FG [a)]	MHG10 [b)]	MHG15 [b)]	MHG30 [b)]	MHG40 [b)]	MHG60 [b)]
Rb_1	0.405±0.006^{c}	0.262±0.001^{d}	0.441±0.007^{bc}	0.503±0.006^{b}	0.718±0.099^{a}	0.507±0.039^{b}
Rb_2	0.233±0.005^{b}	0.138±0.001^{c}	0.102±0.001^{c}	0.128±0.005^{c}	0.344±0.054^{a}	0.251±0.016^{b}
Rc	0.298±0.006^{b}	0.188±0.020^{d}	0.232±0.005^{cd}	0.240±0.002^{c}	0.453±0.064^{a}	0.271±0.012^{bc}
Rd	0.046±0.001^{c}	0.051±0.001^{c}	0.052±0.001^{c}	0.100±0.001^{b}	0.175±0.036^{a}	0.105±0.010^{b}
20S-Rg3			0.007±0.000^{b}	0.009±0.001^{ab}	0.013±0.003^{a}	0.012±0.005^{ab}
20R-Rg3			0.028±0.001^{b}	0.029±0.003^{b}	0.035±0.006^{ab}	0.039±0.005^{a}
Rg5				0.009±0.000^{b}	0.053±0.010^{a}	0.018±0.001^{b}
Rk1				0.001±0.000^{b}	0.011±0.002^{a}	0.002±0.000^{b}

* FG : Fresh ginseng, MHG10 : fresh ginseng treated with microwave-heated for 10 minutes MHG15 : fresh ginseng treated with microwave-heated for 15 minutes, MHG30 : fresh ginseng treated with microwave-heated for 30 minutes, MHG40 : fresh ginseng treated with microwave-heated for 40 minutes, MHG60 : fresh ginseng treated with microwave-heated for 60 minutes, Values represent the mean±S.E. (n=3)

We also found that ginsenosides Rg5 and Rk1 were extracted from 30, 40, and 60 min of microwave-heated ginseng. Consistently, ginseng-exposed with microwave heating for 40 min contained a large amount of ginsenosides Rg5 and Rk1 compared with other microwave heating conditions.

Table 2. The composition of protopanaxatriol (PPT) ginsenoside in fresh ginseng and microwaved-heated ginseng

	Protopanaxatriol (PPT)					
	Microwave processed drying raw ginseng (%,w/w)					
	FG [a)]	MHG10 [b)]	MHG15 [b)]	MHG30 [b)]	MHG40 [b)]	MHG60 [b)]
Re	0.233±0.002^{c}	0.176±0.002^{d}	0.265±0.008^{c}	0.375±0.003^{b}	0.441±0.064^{a}	0.269±0.029^{c}
Rf	0.091±0.002^{c}	0.053±0.002^{d}	0.113±0.002^{bc}	0.123±0.001^{c}	0.193±0.035^{a}	0.100±0.008^{bc}
Rg_1	0.227±0.004^{b}	0.114±0.000^{c}	0.220±0.005^{b}	0.205±0.001^{b}	0.268±0.043^{a}	0.207±0.015^{b}
Rg_2			0.164±0.005^{b}	0.221±0.002^{a}	0.102±0.013^{c}	0.021±0.000^{d}

* FG : Fresh ginseng, MHG10 : fresh ginseng treated with microwave-heated for 10 minutes MHG15 : fresh ginseng treated with microwave-heated for 15 minutes, MHG30 : fresh ginseng treated with microwave-heated for 30 minutes, MHG40 : fresh ginseng treated with microwave-heated for 40 minutes, MHG60 : fresh ginseng treated with microwave-heated for 60 minutes, Values represent the mean±S.E. (n=3).

Ginsenosides Re and Rf in PPT group were also increased approximately two fold in 40 min MHG compared with fresh ginseng (Table 2), while Rg1 was slightly elevated after microwave heating for 40 min. Large amount of Rg2 was also detected at 30 min MHG. Interestingly, MHG were included unique form of ginsenoside such as Rg6, Rh4, Rk3 and F4 (Table 3). These ginsenoside components were significantly increased after microwave heating for 40 min ginseng.

Table 3. The composition of other ginsenosides in fresh ginseng and microwaved-heated ginseng

	Unclassified ginsenoside metabolites					
	Microwave processed drying raw ginseng (%,w/w)					
	FG [a)]	MHG10 [b)]	MHG15 [b)]	MHG30 [b)]	MHG40 [b)]	MHG60 [b)]
Rg6				0.001±0.000[c]	0.003±0.000[a]	0.001±0.001[b]
Rh4			0.00140.000[d]	0.004±0.000[c]	0.017±0.002[a]	0.009±0.001[b]
Rk3			0.001±0.000[c]	0.002±0.000[c]	0.011±0.002[a]	0.005±0.000[b]
F4			0.002±0.000[c]	0.003±0.001[c]	0.013±0.003[a]	0.009±0.002[b]

* FG : Fresh ginseng, MHG10 : fresh ginseng treated with microwave-heated for 10 minutes MHG15 : fresh ginseng treated with microwave-heated for 15 minutes, MHG30 : fresh ginseng treated with microwave-heated for 30 minutes, MHG40 : fresh ginseng treated with microwave-heated for 40 minutes, MHG60 : fresh ginseng treated with microwave-heated for 60 minutes, Values represent the mean±S.E. (n=3).

4. Discussion

The aim of this study is to develop a convenient method for ginseng process using microwave which is able to increase the bioactive ginseng components. Microwave has been commonly used a kitchen appliance manufactured for the purpose of rapid drying, heating, and cooking food [34]. Microwave heating rapidly reaches approximately 100°C in short period of time and initiates the evaporating surface and inside of materials moisture [35]. Many studies have shown that a microwave heating application is able to modify the composition of raw materials due to the microwave-mediated high temperature and drying as a food processing [36,37,38]. Ren et al suggested that the composition change of ginsenoside in ginseng during microwave heating is similar to high temperature steaming processed ginseng constituents [39].

In present study, we showed that rapid microwave heating stimulated a yellow to brown color change in ginseng and subsequently altered the composition of ginsenosides in MHG.

We have previously showed that rapid microwave heating increase a number of ginsenoside contents in fresh ginseng berry [40]. It includes elevated contents of ginsenoside such as Rg2, Rg6, Rh1, and F4 compared with fresh ginseng berry. In addition, we also observed that rapid microwave heating enhance to synthesize the unique form of ginsenosides Rh2 and Rg3, which are not found in fresh ginseng berry.

In this study, we also observed that a large amount of PPD was significantly increased after microwave heating at 40 min. Rb1, Rb2, Rb3, Rd, Rg3, Rh2, Rg5, and Rk1 are a member of PPD group in ginseng. In particular, red ginseng-derived PPD such as Rg3, Rg5, and Rk1 have a strong biomedical function. Ginsenoside Rg3 present in red ginseng has been shown to prevent the progression of cancer, inflammation, and metabolic disease [41,42,43,44]. Ginsenosides Rg5 and Rk1 as major components in red ginseng have also showed a beneficial effect of inflammation, cognitive disorder, diabetes, and tumor progression [45,46,47,48]. After microwave-heated ginseng for 40 min were dramatically enhanced to synthesize the Rg3, Rg5, and Rk1 in our data. However, 60 min treatment of microwave heating decreased total amount of Rg3, Rg5, and Rk1 compared with 40 min MHG.

PPT group were also modified its composition of ginsenoside due to the microwave heating treatment. Microwave heating distributed to alter the total amount of ginsenosides Re and Rg1 until 40 min treatment, while longer exposure (60 min) of microwave heating consistently caused to present the small amount of ginsenosides Re and Rg1 compared with 40 min treatment. Re has been showed to regulate the human intestinal microbiota population [49] and to sensitize the insulin recognition through modulation of mitogen activated phosphatase kinase (MAPK) and nuclear factor-kB signaling pathway [50]. Ginsenoside Rg1 acts as a functional ligand of glucocorticoid receptor [51] and increases the immunomodulation activity in vivo [52].

Our result showed that the composition modification of ginsenoside is due to the rapid microwave heating and indicated a proper treatment time of microwave heating stimulated the synthesis of bioactive ginsenosides. In particular, ginseng treated with microwave heating for 40 min enhance to produce the ginsenoside products which has been specifically isolated from red ginseng. Previous report has been shown microwave heating enhance the unique form of ginsenosides with a various microwave incubation times [53]. Our result is slightly different fresh ginseng incubation time in microwave compare to other reports [35,39]. A period of microwave heating can vary depending on the material size, surface area and its moisture contents [54].

In conclusion, we proposed that rapid microwave heating approach alters ginsenoside composition in ginseng similar to traditional preparation method of red ginseng. Although further study need to perform to make in mass quantities of MHG, our proposed method might bring benefits to produce high quantity of bioactive ginsenosides with a convenient and highly cost effective process in ginseng industry.

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