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Metabolite profiling approach for assessing the effects of colored light-emitting diode lighting on the adventitious roots of ginseng (*Panax ginseng* C. A. Mayer)

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Abstract

Metabolome analysis was carried out to evaluate the effects of light-emitting diode (LED) spectra on the metabolic processes of ginseng (*Panax ginseng* C. A. Mayer) adventitious roots. In total, 35 hydrophilic and 11 lipophilic metabolites were identified in ginseng roots irradiated with red (630 nm), blue (465 nm) LED light or fluorescent lamp (FL) light, by gas chromatography–time-of-flight mass spectrometry. Principal components analysis results using the 46 metabolites showed differentiation between the metabolomes of ginseng roots irradiated with red LED, blue LED, and FL light, indicating that metabolic changes were occurred in the ginseng roots by light spectral quality. The corresponding loading indicated that LED light-irradiated ginseng roots had higher sucrose and lower amino acids compared to FL-irradiated ginseng roots. The quantitative results revealed that ginseng roots irradiated with blue LED light had higher concentrations of α-tocopherol and β-amyrin, as well as phenolic acids compared with FL-irradiated ginseng roots. This is the first study to determine the comprehensive metabolic changes in response to LED light in ginseng adventitious roots and to demonstrate the utility of the metabolite profiling approach employed in this study for detecting environmental effects on the plant metabolome.

Keywords: light-emitting diode; lipophilic compounds; metabolomics; *Panax ginseng*; phenolic acids; principal components analysis.
Abbreviations: FL- fluorescent lamp; GC-TOFMS- gas chromatography–time-of-flight mass spectrometry; LED- light-emitting diode; TBDMCS- *tert*-butyldimethylchlorosilane; MSTFA- *N*-methyl-*N*-trimethylsilyltrifluoroacetamide; MTBSTFA- *N*-(*tert*-butyldimethylsilyl)-*N*-methyltrifluroacetamide; PCA- principal components analysis.

Introduction

Roots from ginseng (*Panax ginseng*), an herbal plant, have been used extensively as medicine and functional food for thousands of years. The anti-oxidative, immunomodulatory, and neuroprotective properties of ginseng have been demonstrated in numerous studies that mainly focused on ginsenosides as functional components. However, other substances such as phenolic compounds, polyacetylene, and alkaloids have recently received attention for their various pharmacological activities (Jung et al., 2002; Block and Mead, 2003; Radad et al., 2006; Lim et al., 2010). Since ginseng production is difficult due to its long cultivation and susceptibility to disease, developing ways to improve the quality of ginseng is very important. Ali et al. (2006) and Thanh et al. (2006) attempted to increase ginsenoside production by supplying copper and oxygen while Yu et al. (2005) investigated the optimal temperature and light conditions for biomass accumulation and ginsenoside production. Light is one of the most important factors affecting plant development and physiology as the sole energy source. With the advent of light-emitting diodes (LEDs) with the potential to produce high-fluence-rate lights at specific wavelengths, studies regarding the impact of different light spectra on physiological plant processes have recently increased (Yu et al., 2005; Park et al., 2012a). Although these studies have also been applied to ginseng, they have concentrated on ginsenoside production and therefore no overall metabolite analysis has been conducted to explore the effects of light spectral quality on metabolic processes. This study aimed to evaluate the effects of specific emission spectra from different LED light sources on metabolic processes in ginseng adventitious roots using gas chromatography–time-of-flight mass spectrometry (GC-TOFMS). This technique has been shown to be useful for the rapid and highly sensitive detection of plant metabolites from the central pathways of primary metabolism (Carreno-Quintero et al., 2012). The metabolite profiles obtained from ginseng roots irradiated with different LED light spectra were analyzed by principal components analysis (PCA). In addition, absolute concentrations of phenolic acids and lipophilic compounds including policosanols, tocopherols, and phytosterols were quantified in ginseng roots.

Results and discussion

Contents of phenolic acids in ginseng adventitious roots irradiated with LED lights

In plants, the synthesis of secondary metabolites is strongly influenced by surrounding environmental factors such as temperature, water, and light (Zhao et al., 2005). Phenolic

Table 1. Contents (μg/g on dry weight basis) of soluble and insoluble phenolic acids in ginseng (*Panax ginseng*) adventitious roots irradiated with different light emission spectra.

	Soluble			Insoluble			Total		
	FL	Red (630 nm)	Blue (465 nm)	FL	Red (630 nm)	Blue (465 nm)	FL	Red (630 nm)	Blue (465 nm)
p-Hydroxybenzoic acid	31.76±2.66a	30.76±3.67a	33.28±1.31a	86.81±10.90a	55.69±0.46c	70.83±1.22b	118.57±12.10	86.45±3.38	104.12±2.41
Vanillic acid	11.15±0.55b	10.38±0.35c	15.86±0.04a	21.94±0.41b	16.55±0.66c	25.23±1.06a	.33.09±0.93	26.93±1.00	41.09±1.10
Syringic acid	0.78±0.10b	0.54±0.12b	2.02±0.19a	2.84±0.08b	1.43±0.14c	4.40±0.51a	3.62±0.17	1.97±0.25	6.42±0.68
p-Coumaric acid	29.04±3.22c	80.38±19.07b	132.85±23.68a	46.82±6.04c	105.86±4.43b	181.20±28.56a	75.87±7.98	186.25±23.09	314.05±54.92
Ferulic acid	97.21±7.80b	109.41±13.56b	266.36±39.62a	222.33±24.77b	203.41±13.09b	320.53±44.83a	319.54±31.91	312.82±18.74	586.89±84.19
Sinapic acid	12.34±0.20b	12.53±0.86b	16.14±0.65a	19.60±2.68a	14.48±0.98b	21.64±1.19a	31.94±2.74	27.01±1.74	37.78±1.64
Sum	182.30±13.56	244.00±37.62	466.52±65.49	400.33±44.89	397.43±19.75	623.83±77.38	582.62±50.92	641.43±41.34	1090.35±135.81

Different letters represent significant ($p < 0.05$) differences between means according to ANOVA combined with Duncan's multiple range test. Each value represents the mean ± standard deviation ($n = 3$). FL=White fluorescent lamp.

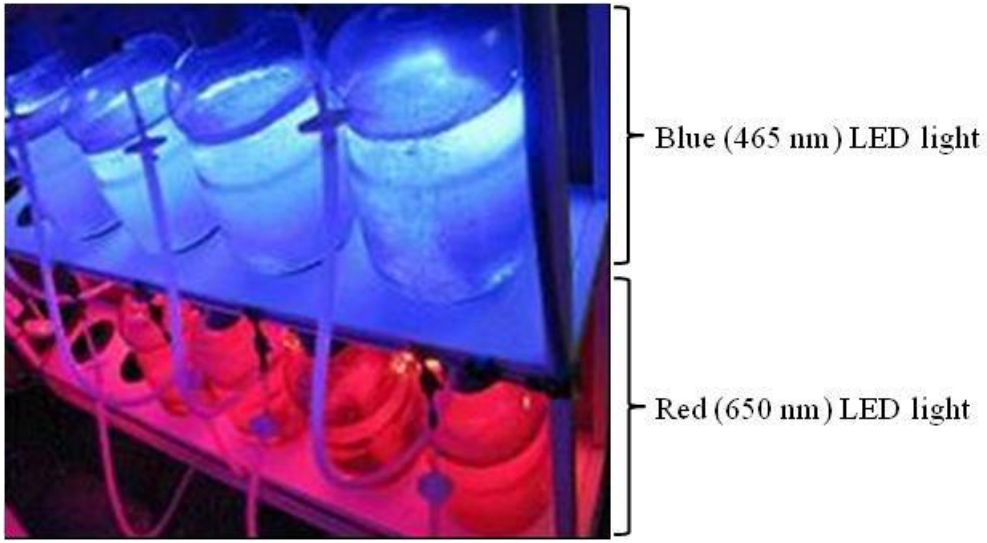

Fig 1. Image of ginseng (*Panax ginseng*) adventitious roots cultivated under light-emitting diode (LED) irradiation. The LED treatments were selected to provide blue (465 nm, upper) and red (630 nm, lower) light in the spectra.

compounds comprise important secondary metabolites with many physiological functions including antioxidant, antitumor, and anti-inflammatory activities as radical scavengers (Rice-Evans et al., 1997; Panda et al., 2011). In this study, the adventitious roots of ginseng (*Panax ginseng*) were cultivated under red (630 nm) or blue (465 nm) LED light irradiation for 5 weeks to determine the effects of different light spectra on phenolic acid production (Fig. 1). Six types of phenolic acid were identified by GC-TOFMS (Table 1). The insoluble (bound form) levels were higher than the soluble (free and esterified forms) levels in all ginseng samples. The major portion of phenolic acids in ginseng roots consisted of ferulic, *p*-coumaric, and *p*-hydroxybenzoic acids. Compared to white FL-irradiated ginseng roots, roots irradiated with two different LED lights had higher concentrations of total phenolic acids, which increased by 87% in blue LED light-irradiated ginseng roots. A significant increase was presented only in the *p*-coumaric acid content in red LED light ginseng roots, while *p*-coumaric and ferulic acids were markedly increased in blue LED light-irradiated ginseng roots. These results were similar to those reported in previous studies on the impact of LED illumination in which blue LED light irradiation resulted in an increase in total phenolic levels of barley leaf and sprouted seeds of lentil and wheat (Lee et al., 2010; Samuolienė et al., 2011) indicating that LED light irradiation was carried out accurately in this study.

Contents of hydrophilic and lipophilic metabolites in ginseng adventitious roots irradiated with LED lights

Photosynthetic organisms use light energy to drive the synthesis of sugar and other organic compounds such as lipids and proteins that are used to provide energy for the organism. Therefore, the metabolites synthesized were directly involved in the organism's normal growth, development, and phenotype (von Schaewen et al., 1990). To investigate the effects of different light spectra on metabolite content of ginseng roots, we examined the profiles of hydrophilic and lipophilic metabolites in FL, red, and blue LED light-irradiated ginseng roots. GC-TOFMS was used to analyze low-molecular-weight metabolites, and ChromaTOF software (LECO) was used to assist with peak locations. Peaks were identified by comparison with reference compounds and the use of an in-house library (Kim et al., 2013a). In total, 35 hydrophilic (i.e., 17 amino acids, 11 organic acids, 4 sugars, 2 sugar alcohols, and 1 amine) and 11 lipophilic metabolites (i.e., 6 fatty acids, 4 phytosterols, and 1 tocopherol) were detected in ginseng roots (Fig. 2). Quantification was performed using selected ions as described in Table (2). The quantitative calculations of all analytes were based on the peak area ratios relative to that of the IS. Data for the 46 metabolites were subjected to PCA to examine differences in metabolite profiles between samples that were cultivated with different LED light irradiation (Fig. 3). The first and second components explained 51.3% and 28.1% of the variation, and the metabolomes of FL light-irradiated ginseng roots were completely separated from the metabolomes of LED light-irradiated ginseng roots by component 1. This variation was mainly attributable to sucrose and amino acids of which the corresponding loading was positive for sucrose and negative for all amino acids with the exception of glutamic and pyroglutamic acids. The loading indicated that sucrose was higher in red and blue LED light-irradiated ginseng roots than in FL light-irradiated ginseng roots, and most amino acids were lower in LED light-irradiated ginseng roots than in FL light-irradiated ginseng roots. Sucrose is a primary product of photosynthesis and its content in plant is directly involved with the efficiency of photosynthesis and productivity of related metabolite biosynthesis such as anthocyanin and carotenoids. The significant relationship between sucrose and carbon-rich secondary metabolites were demonstrated in our recent studies in which the black rice containing relatively high flavonoids and phenolic acids, had higher concentration of sucrose compared to the white rice (Kim et al., 2010, 2013b; Park et al., 2012b). In addition, in component 1, the corresponding loading was positive for all measured tocopherol and phytosterols, and negative for all fatty acids. This result is the first to reveal overall metabolic changes in response to specific emission spectra from different LED light sources in ginseng roots, demonstrating the usefulness of this metabolite profiling approach in studies investigating the compositional changes of core primary metabolites. To confirm the absolute quantity of lipophilic metabolites, the three types of ginseng roots samples were extracted by alkaline hydrolysis to release bound lipophilic compounds. Identification and quantification of the detected compounds were performed using methods reported by our group (Kim et al., 2012). Thirteen lipophilic compounds (i.e., 6 policosanols, 5 phytosterols, and 2 tocopherols) were identified in ginseng roots (Table 3). The most notable findings were in the α-tocopherol and β-amyrin content, which was 2.54- and 1.94-fold higher in blue LED light-irradiated ginseng roots compared to those in FL light-irradiated ginseng roots. α-Tocopherol and β-amyrin have been found to have anti-oxidative effects *in vivo* (Yamada et al., 1999; Oliveira et al., 2005).

Materials and methods

Samples and Chemicals

Ginseng (*Panax ginseng* C. A. Mayer) adventitious roots were obtained from the Oriental Medicinal Materials & Processing Department, Kyung Hee University, Korea. All chemicals used in this study were analytical grade. Methanol and chloroform, which were used as extraction solvents, were purchased from J.T. Baker (Phillipsburg, NJ, USA). Ribitol, 5α-cholestane, sinapic acid, vanillic acid, eicosanol, heneicosanol, docosanol, tricosanol, tetracosanol, octacosanol, campesterol, cholesterol, stigmasterol, β-sitosterol, β-amyrin, and *N*-methyl-*N*-trimethylsilyltrifluoroacetamide (MSTFA) were obtained from Sigma Chemical Co. (St. Louis, MO, USA). Methoxyamine hydrochloride was purchased from Thermo Fisher Scientific (Pittsburgh, PA, USA). Syringic, 3,4,5-trimethoxycinnamic, *p*-hydroxybenzoic, ferulic and acetic acids were acquired from Wako Pure Chemical Industries, Ltd. (Osaka, Japan). *p*-Coumaric acid was obtained from MP Biomedicals (Solon, OH, USA). Pyridine and *N*-(*tert*-butyldimethylsilyl)-*N*-methyltrifluroacetamide (MTBSTFA) with 1% *tert*-butyldimethylchlorosilane (TBDMCS) were purchased from Thermo Fisher Scientific. Tocopherols were purchased from Merck (Darmstadt, Germany).

Bioreactor Culture and LED Treatment

Ginseng adventitious roots were cultivated according to the procedure described by Lee et al. (2009). Ginseng roots were cut into 0.5–2.0-cm slices and cultured in SH (Sheck and Hildebrant, 1972) liquid media containing 30 g/l sucrose and 2 mg/l indole-3-butyric acid (IBA); the pH was then adjusted to 5.75–5.80. An airlift bioreactor culture was initiated with 15-L inoculation for 5 weeks. A LED-10M/AHH-BL and LED-10M/HP-R device was used as the LED light source and was manufactured by KM Electronic Supplier (KM1235; Seoul, Korea). The LED treatments were selected to provide red (630 nm) and blue (465 nm) light in the spectra (Fig. 1). For the

Table 2. Metabolites identified in GC-TOFMS chromatograms from ginseng (*Panax ginseng*) adventitious roots extracts.

No.	Compound	RT	RRT	Quantification ion
Hydrophilic compounds				
1	Pyruvic acid	4.56	0.426	174
2	Lactic acid	4.66	0.435	147
3	Alanine	5.15	0.481	116
4	Glycolic acid	6.26	0.585	147
5	Valine	6.37	0.595	144
6	Ethanolamine	6.89	0.644	174
7	Glycerol	6.92	0.647	218
8	Phosphoric acid	6.93	0.648	299
9	Isoleucine	7.15	0.668	158
10	Proline	7.23	0.676	142
11	Glycine	7.29	0.681	174
12	Succinic acid	7.37	0.688	147
13	Glyceric acid	7.47	0.698	147
14	Fumaric acid	7.70	0.720	245
15	Serine	7.75	0.724	204
16	Threonine	7.99	0.746	219
17	*β*-Alanine	8.41	0.786	174
18	Malic acid	8.89	0.831	147
19	Aspartic acid	9.17	0.857	100
20	Methionine	9.22	0.861	176
21	Pyroglutamic acid	9.28	0.867	156
22	4-Aminobutyric acid	9.29	0.869	174
23	Glutamic acid	9.97	0.931	246
24	Phenylalanine	10.09	0.943	218
25	Xylose	10.18	0.951	103
26	Asparagine	10.37	0.969	116
27	Glutamine	11.15	1.042	156
28	Shikimic acid	11.29	1.055	204
29	Citric acid	11.41	1.066	273
30	Quinic acid	11.67	1.090	345
31	Fructose	11.77	1.100	103
32	Galactose	11.90	1.112	147
33	Inositol	13.22	1.236	305
34	Tryptophan	14.06	1.314	202
35	Sucrose	16.16	1.510	217
Lipophilic compounds				
36	Hexadecanoic acid	4.12	0.348	313
37	*cis,cis*-9,12-Octadecadienoic acid	5.21	0.440	337
38	*cis*-9-Octadecadienoic acid	5.23	0.442	339
39	Octadecanoic acid	5.39	0.456	341
40	Eicosanoic acid	6.77	0.572	369
41	Docosanoic acid	8.16	0.690	397
42	*α*-Tocopherol	11.54	0.976	237
43	Campesterol	12.54	1.060	343
44	Stigmasterol	12.73	1.077	394
45	*β*-Sitosterol	13.28	1.123	357
46	*β*-Amyrin	13.63	1.153	218

Numbers represent the compound index for chromatogram peaks shown in Figure 2. RT=Retention time (min). RRT=Relative retention time (retention time of the analyte/retention time of the IS). Quantification ion: specific mass ion used for quantification.

control treatment, the roots were cultivated under white fluorescent lamp for 5 weeks. All cultures were grown under the photon flux density of 24 μmol $m^{-2}s^{-1}$.

Metabolites Analysis

Soluble (free and esterified forms) and insoluble (bound form) phenolic acids were extracted according to the procedure described by Park et al. (2012b) with slight modifications. The powdered samples (0.1 g) were extracted twice by water-based sonication for 5 min at room temperature and incubation at 30°C for 10 min with 1 ml of 85% methanol containing 2 g/l BHA. After centrifugation at 13,000 rpm for 10 min at 4°C, the combined extracts and residue were analyzed to determine the soluble and insoluble phenolic acids, respectively. Fifty microliters of 3,4,5-trimethoxycinnamic acid (100 μg/ml) was added as an internal standard (IS), and the mixture was hydrolyzed with 1 ml 5 N NaOH at 30°C under nitrogen gas for 4 h. Each hydrolyzed sample was adjusted to pH 1.5–2.0 with 6 M HCl, extracted with ethyl acetate, and evaporated in a centrifugal concentrator (CVE-2000; Eyela, Tokyo, Japan). For derivatization, 40 μl MTBSTFA containing 1% TBDMCS and 40 μl pyridine were added to the dried extracts followed by incubation at 60°C for 30 min at a mixing frequency of 1,200

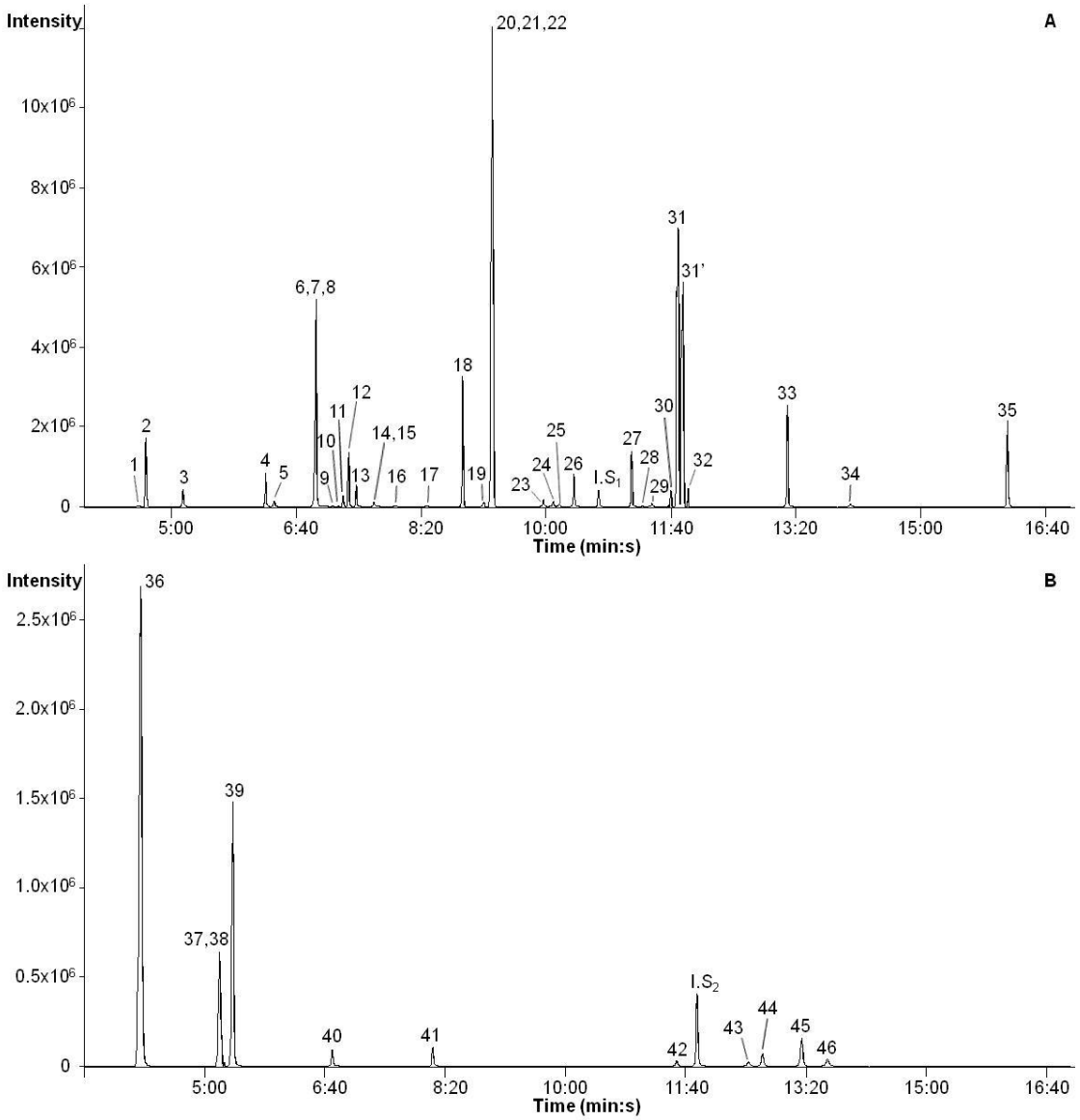

Fig 2. Selected ion chromatograms of hydrophilic (A) and lipophilic (B) metabolites extracted from ginseng (*Panax ginseng*) adventitious roots as MO/TMS derivatives separated on a 30 m × 0.25-mm i.d. fused silica capillary column coated with 0.25 μm CP-SIL 8 CB low bleed. Peak identification: 1, pyruvic acid; 2, lactic acid; 3, alanine; 4, glycolic acid; 5, valine; 6, ethanolamine; 7, glycerol; 8, phosphoric acid; 9, isoleucine; 10, proline; 11, glycine; 12, succinic acid; 13, glyceric acid; 14, fumaric acid; 15, serine; 16, threonine; 17, β-alanine; 18, malic acid; 19, aspartic acid; 20, methionine; 21, pyroglutamic acid; 22, 4-aminobutyric acid; 23, glutamic acid; 24, phenylalanine; 25, xylose; 26, asparagine; 27, glutamine; 28, shikimic acid; 29, citric acid; 30, quinic acid; 31, fructose; 31′, fructose; 32, galactose; 33, inositol; 34, tryptophan; 35, sucrose; 36, hexadecanoic acid; 37, cis,cis-9,12-octadecadienoic acid; 38, cis-9-octadecadienoic acid; 39, octadecanoic acid; 40, eicosanoic acid; 41, docosanoic acid; 42, α-tocopherol; 43, campesterol; 44, stigmasterol; 45, β-sitosterol; 46, β-amyrin; IS_1, internal standard, ribitol; IS_2, internal standard, 5α-cholestane.

rpm using a thermomixer comfort (model 5355; Eppendorf AG, Hamburg, Germany). GC-TOFMS procedure was performed, according to the method previously reported (Park et al., 2012b). Policosanols, tocopherols, and phytosterols were analyzed according to the procedure described by Kim et al. (2012). Polar and non-polar metabolite profiling were performed as described previously (Kim et al., 2013a).

Statistical Analysis

All analyses were performed at least in triplicate. The experimental data were analyzed by analysis of variance (ANOVA) and significant differences among the means were determined by Duncan′s multiple-range test (SAS 9.2; SAS Institute, Cary, NC, USA). Quantification data acquired from GC-TOFMS were subjected to PCA (SIMCA-P version 12.0; Umetrics, Umeå, Sweden) to evaluate differences among groups of multivariate data. The PCA output consisted of score plots to visualize the contrast between different samples and loading plots to explain the cluster separation.

Conclusion

This study demonstrates the effects of different light spectra on metabolite profiles of ginseng adventitious roots. Based on

Table (3). Contents (mg/100 g on dry weight basis) of lipophilic compounds in ginseng (*Panax ginseng*) adventitious roots irradiated with different light emission spectra.

	FL	Red (630 nm)	Blue (465 nm)
Policosanols			
C20-ol	216.85±81.37a	261.84±46.93a	146.23±29.71a
C21-ol	1.35±0.91a	1.70±0.49a	0.82±0.38a
C22-ol	8.44±6.37a	11.11±4.10a	4.11±2.65a
C23-ol	5.41±0.56a	5.78±0.35a	5.33±0.31a
C24-ol	11.43±0.74a	11.49±0.37a	10.89±0.28a
C28-ol	11.12±0.89a	10.30±0.32a	10.01±0.58a
Sum	254.60±90.43	302.22±51.80	177.40±32.94
Tocopherols			
α-Tocopherol	8.64±3.44b	4.34±0.92b	21.96±1.76a
β-Tocopherol	ND	ND	0.17±0.01
Sum	8.64±3.44	4.34±0.92	22.13±1.76
Phytosterols			
β-Amyrin	61.28±8.38b	57.22±2.40b	119.37±13.90a
Campesterol	64.43±8.86a	73.99±12.67a	38.84±2.60b
Cholesterol	2.30±0.41b	3.63±0.27a	3.19±0.60ab
β-Sitosterol	700.43±143.54a	840.30±136.42a	795.20±44.71a
Stigmasterol	449.21±51.50ab	538.20±89.52a	383.15±59.28b
Sum	1277.66±211.20	1513.35±239.79	1339.75±119.78

Different letters represent significant ($p < 0.05$) differences between means according to ANOVA combined with Duncan's multiple range test. Each value represents the mean ± standard deviation ($n = 3$). FL=White fluorescent lamp. C20-ol=eicosanol. C21-ol=heneicosanol. C22-ol=docosanol. C23-ol=tricosanol. C24-ol=tetracosanol. C28-ol=octacosanol. ND=Not detected.

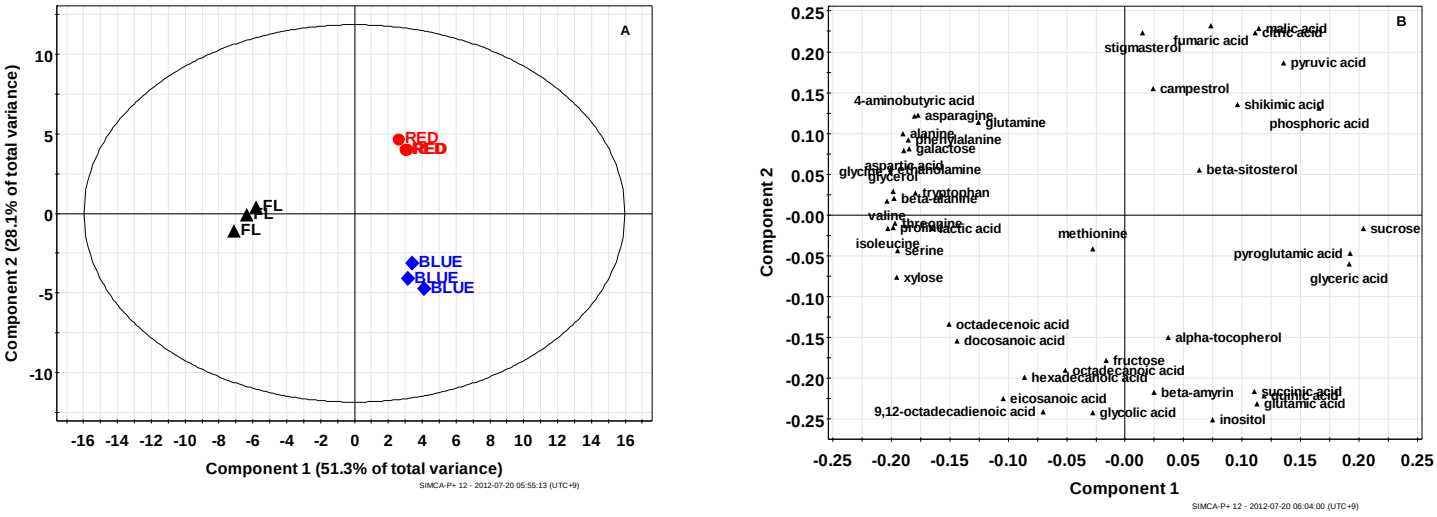

Fig 3. Score (A) and loading (B) plots of principal components 1 and 2 of the PCA results obtained from the data on 46 metabolites in ginseng (*Panax ginseng*) adventitious roots irradiated with different LED lights. FL, red, and blue indicate ginseng roots irradiated with white fluorescent lamp, red (650 nm) LED light, and blue (465 nm) LED light, respectively.

PCA results using 46 metabolites from the FL, red, and blue light-irradiated ginseng roots, a significant difference was observed in the metabolite composition of sucrose, amino acids, fatty acids, tocopherols, and phytosterols. The blue light-irradiated roots had high *α*-tocopherol and *β*-amyrin levels and also contained high phenolic acid levels compared to FL and red light-irradiated roots. The results of this study suggest that metabolite profiling combined with chemometrics can be a powerful tool for detecting environmental effects on the plant metabolome. Since *α*-tocopherol, *β*-amyrin, and phenolic acids have received attention as health-promoting substances due to their antioxidant activities, blue light could be a useful source for the production of ginseng roots with higher nutritional value.

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