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Research Article

Method development for simultaneous analytical method for ten ginsenosides in soft-gel dietary supplements containing *Panax* spp. by LC-MS/MS

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Abstract

A liquid chromatography coupled with tandem mass spectrometry (LC-MS/MS) method was developed for the simultaneous quantification of ginsenosides Rb1, Rb2, Rc, Rd, Re, Rf, Rg1, Rg3, notoginsenoside R1 and majonoside R2 in dietary supplement products containing ginseng. A Waters ACQUITY UPLC BEH C18 column (100 mm × 2.1 mm, 1.7 µm) was employed as the separation column and maintained at 40°C during analysis. The mobile phase consisted of 0.1% formic acid and acetonitrile, delivered under an optimized gradient program. Detection was by tandem mass spectrometry using electrospray ionization in the positive ion mode and multiple reaction monitoring (MRM). The sample were defatted with hexane before extraction with 50% methanol at 75°C for 30 min by sonication. The method was validated following AOAC guidelines and Commission Decision 2002/657/EC. The results demonstrated good specificity, linearity over the range of 100 - 2000 ng/mL, the detection limit and quantitative limit of the method are 1.43 - 1.85 and 4.18 - 5.41 µg/g. The validated method was successfully applied to determine ginsenoside content in ten different ginseng-based dietary supplements available on the Vietnamese market.

Keywords: *ginsenoside, dietary supplements, ginseng, LC-MS/MS.*

1. INTRODUCTION

The genus *Panax*, belonging to the family Araliaceae, comprises several well-known plant species that have been widely used in traditional medicine due to their significant pharmacological properties. Among them, the species most commonly available on the Vietnamese market include *Panax ginseng* (Korean ginseng), *Panax notoginseng* (Tienchi ginseng), *Panax quinquefolius* (American ginseng), and *Panax vietnamensis* (Vietnamese ginseng). These species are considered rare and high-value medicinal materials and are extensively utilized as foods, dietary supplements, and herbal medicines in various forms, such as ginseng-infused alcohol and oral dosage forms [1]. Clinical and pharmacological studies have demonstrated that most of their bioactivities are primarily attributed to ginsenosides, a major group of bioactive constituents in ginseng, which have been reported to exhibit antioxidant, anti-inflammatory, and antimicrobial activities, as well as protective effects against cardiovascular diseases, obesity, and diabetes [1, 2].

The quality of *Panax*-derived medicinal materials and related products is commonly evaluated based on the content of characteristic ginsenosides. For example, ginsenosides Rb1, Re, Rf, and Rg1 are widely used as quality markers for Korean ginseng [3-6]; Rb1, Rg1, and Rg3 for red ginseng products [7]; Rb1, Rb2, Rc, Rd, Re, and Rg1 for American ginseng [8-10]; Rb1, Rg1, and notoginsenoside R1 for *P. notoginseng* [11]; and Rb1, Rg1, together with majonoside R2, for Vietnamese ginseng (*P. vietnamensis*) [12].

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In recent years, the demand for dietary supplements containing *Panax*-derived medicinal materials has increased substantially. However, the analysis of ginsenosides in dietary supplement matrices remains highly challenging. These challenges arise from the structural complexity of ginsenosides, their generally low concentrations in finished products, and potential interactions with other components present in complex matrices. Conventional analytical techniques, such as high-performance liquid chromatography (HPLC), have been widely applied for ginsenoside determination; nevertheless, they often suffer from limited sensitivity and insufficient chromatographic resolution for structurally similar compounds, including ginsenosides Rb1, Rb2, Rc, Rd, Re, Rg1, Rg3, notoginsenoside R1, and majonoside R2. These limitations are particularly pronounced for soft capsule dietary supplements, which are characterized by high contents of oils, waxes, and additional herbal ingredients, further complicating sample preparation and chromatographic analysis using HPLC-based methods. Therefore, the development of an advanced analytical approach capable of simultaneously determining multiple ginsenosides in soft capsule dietary supplements is essential to improve quantitative performance and analytical reliability, thereby enabling accurate quality evaluation and differentiation of ginseng-containing products.

In this study, a liquid chromatography-tandem mass spectrometry (LC-MS/MS) method was selected for the simultaneous determination of ten ginsenosides (Rb1, Rb2, Rc, Rd, Re, Rf, Rg1, Rg3, notoginsenoside R1, and majonoside R2) in selected ginseng-containing dietary supplements. This method not only enables rapid and effective quality control of commercial products but also contributes to the establishment of analytical benchmarks and quality management frameworks for dietary supplements currently available on the Vietnamese market.

2. MATERIALS AND METHODS

2.1. Materials and equipment

2.1.1. Equipment

The study employed a high-performance liquid chromatography system coupled with a triple quadrupole tandem mass spectrometer (LC-MS/MS), H-Class-Xevo TQD (Waters, USA). Supporting laboratory equipment included an Elma ultrasonic bath and a Hermle Z326K centrifuge, which were used throughout sample preparation and analysis.

2.1.2. Study samples

The study samples included softgel capsules of dietary supplements containing species of the genus Panax, including *Panax ginseng, Panax notoginseng, Panax vietnamensis*, and *Panax quinquefolius*. These samples were purchased in Hanoi.

Based on a review of the ingredient compositions of *Panax*-containing soft capsule dietary supplements and other herbal ingredients commonly co-formulated with *Panax* species as specified in the Essential Medicines List under Circular No. 28/2024/TT-BYT of the Ministry of Health, a blank matrix was prepared for method development and validation. The blank matrix consisted of a mixture of 1 g each of the following raw materials: Citri Reticulatae Pericarpium, Cimicifugae Rhizoma, Bupleuri Radix, Ziziphi Jujubae Fructus, Cinnamomi Cortex, Zingiberis Rhizoma, Eucommiae Cortex, Acanthopanacis Cortex, Longan Arillus, Lycii Fructus, Cistanches Herba, Rehmanniae Radix, Sophorae Flos, Leonuri Herba, *Ganoderma lucidum*, Mel (*Apis* spp.), Polygalae Radix, Ziziphi Spinosae Semen, *Cordyceps sinensis*, and Taxilli herba. and vitamin E.

2.1.3. Chemicals and reagents

The chemicals used in this study included analytical reference standards supplied by Biopurify (China), namely ginsenoside Rb1 (Lot: PRF24030705, purity 99.8%), ginsenoside Rb2 (Lot: PRF21041223, purity 99.1%), ginsenoside Rc (Lot: PRF24053102, purity 99.4%), ginsenoside Rd (Lot: PRF24030705, purity 99.8%), ginsenoside Re (Lot: PRF24082741, purity 99.7%), ginsenoside Rf (Lot: PRF20040302, purity 98.8%), ginsenoside Rg1 (Lot: PRF24030705, purity 99.8%), ginsenoside Rg3 (Lot: PRF25031844, purity 99.3%), notoginsenoside R1 (Lot: PRF10061702, purity 99.8%), and majonoside R2 (Lot: PV010724, purity 98.1%).

Other reagents included acetonitrile, methanol, and formic acid of LC-MS/MS analytical grade purchased from Merck (Germany). Deionized water was used throughout the study. Stock standard solutions of

ginsenoside Rb1, Rb2, Rc, Rd, Re, Rf, Rg1, Rg3, notoginsenoside R1, and majonoside R2 at a concentration of 10 µg/mL were prepared in methanol and stored at 2 - 8°C. Mixed calibration standard solutions containing the ten ginsenosides at concentrations ranging from 100.0 to 2000 ng/mL were freshly prepared prior to analysis by dilution in methanol-water (1 : 1, v/v).

2.2. Method

2.2.1. Analytical method

LC-MS/MS was employed for the simultaneous determination of ten ginsenosides in dietary supplement samples. This advanced analytical technique offers high sensitivity, accuracy, and selectivity, making it well suited to the simultaneous quantification of multiple ginsenosides in complex dietary supplement matrices.

2.2.2. Sample preparation method

Ultrasonic extraction was selected as the sample preparation method. Based on a review of the literature [14-17], the proposed sample preparation procedure was as follows: the sample was homogenized, and an accurately weighed portion of 0.5 - 2.0 g was transferred into a 50 mL centrifuge tube. A defatting solvent was added, followed by vortex mixing for 5 s and centrifugation at 6000 rpm at 4°C for 5 min. The supernatant was discarded, and an extraction solvent was added to the residue. The mixture was subjected to ultrasonic extraction for 30 min. The extraction was repeated using the optimized extraction volume, and the combined extracts were transferred to a volumetric flask. The extract was then filtered through a 0.45 µm membrane filter and diluted to an appropriate concentration prior to LC-MS/MS analysis.

The investigated parameters were evaluated using a univariate approach on the blank matrix prepared as described in **Section 2.1.2** and spiked with the analytes at a concentration of 5 mg/g. Each parameter was examined independently by varying one factor at a time while keeping all other parameters constant. The specific parameters investigated are described as follows.

Defatting solvents include chloroform, hexane, and diethyl ether. Extraction solvents includes 30% methanol, 50% methanol, 70% methanol, methanol, and ethanol. Extraction volumes are 25 mL, 50 mL, and 100 mL. Each condition was performed in triplicate.

2.2.3. Method validation

Method validation was conducted in accordance with the guidelines of the Association of Official Analytical Collaboration (AOAC, 2016) [13]. The validation parameters included system suitability, specificity, limit of detection (LOD), limit of quantification (LOQ), linearity range and calibration curves, accuracy (evaluated through recovery), and precision (assessed by repeatability, expressed as relative standard deviation, RSD%, at three different concentration levels).

2.2.4. Data processing method

Analytical data were processed using MassLynx software supplied with the Waters LC-MS/MS system, and statistical analyses were performed using Microsoft Excel 2019.

3. RESULTS AND DISCUSSION

3.1. LC-MS/MS analysis condition survey

3.1.1. MS condition optimization

Based on the literature [14] and the chemical structures of the target analytes, MS/MS conditions were investigated using electrospray ionization in positive mode (ESI+) and operated in multiple reaction monitoring (MRM) mode. Individual standard solutions of each analyte at a concentration of 50.0 ng/mL were directly infused into the mass spectrometer without chromatographic separation. The product ion exhibiting the highest signal intensity was selected for quantification, while the second most intense product ion was used for confirmation.

The precursor ions, product ions, and optimized MS/MS parameters for each analyte are summarized in **Table 1**.

Table 1. *Mass spectrometric conditions of ginsenosides*

Analyte	Precursor ion (m/z)	Product ion (m/z)	Collision energy (eV)
Rb_1	1131.5	**365.0**/789.5	56/54
Rb_2	1101.5	**335.0**/789.5	66/58
Rc	1101.5	**335.0**/789.5	58/50
Rd	969.5	**203.0**/789.5	42/50
Re	969.5	**789.5**/203.0	42/50
Rf	823.5	**365.0**/245.0	54/46
Rg_1	823.5	**203.0**/643.5	46/38
Rg_3	807.5	**365.0**/245.5	56/56
R_1	955.9	**203.0**/775.5	52/40
R_2	787.5	**143.0**/439.5	18/20

Note: Bold values- Product ions used for quantification

The results of the MS condition survey presented in **Table 1** show mass overlap between ginsenoside Rb2 and Rc, as well as between ginsenoside Rd and Re. This phenomenon arises from the high structural similarity of these ginsenosides, which differ only in the stereochemical orientation of certain chiral carbon atoms in their molecular structures. Therefore, to enable the simultaneous determination of these four compounds, optimization of the mobile phase gradient is required to ensure adequate chromatographic separation.

3.1.2. LC condition optimization

Based on a review of the literature [14-17] and an evaluation of different mobile phase systems on the LC-MS/MS instrument, chromatographic separation was performed using an Acquity C18 column (100 mm × 2.1 mm, 1.7 µm) from Waters. The survey results are presented in **Table 2**. The performance of each condition was evaluated based on the total signal response of the ten ginsenosides obtained from the analysis of mixed standard solutions at the same concentration.

Table 2. *Results of mobile phase optimization*

Mobile phase	Total signal intensity of ten ginsenosides
Acetonitril - 0.1%Acid formic	13070
Acetonitril - 0.1%Acid acetic	5382
Acetonitril - 0.05%Acid formic	3819
Acetonitril - 0.2%Acid formic	2157
Acetonitril - Water	2802

Based on the comparison of mobile phase systems presented in **Table 2**, the mobile phase consisting of 0.1% formic acid and acetonitrile was selected for subsequent investigations.

From this mobile phase system, a gradient elution program was developed according to the differences in retention behavior and polarity of the ginsenosides in order to enable the simultaneous determination of ten ginsenosides while ensuring adequate chromatographic separation of compounds with identical m/z values. The detailed gradient program is presented in **Table 3**, in which mobile phase A was 0.1% formic acid and mobile phase B was acetonitrile.

***Table 3**. Mobile phase gradient program*

Time (min)	%A	%B
0.0	73	27
7.0	64	36
13.0	62	38
14.0	5	95
15.5	5	95
15.6	73	27
17.0	73	27

The chromatographic conditions were set as follows: a flow rate of 0.4 mL/min, an injection volume of 2 µL, and a column temperature of 40°C. The chromatogram of the mixed standard solution obtained under the optimized conditions is shown in **Figure 1**.

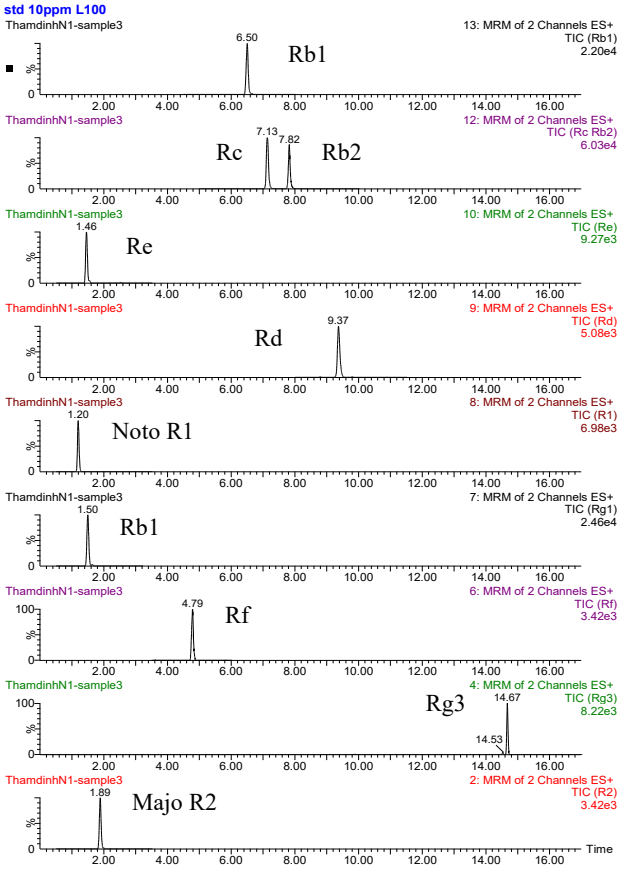

***Figure 1.** Chromatogram of the mixed standard solution of ten ginsenosides*

3.2. Sample preparation optimization

3.2.1. Optimization of defatting solvents

The results of the evaluation of the effect of defatting solvent type, using chloroform, hexane, and diethyl ether, are presented in **Figure 2**.

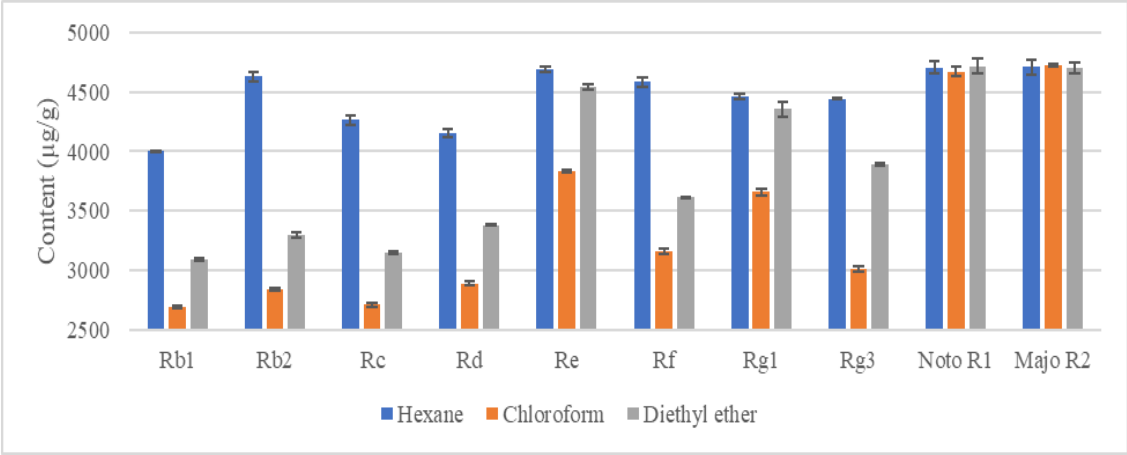

Figure 2. *Results of optimization of defatting solvents*

As shown in **Figure 2**, *n*-hexane provided the highest recovery for the majority of ginsenosides. This result is consistent with previously reported studies on the solubility characteristics of ginsenosides [19].

3.2.2. Optimization of extraction solvent

The evaluation of extraction solvents, including 30% methanol, 50% methanol, 70% methanol, methanol, and ethanol, yielded the ginsenoside contents as presented in **Figure 3**.

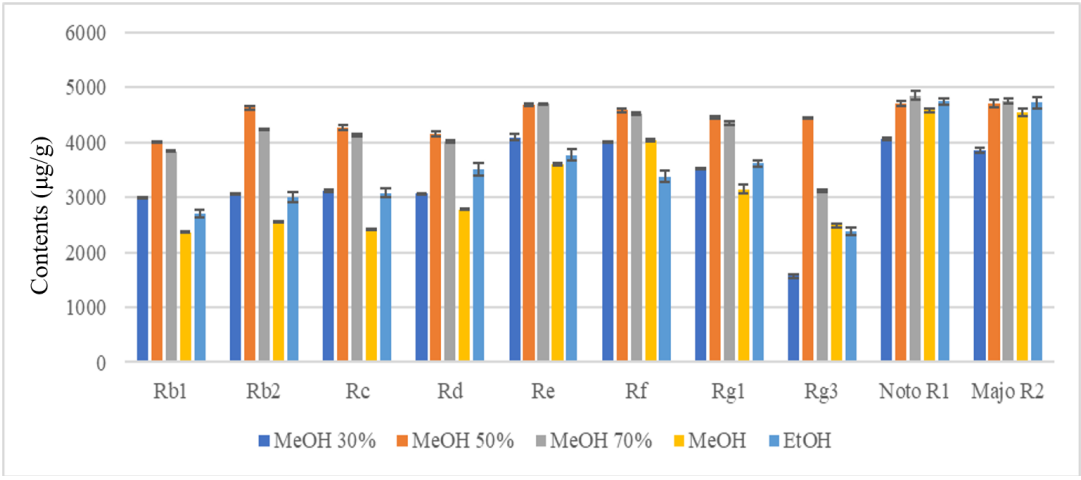

Figure 3. *Results of extraction solvent evaluation*

Based on the experimental results, 50% methanol provided the highest extraction yields for most ginsenosides. The decrease in analyte recovery observed at higher methanol proportions may be attributed to the reduced water content, which limits matrix swelling; the presence of water facilitates the swelling of excipients and cellular structures in the sample, thereby enhancing extraction efficiency [20].

3.2.3. Optimization of extraction solvent volume

Three extraction solvent volumes (25, 50, and 100 mL) were evaluated. The corresponding total ginsenoside contents obtained after extraction were 1.67, 4.75, and 4.80 mg/g, respectively. The results indicate that ginsenoside extraction reached saturation at a solvent volume of 50 mL. Therefore, to reduce solvent consumption and cost while improving the method's limit of quantification, an extraction solvent volume of 50 mL was selected for subsequent analyses.

After optimization of the experimental conditions, the final sample preparation procedure was established as follows. Approximately 20 soft capsules containing ginseng were homogenized. An accurately weighed portion of about 1.0 g of the homogenized sample was transferred into a 50 mL centrifuge tube. About 10 mL of *n*-hexane was added, followed by thorough mixing and centrifugation at 6000 rpm for 5 min. The supernatant

was discarded, and the residue was allowed to air-dry. Subsequently, approximately 35 mL of 50% methanol was added as the extraction solvent, and the mixture was subjected to ultrasonic extraction at 75°C for 30 min. After centrifugation at 6000 rpm for 5 min, the extract was transferred into a 50 mL volumetric flask. The residue was re-extracted a second time with 10 - 15 mL of the same extraction solvent. The combined extracts were made up to volume with 50% methanol. The final extract was filtered and appropriately diluted prior to LC-MS/MS analysis.

3.3. Method validation

3.3.1. System suitability

System suitability was evaluated based on the repeatability (RSD%) of retention times and peak areas obtained from six consecutive injections of a mixed standard solution containing ten ginsenosides, each at a concentration of 500 ng/mL, into the LC-MS/MS system. The results showed that the RSD values for retention times were below 1.0%, while the RSD values for peak areas ranged from 0.54% to 2.61%, meeting the acceptance criteria specified in AOAC 2016 [13].

3.3.2. Matrix effect evaluation

A mixed standard solution containing ten ginsenosides at a concentration of 500 ppb was analyzed in 50% methanol and in the blank matrix extract prepared as described in Section 2.1.2. The signal responses of the analytes obtained from the two solutions were compared, and the results are presented in **Table 4**.

Table 4. *Matrix effect evaluation*

Analyte	Response in standard solution	Response in blank matrix extract	% Matrix effect
Rb_1	7998	8158	102
Rb_2	4732	4640	98.1
Rc	20038	20208	101
Rd	17578	17224	98.0
Re	2054	1972	96.0
Rf	1619	1633	101
Rg_1	1433	1368	95.4
Rg_3	1120	1038	92.7
R_1	1647	1568	95.2
R_2	419	399	95.3

The results in **Table 4** indicate that the matrix effect on the analytical response of the target analytes was negligible.

3.3.3. Specificity

The results in **Table 1** show that each analyte was characterized by one precursor ion and two product ions; therefore, all analytes achieved an identification point (IP) value of 5. In addition, method specificity was further confirmed by the analysis of blank matrix samples, standard solutions, and spiked samples (**Figure 4**). The results demonstrated that no signals corresponding to the target analytes were observed in the blank samples, and no statistically significant differences were found in the retention times of the analytes between the standard solutions and the spiked matrix samples, confirming the adequate specificity of the proposed method.

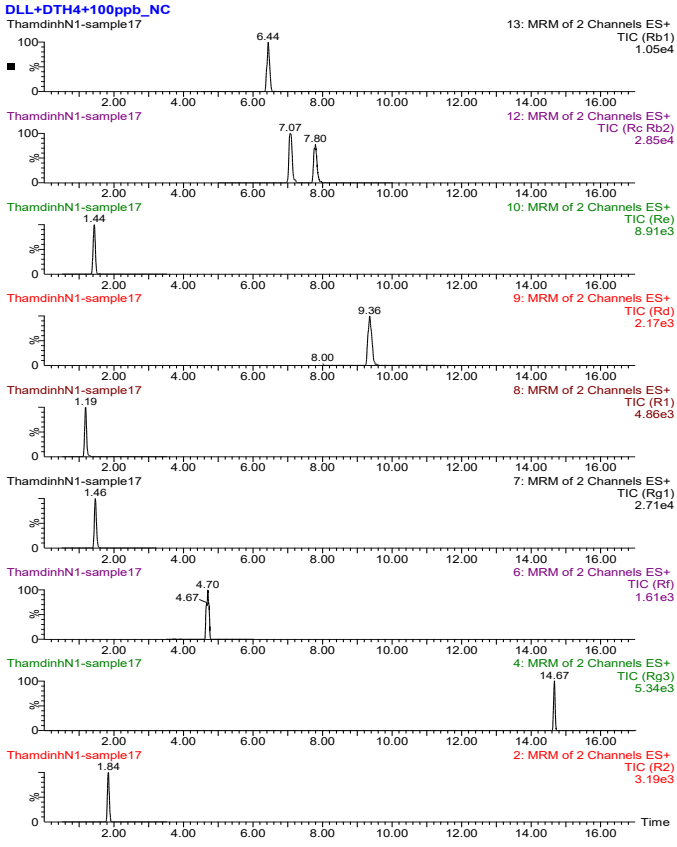

Figure 4. *Chromatograms of the analysis of 10 ginsenosides in spike blank matrix sample: The compounds appearing in the chromatogram from top to bottom are, respectively: ginsenoside Rb1; ginsenosides Rc and Rb2; ginsenoside Re; ginsenoside Rd; notoginsenoside R1; ginsenoside Rg1; ginsenoside Rf; and majonoside.*

3.3.4. Calibration curve

Based on the selected analytical conditions, calibration curves for the ten ginsenosides were established by evaluating the linear relationship between peak area and analyte concentration over the range of 100 - 2000 ng/mL. The regression equations and corresponding correlation coefficients for each analyte are presented in **Table 5**, where *x* represents the analyte concentration and *y* denotes the peak area.

Table 5. *Calibration equations and correlation coefficients of ginsenosides*

Analyte	Calibration equation	Correlation coefficient R^2
Rb_1	y = 18.493x - 411.406	0.998
Rb_2	y = 39.444x - 982.953	0.998
Rc	y = 44.836x -1047.990	0.998
Rd	y = 3.353x + 24.766	0.998
Re	y = 4.198x + 16.473	0.999
Rf	y = 2.170x - 17.970	0.999
Rg_1	y = 9.922x - 84.624	0.999
Rg_3	y = 2.831x + 176.574	0.999
R_1	y = 2.878x - 19.569	0.999
R_2	y = 0.818x - 1.586	0.999

The results presented in **Table 5** show that the calibration equations of all analytes exhibit correlation coefficients (R^2) greater than 0.995. Therefore, within the investigated concentration range, a good linear relationship exists between peak area and the corresponding analyte concentration.

3.3.5. Limit of Detection (LOD) and Limit of Quantification (LOQ)

The LOD and LOQ of the method were determined by analyzing blank samples spiked at a concentration level of 5 µg/g, with ten parallel determinations. The R value was calculated in the range of 4 - 10. The LOD and LOQ results are presented in **Table 6**.

Table 6. *Limits of detection (LOD) and limits of quantification (LOQ)*

Analyte	LOD (µg/g)	LOQ (µg/g)	R
Rb_1	1.43	4.18	9.68
Rb_2	1.57	4.58	8.79
Rc	1.55	4.51	8.80
Rd	1.85	5.41	7.43
Re	1.73	5.03	8.14
Rf	1.61	4.69	8.73
Rg_1	1.72	5.01	8.10
Rg_3	1.70	4.95	8.20
R_1	1.60	4.67	8.73
R_2	1.79	4.93	7.68

The results in **Table 6** indicate that the LOQ values of the analytes ranged from 4.18 to 5.41 µg/g. These values are suitable for the determination of ginsenosides in dietary supplement products.

3.3.6. Precision and Accuracy of the method

Accuracy was evaluated through recovery (H%), while precision was assessed in terms of repeatability using the relative standard deviation (RSD%). This evaluation was carried out by analyzing blank samples spiked with standards at three concentration levels (5.00, 250, and 500 µg/g). Each level was analyzed in six replicates following the sample preparation procedure selected in **Section 3.2**. The results of the precision and accuracy assessment are summarized in **Table 7**.

The results presented in **Table 7** show that the recoveries of the analytes ranged from 90.9 to 106%, while the RSD values ranged from 1.14 to 4.36%. These results meet the AOAC 2016 requirements for recovery at concentration levels of 1.00 - 10.0 µg/g and 10.0 - 100 µg/g (80.0 - 110% and 90.0 - 107%, respectively), as well as the repeatability criteria at concentration levels of 1.00 - 10.0 µg/g and 100 - 1000 µg/g (7.30% and 3.70%, respectively) [13].

Further analyses were performed on matrix-matched spiked samples at three concentration levels (5, 25, and 50 µg/g) for each ginsenoside on two different days by two different analysts, with six replicates at each level. Comparison of the results between the two analytical runs showed that the intermediate precision of the ginsenosides ranged from 1.28 to 4.21%. Therefore, the method demonstrates acceptable intermediate precision in accordance with AOAC 2016 guidelines [13].

Table 7. *Results of precision and accuracy evaluation*

Analyte	Spiked level (µg/g)	Recovery (H%)	Repeatability (RSD%)
	5.00	92.9 - 102	3.04
Rb_1	250	94.9 - 101	2.17
	500	95.9 - 102	1.85
	5.00	92.8 - 102	2.89
Rb_2	250	97.2 - 103	2.23
	500	95.2 - 100	1.62
	5.00	91.3 - 102	3.76
Rc	250	94.0 - 102	2.68
	500	96.9 - 102	1.50
	5.00	90.9 - 104	4.36
Rd	250	97.1 - 102	1.56
	500	94.3 - 100	1.94
	5.00	93.5 - 104	3.61
Re	250	95.4 - 101	1.85
	500	95.0 - 103	2.41
	5.00	95.7 - 106	3.49
Rf	250	94.9 - 102	2.34
	500	94.3 - 101	2.16
	5.00	92.7 - 105	3.87
Rg_1	250	95.4 - 104	2.73
	500	94.1 - 101	2.17
	5.00	91.3 - 101	4.07
Rg_3	250	96.1 - 101	1.97
	500	96.5 - 99.6	1.14
	5.00	93.2 - 103	3.34
R_1	250	95.8 - 102	2.39
	500	95.2 - 102	2.18
	5.00	93.8 - 102	2.63
R_2	250	95.7 - 102	1.97
	500	96.6 - 102	1.60

3.4. Ginsenoside contents in raw materials and ginseng-containing dietary supplements

After evaluation, this method met all the necessary criteria and was applied to determine 10 ginsenosides in 14 samples of dietary supplements purchased at a Hanoi market. **Figure 5** shows typical chromatograms of the analyzed samples, and **Table 8** summarizes the quantified ginsenoside content.

Table 8. *Results of analysis of real samples*

Sample	Added raw material	Rb1 (µg/g)	Rb2 (µg/g)	Rc (µg/g)	Rd (µg/g)	Re (µg/g)	Rf (µg/g)	Rg1 (µg/g)	Rg3 (µg/g)	Noto R1 (µg/g)	Majo R2 (µg/g)
1	American ginseng	89.1	30.4	30.1	54.2	34.2	46.7	132	24.3	-	-
2	American ginseng	4567	871	781	723	1234	54.6	7634	635.4	-	-
3	American ginseng	1341	43.4	49.1	42.1	320	24.3	981	-	-	-
4	Red ginseng	54.1	43.5	35.6	76.7	87.6	23.4	1234	105.1	-	-
5	Red ginseng	401	34.2	43.5	23.5	154	43.2	1542	408.6	-	-
6	Ginseng	1672	-	-	-	23.5	-	1765	-	-	-
7	Ginseng	56.1	-	-	-	25.1	27.4	154	-	-	-
8	Ginseng	89.1	-	-	-	-	-	116	-	-	-
9	Ginseng	176	-	-	9.6	55.4	-	183	-	-	-
10	Ginseng	324	-	-	29.9	42.1	26.4	145	-	-	-
11	Vietnamese ginseng	187	54.2	53.7	101	116	234	487	-	240	587
12	Vietnamese ginseng	156	46.5	64.3	90.4	87.5	57.8	206	-	43.2	872
13	Vietnamese ginseng	781	65.7	87.9	421	90.1	98.2	981	-	87.1	1102
14	Tienchi ginseng	430	42.5	56.2	65.4	76.1	143.5	872.1	-	540	-

The results in **Table 8** show that ginsenosides were detected in all dietary supplement samples at different levels. All samples exhibited a high proportion of ginsenosides Rb1 and Rg1 among the detected ginsenosides, which is consistent with previous studies. Variations in ginsenoside composition among samples can be attributed to differences in cultivation regions, harvesting time, and processing methods. In samples supplemented with red ginseng, the presence of ginsenoside Rg3 was observed, a characteristic compound formed during the heat-steaming process due to hydrolysis of glucose moieties at the C-20 position of ginsenoside Rb1. Samples containing American ginseng showed the presence of ginsenosides Rb1, Rb2, Rc, Rd, Re, and Rf, consistent with the specifications of the United States Pharmacopeia. For samples supplemented with *Panax notoginseng*, notoginsenoside R1 was detected as a specific marker distinguishing this species from other ginsengs. Notably, samples containing *Panax vietnamensis* exhibited the presence of all ten ginsenosides, including majonoside R2, a compound unique to Vietnamese ginseng.

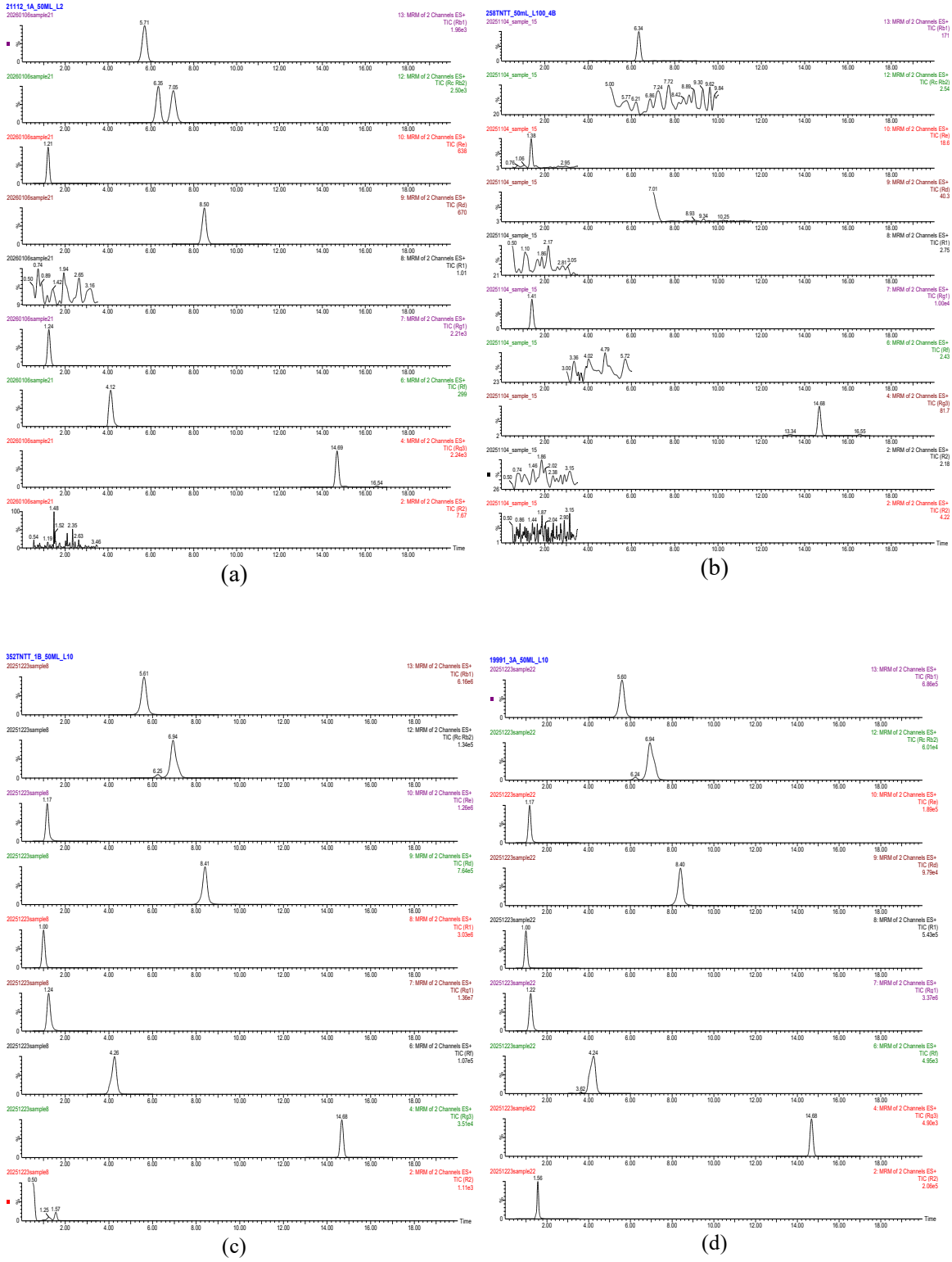

Figure 5. *Chromatograms of real sample analysis: (a) sample containing American ginseng; (b) sample containing ginseng; (c) sample containing Panax notoginseng; (d) sample containing Panax vietnamensis*

4. CONCLUSION

This study successfully developed a rapid and effective LC-MS/MS method for the simultaneous determination of ten ginsenosides (Rb1, Rb2, Rc, Rd, Re, Rf, Rg1, Rg3, notoginsenoside R1, and majonoside R2) in soft capsule dietary supplement samples. The method demonstrated high specificity, low limits of detection, and satisfactory accuracy and precision in accordance with AOAC 2016 guidelines. The validated method was applied to the analysis of 14 ginsenoside-containing dietary supplement samples submitted to the National Institute for Food Control from June to December 2025. The results indicated that ginsenosides were detected in all samples, with total contents ranging from 0.205 to 16.5 mg/g. Overall, the LC-MS/MS method proved to be a powerful analytical tool for the determination of ginsenosides in dietary supplements, with significant potential for quality control and for identifying the ginseng species used in products, thereby contributing to consumer protection.

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