AOAC SMPR® 2017.014

Standard Method Performance Requirements (SMPRs®) for Determination of Select Ginsenosides in Dietary Supplements and Dietary Ingredients

Intended Use: Quality assurance and compliance to Current Good Manufacturing Practices (CGMPs) and possibly detection of adulterants and enforcement of Convention of International Trade in Endangered Species of Wild Fauna and Flora (CITES)

1 Purpose

AOAC SMPRs describe the minimum recommended performance characteristics to be used during the evaluation of a method. The evaluation may be an on-site verification, a single-laboratory validation, or a multi-site collaborative study. SMPRs are written and adopted by AOAC stakeholder panels composed of representatives from industry, regulatory organizations, contract laboratories, test kit manufacturers, and academic institutions. AOAC SMPRs are used by AOAC expert review panels in their evaluation of validation study data for methods being considered for *Performance Tested Methods*^{SM} or AOAC *Official Methods of Analysis*^{SM}, and can be used as acceptance criteria for verification at user laboratories. [Refer to Appendix F: *Guidelines for Standard Method Performance Requirements*, *Official Methods of Analysis of AOAC INTERNATIONAL* (2016) 20th Ed., AOAC INTERNATIONAL, Rockville, MD, USA.]

2 Applicability

Determination of the individual ginsenosides Rb_1, Rb_2, Rc, Rd, Rf, Re, Rg_1 and optionally pseudoginsenoside (F11) and notoginsenoside R_1 in *Panax ginseng* and *P. quinquefolius,* and optionally *P. notoginseng* raw materials, dietary ingredients, and dietary supplements materials as listed in Table 1.

Optionally the method should provide guidance for differentiation of species and plant parts based on quantitative ratios of ginsenosides and/or species-specific ginsenosides.

3 Analytical Technique

Any analytical technique that meets the following method performance requirements is acceptable.

4 Definitions

Dietary ingredient.—A vitamin; a mineral; an herb or other botanical; an amino acid; a dietary substance for use by man to supplement the diet by increasing total dietary intake; or a concentrate, metabolite, constituent, extract, or combination of any of the above dietary ingredients. {United States Federal Food Drug and Cosmetic Act §201(ff) [U.S.C. 321 (ff)]}

Dietary supplement.—A product intended for ingestion that contains a "dietary ingredient" intended to add further nutritional value to (supplement) the diet. Dietary supplements may be found in many forms, such as tablets, capsules, softgels, gelcaps, liquids, or powders.

Ginsenosides.—See Figure 1.

Limit of quantitation (LOQ).—Minimum concentration or mass of analyte in a given matrix that can be reported as a quantitative result.

Pseudoginsenoside (F11).—*See* Figure 2.

Raw materials.—Fresh, dried or cut plant materials.

Recovery.—Fraction or percentage of spiked analyte that is recovered when the test sample is analyzed using the entire method.

Repeatability.—Variation arising when all efforts are made to keep conditions constant by using the same instrument and operator and repeating during a short time period. Expressed as the repeatability standard deviation (SD_r); or % repeatability relative standard deviation ($\%RSD_r$).

Reproducibility.—The standard deviation or relative standard deviation calculated from among-laboratory data. Expressed as the reproducibility standard deviation (SD_R); or % reproducibility relative standard deviation ($\%RSD_R$).

5 Method Performance Requirements

See Tables 2 and 3.

6 System Suitability Tests and/or Analytical Quality Control

Suitable methods will include blank check samples, and check standards at the lowest point and midrange point of the analytical range. A control sample must be included.

7 Reference Material(s)

NIST Standard Reference Material (SRM) 3384
NIST *Panax ginseng* (Asian ginseng) Rhizome
NIST SRM 3385 *Panax ginseng* (Asian ginseng) Extract
See Table 4 for a list of sources of plant materials.
See Table 5 for a list of sources of individual ginsenosides, protopanaxdiol, and pseudoginsenosides.

Refer to Annex F: *Development and Use of In-House Reference Materials* in Appendix F: *Guidelines for Standard Method Performance Requirements*, *Official Methods of Analysis of AOAC INTERNATIONAL* (2016) 20th Ed., AOAC INTERNATIONAL, Rockville, MD, USA (http://www.eoma.aoac.org/app_f.pdf)

8 Validation Guidance

All target analytes and all matrixes listed in Table 1 plus all claimed matrices shall be evaluated. One analyte per matrix is acceptable provided all analytes are represented in the complete evaluation.

Appendix D: *Guidelines for Collaborative Study Procedures to Validate Characteristics of a Method of Analysis*, *Official Methods of Analysis of AOAC INTERNATIONAL* (2016) 20th Ed., AOAC INTERNATIONAL, Rockville, MD, USA (http://www.eoma.aoac.org/app_d.pdf)

Appendix K: *Guidelines for Dietary Supplements and Botanicals*, *Official Methods of Analysis of AOAC INTERNATIONAL* (2016) 20th Ed., AOAC INTERNATIONAL, Rockville, MD, USA (http://www.eoma.aoac.org/app_k.pdf). Also at: *J. AOAC Int*. **95**, 268(2012); DOI: 10.5740/jaoacint.11-447

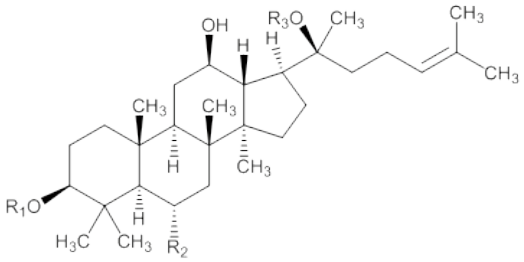
9 Maximum Time-to-Determination

No maximum time.

Approved by the AOAC Stakeholder Panel on Dietary Supplements (SPDS) on September 22, 2017. Final Version Date: September 22, 2017.

Table 1. Required matrixes

Powdered root
Powdered extract
Tablets
Capsules
Combination: Ginseng and one of, e.g., *Ginkgo biloba*, *Eleutherococcus senticosus, Rhodiola rosea*



SAPONIN	R_1	R_2	R_3	R_4
Ginsenoside Rb1	β-D-Glc*p*-(1→2)-β-D-Glc*p*	H	β-D-Glc*p*-(1→6)-β-D-Glc*p*	
Ginsenoside Rb2	β-D-Glc*p*-(1→2)-β-D-Glc*p*	H	α-L-Ara*p*-(1→6)-β-D-Glc*p*	
Ginsenoside Rc	β-D-Glc*p*-(1→2)-β-D-Glc*p*	H	α-L-Ara*f*-(1→6)-β-D-Glc*p*	
Ginsenoside Rd	β-D-Glc*p*-(1→2)-β-D-Glc*p*	H	β-D-Glc*p*	
Ginsenoside Re	H	R_4O	β-D-Glc*p*	α-L-Rha*p*-(1→2)-β-D-Glc*p*
Ginsenoside Rf*	H	R_4O	H	β-D-Glc*p*-(1→2)-β-D-Glc*p*
Ginsenoside Rg1	H	R_4O	β-D-Glc*p*	β-D-Glc*p*
Ginsenoside Rg2**	H	R_4O	H	α-L-Rha*p*-(1→2)-β-D-Glc*p*
Notoginsenoside R1***	H	R_4O	β-D-Glc*p*	β-D-Glc*p*-(1→2)-β-D-Xyl*p*

*Asian Ginseng only **American Ginseng only *** Tienchi Ginseng only

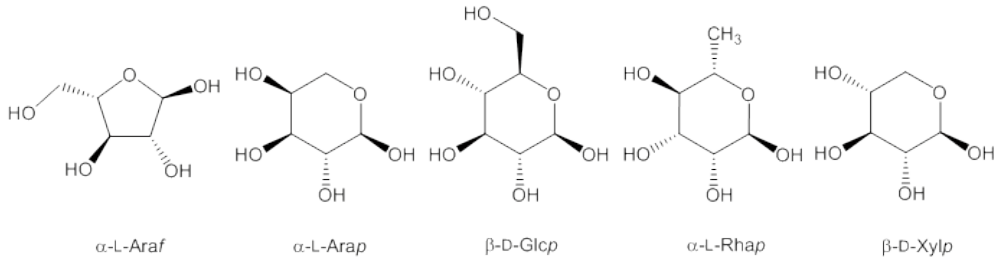


Figure 1. Molecular structures of ginsenosides.

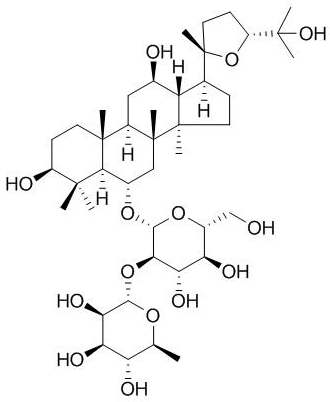


Figure 2. Molecular structure of pseudoginsenoside (F11).

Table 2. Analytical range and LOQ[a]

Parameter	Acceptance criteria
Analytical range, mg/g	0.5–200
Limit of quantitation, mg/g	≤0.5

[a] Reported as individual ginsenosides.

Table 3. Method performance requirements[a,b]

Parameter	Acceptance criteria
Recovery, %	90–110
RSD_r, %	≤7.5
RSD_R, %	≤10

[a] Reported as individual ginsenosides.

[b] It is recognized that the individual ginsenosides will vary. Individual presence and levels are dependent upon species.

Table 4. Sources of plant materials

Product name	Product description	Manufacturer	Product code
AHP monograph: American ginseng root (PDF)	AHP monograph for *Panax quinquefolius*	American Herbal Pharmacopoeia	502
Elutherococcus senticosus, root	Common name: Siberian ginseng	Alkemist	903528
	Genus species: *Eleutherococcus senticosus*		
	Plant part: root		
	Physical form: cut and sifted		
	Latin name: *Eleutherococcus senticosus* (Rupr. & Maxim.) Maxim. [Araliaceae]		
Elutherococcus senticosus, root (AHP)	Common name: Eleuthero (Siberian ginseng); ci wu jia	American Herbal Pharmacopoeia	596473
	Genus species: *Eleutherococcus senticosus*		
	Plant part: root		
	Physical form: whole		
Panax ginseng (red), root	Common name: Asian ginseng (hong shen; ren shen)	American Herbal Pharmacopoeia	530358
	Genus species: *Panax ginseng* (red)		
	Plant part: root		
	Physical form: whole		
Panax ginseng (white), root	Common name: Asian ginseng (bai ren shen; ren shen)	American Herbal Pharmacopoeia	536137
	Genus species: *Panax ginseng* (white)		
	Plant part: root		
	Physical form: whole		
Panax ginseng, root	Common name: Asian ginseng	Alkemist	945031
	Genus species: *Panax ginseng*		
	Plant part: root		
	Physical form: cut and sifted		
	Latin name: *Panax ginseng* C.A. Mey [Araliaceae]		
Panax pseudoginseng, root	Common name: Tienchi ginseng (tien qi; san qi)	American Herbal Pharmacopoeia	545272
	Genus species: *Panax pseudoginseng*		
	Plant part: root		
	Physical form: whole		
Panax quinquefolius, root	Common name: American ginseng	Alkemist	964728
	Genus species: *Panax quinquefolius*		
	Plant part: root		
	Physical form: whole/dry		
	Latin name: *Panax quinquefolius* L. [Araliaceae]		
Panax quinquefolius, root (AHP)	Common name: American ginseng (xi yang shen)	American Herbal Pharmacopoeia	514442
	Genus species: *Panax quinquefolius*		
	Plant part: root		
	Physical form: whole		

Table 5. Sources of individual ginsenonsides, protopanaxdiol, and pseudoginsenosides

Product name	Product code	CAS No.
Ginsenoside CK	0150S	[39262-14-1]
Ginsenoside CK 25 mg	0150S 25 mg	[39262-14-1]
Ginsenoside Rb_1	0105S	[41753-43-9]
Ginsenoside Rb_1 25 mg	0105S 25 mg	[41753-43-9]
Ginsenoside Rb_2	0104S	[11021-13-9]
Ginsenoside Rb_2 25 mg	0104S 25 mg	[11021-13-9]
Ginsenoside Rb_3	0151S	[68406-26-8]
Ginsenoside Rb_3 25 mg	0151S 25 mg	[68406-26-8]
Ginsenoside Rc	0106S	[11021-14-0]
Ginsenoside Rc 25 mg	0106S 25 mg	[11021-14-0]
Ginsenoside Rd	0102S	[52705-93-8]
Ginsenoside Rd 25 mg	0102S 25 mg	[52705-93-8]
Ginsenoside Re	0103S	[52286-59-6]
Ginsenoside Re 25 mg	0103S 25 mg	[52286-59-6]
Ginsenoside Rf	0107S	[52286-58-5]
Ginsenoside Rf 25 mg	0107S 25 mg	[52286-58-5]
Ginsenoside Rg_1	0101S	[22427-39-0]
Ginsenoside Rg_1 25 mg	0101S 25 mg	[22427-39-0]
Ginsenoside Rg_2	0108S	[52286-74-5]
Ginsenoside Rg_2 25 mg	0108S	[52286-74-5]
Ginsenoside Rg_3	0152S	[14197-60-5]
Ginsenoside Rg_3 25 mg	0152S 25 mg	[14197-60-5]
Ginsenoside Rh_1	0153S	[63223-86-9]
Ginsenoside Rh_1 25 mg	0153S 25 mg	[63223-86-9]
Ginsenoside Rh_2	0154S	[78214-33-2]
Ginsenoside Rh_2 25 mg	0154S 25 mg	[78214-33-2]
Protopanaxadiol	2308	[7755-01-3]
Protopanaxatriol	2307	[1453-93-6]
Pseudoginsenoside F11	0155S	[69884-00-0]