J Ginseng Res 39 (2015) 287–298

Contents lists available at ScienceDirect

Journal of Ginseng Research

journal homepage: http://www.ginsengres.org

Review article

Chemical diversity of ginseng saponins from *Panax ginseng*

Byong-Kyu Shin, Sung Won Kwon, Jeong Hill Park*

College of Pharmacy, Seoul National University, Seoul, Korea

ARTICLE INFO

Article history:
Received 5 November 2014
Received in Revised form
23 December 2014
Accepted 25 December 2014
Available online 10 January 2015

Keywords:
Araliaceae
dammarane
ginsenoside
Panax ginseng
triterpene

ABSTRACT

Ginseng, a perennial plant belonging to the genus *Panax* of the Araliaceae family, is well known for its medicinal properties that help alleviate pathological symptoms, promote health, and prevent potential diseases. Among the active ingredients of ginseng are saponins, most of which are glycosides of triterpenoid aglycones. So far, numerous saponins have been reported as components of *Panax ginseng*, also known as Korean ginseng. Herein, we summarize available information about 112 saponins related to *P. ginseng*; >80 of them are isolated from raw or processed ginseng, and the others are acid/base hydrolysates, semisynthetic saponins, or metabolites.

1. Introduction

Ginseng has been one of the most important components in a number of East Asian herbal remedies. In fact, the term ginseng, without any modifier, refers particularly to the species *Panax ginseng* Meyer or sometimes even more specifically to the root of the plant species. As the name ginseng carries authority and veneration in East Asian medicine, other plants that have some properties in common with *P. ginseng* have been allegedly called "ginseng". Eventually, ginseng has become a blanket term that encompasses >10 species of perennial plants belonging to the genus *Panax* of the family Araliaceae [1,2]. Currently, 14 plants, including 12 species and two infraspecific taxa, have been recognized as members of the genus *Panax*, as shown in Table 1 [3]. Some of the *Panax* plants have common names, which stem from their countries of origin: *P. ginseng*, *Panax japonicus*, *Panax notoginseng*, *Panax quinquefolius*, and *Panax vietnamensis* are also called Korean ginseng, Japanese ginseng, Chinese ginseng, American ginseng, and Vietnamese ginseng, respectively. Of the *Panax* plants, Korean ginseng, Chinese ginseng, and American ginseng have been commercially cultivated; Vietnamese ginseng has recently been introduced for agriculture. Most ginseng species are native to Asia, especially East Asia. Thus, the use of equivocal names, such as Asian ginseng that often refers to *P. ginseng*, is discouraged.

While the variety of species renders some pharmacological effects specific to certain species, ginseng, in general, displays restorative, tonic, and revitalizing properties [4]. Thus far, >6,000 articles regarding the traditional uses, chemical constituents, and biological and pharmacological effects of ginseng have been published since Petkov [5] reported the pharmacological properties of *P. ginseng* extracts in the 1950s. Such pharmacological activities of ginseng have been found to be mainly attributed to ginseng saponins, also known as ginsenosides [6–11].

Since the first isolation of six ginsenosides from *P. ginseng* in the 1960s [12], plenty of ginsenosides have been isolated and identified from the species. In this review, we recapitulate the chemical structures, molecular masses, and monoisotopic masses of saponins from various parts of *P. ginseng*, including roots, flower buds, fruits, and leaves. In addition, we furnish available information about artifactual saponins formed during physicochemical and/or biological treatment and compounds synthesized from saponins isolated from *P. ginseng*.

* Corresponding author. College of Pharmacy, Seoul National University, 1 Gwanak-ro, Gwanak-gu, Seoul 151-742, Korea.
E-mail address: hillpark@snu.ac.kr (J.H. Park).

p1226-8453 e2093-4947/$ – see front matter
http://dx.doi.org/10.1016/j.jgr.2014.12.005

Table 1
Scientific and common names of *panax* plants

Scientific name	Rank	Common name
Panax bipinnatifidus Seem	Species	
Panax bipinnatifidus var. *angustifolius*	Infraspecific taxon	
Panax bipinnatifidus var. *bipinnatifidus*	Infraspecific taxon	
Panax ginseng C. A. Mey.	Species	Korean ginseng, Ginseng
Panax japonicus (T. Nees) C. A. Mey.	Species	Japanese ginseng
Panax notoginseng (Burkill) F. H. Chen	Species	Chinese ginseng, sanchi
Panax pseudoginseng Wall.	Species	
Panax quinquefolius L.	Species	American ginseng
Panax sokpayensis Shiva K. Sharma & Pandit	Species	
Panax stipuleanatus H. T. Tsai & K. M. Feng	Species	
Panax trifolius L.	Species	
Panax vietnamensis Ha & Grushv.	Species	Vietnamese ginseng
Panax wangianus S. C. Sun	Species	
Panax zingiberensis C. Y. Wu & Feng	Species	

2. Classification of ginseng saponins according to their genin structures

Most ginseng saponins are believed to be biosynthesized from 2,3-oxidosqualene, which is also the precursor of β-sitosterol, a steroid commonly found in plants [13]. It has been suggested that the action of three different enzymes on 2,3-oxidosqualene leads to the formation of cycloartenol, dammarenediol-II, and β-amyrin, the latter two of which are eventually biotransformed into ginseng saponins. Fig. 1 shows the proposed biosynthetic pathway of ginseng saponins and β-sitosterol. Dammarenediol-II is the precursor of dammarane-type saponins, including ginsenosides Rb1, Rb2, Re, and Rg1, which account for a significant portion of saponins found in ginseng species. Dammarane-type saponins are further classified into various groups. By contrast, oleanane-type saponins are biosynthesized from β-amyrin. In *P. ginseng*, however, oleanane-type saponins other than ginsenoside Ro are rare and often practically undetectable.

Table 2 [14–67] displays the molecular formulas, molecular masses, monoisotopic masses, and parts of ginseng saponins, isolated from or related to *P. ginseng*, that are used. We categorize the ginseng saponins based upon the position of hydroxyl group(s) and/or double bond(s) of their genins.

2.1. Protopanaxadiol, protopanaxatriol, and their glycosides

As shown in Fig. 1, dammarenediol-II is hydroxylated to protopanaxadiol (PPD), 3β,12β,20-trihydroxydammar-24-ene. Ultimately, a number of saponins are biosynthesized by O-glycosylation of PPD that involves the attachment of saccharide(s) to C-3 and/or C-20. Typical PPD-type saponins include ginsenosides Rb1, Rb2, Rc, and Rd, which are found in the roots [19,20], flower buds [21], and leaves [21] of *P. ginseng*.

PPD may further be hydroxylated to protopanaxatriol (PPT), 3β,6α,12β,20-tetrahydroxydammar-24-ene. A variety of saponins are biosynthesized by O-glycosylation of PPT that involves the attachment of saccharide(s) to C-6 and/or C-20. Typically, the hydroxyl group at C-3 remains free in PPT-type ginsenosides. The two most abundant PPT-type saponins in *P. ginseng* are ginsenosides Re and Rg1.

Fig. 2A illustrates the structures of PPD- and PPT-type saponins. While most naturally occurring ginsenosides are of the (*S*)-configuration at C-20, some artifactual ginsenosides exist in two epimeric forms at the carbon.

2.2. Peroxidation products of PPD- and PPT-type saponins

Some saponins isolated from the flower buds of *P. ginseng* have an aglycone that is believed to be produced via the peroxidation of PPD or PPT [68]. In most cases, the peroxidation occurs at or around the double bond between C-24 and C-25, and eventually leads to various structures. Fig. 2B, C show the structures of ginsenosides whose genin appears to be produced via the peroxidation of PPD or PPT. Fig. 2B-(a) shows the structures of some saponins that have a hydroperoxyl group at C-24 and a double bond between C-25 and C-26. Fig. 2B-(b) contains the genin structure that has a hydroxyl group at C-24, which would be reduced from the hydroperoxyl group shown in Fig. 2B-(a). In addition, Fig. 2B-(c) shows the structure of floralginsenoside Ta, a glycoside of 3β,6α,12β,20-tetrahydroxydammar-24-one-25-ene, which may be considered to be formed by the dehydration of floralginsenoside Ka, whose structure is illustrated in Fig. 2B-(a).

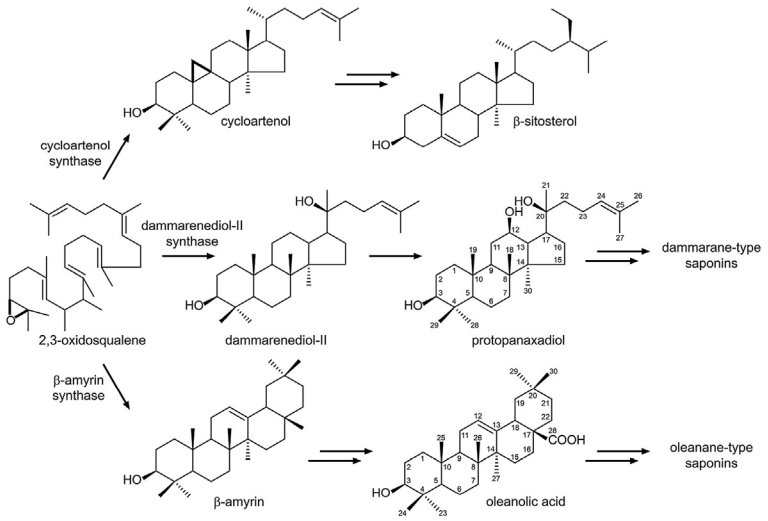


Fig. 1. Biosynthetic pathways of ginseng saponins. 2,3-Oxidosqualene may be cyclized into three different compounds, two of which are dammarenediol-II and β-amyrin, the precursor of dammarane-type saponins and oleanane-type saponins, respectively.

Table 2
Useful information about saponins isolated from *p. ginseng*, synthetic saponins, and saponin metabolites

No.	Saponin	Formula	Backbone (Fig. 2)	Molecular mass (*u*) [1)]	Monoisotopic mass (u) [1)]	Plant part (process)	Refs
	Saponins from Panax ginseng						
1	Protopanaxadiol	$C_{30}H_{52}O_3$	A	460.73	460.3916	(Hydrolysis)	[14,15]
2	Ginsenoside F2	$C_{42}H_{72}O_{13}$	A	785.01	784.4973	Leaves	[16]
3	Ginsenoside Ra1	$C_{58}H_{98}O_{26}$	A	1,211.38	1,210.6346	Roots	[17]
4	Ginsenoside Ra2	$C_{58}H_{98}O_{26}$	A	1,211.38	1,210.6346	Roots	[17]
5	Ginsenoside Ra3	$C_{59}H_{100}O_{27}$	A	1,241.41	1,240.6452	Roots	[18]
6	Ginsenoside Rb1	$C_{54}H_{92}O_{23}$	A	1,109.29	1,108.6029	Roots	[19–22]
7	Ginsenoside Rb2	$C_{53}H_{90}O_{22}$	A	1,079.27	1,078.5924	Roots	[19–21]
8	Ginsenoside Rb3	$C_{53}H_{90}O_{22}$	A	1,079.27	1,078.5924	Roots	[23]
9	Ginsenoside Rc	$C_{53}H_{90}O_{22}$	A	1,079.27	1,078.5924	Roots	[19–21]
10	Ginsenoside Rd	$C_{48}H_{82}O_{18}$	A	947.15	946.5501	Roots	[19–21,24]
11	Ginsenoside Rg3	$C_{42}H_{72}O_{13}$	A	785.01	784.4973	Steamed roots	[20,25]
12	Ginsenoside Rh2	$C_{36}H_{62}O_8$	A	622.87	622.4445	Steamed roots	[25]
13	Ginsenoside Rs1	$C_{55}H_{92}O_{23}$	A	1,121.31	1,120.6029	Roots	[20]
14	Ginsenoside Rs2	$C_{55}H_{92}O_{23}$	A	1,121.31	1,120.6029	Roots	[20]
15	Ginsenoside Rs3	$C_{44}H_{74}O_{14}$	A	827.05	826.5079	Steamed roots	[26]
16	Malonylginsenoside Ra3	$C_{62}H_{102}O_{30}$	A	1,327.46	1,326.6456	Roots	[27]
17	Malonylginsenoside Rb1	$C_{57}H_{94}O_{26}$	A	1,195.34	1,194.6033	Roots	[28]
18	Malonylginsenoside Rb2	$C_{56}H_{92}O_{25}$	A	1,165.31	1,164.5928	Roots	[28]
19	Malonylginsenoside Rc	$C_{56}H_{92}O_{25}$	A	1,165.31	1,164.5928	Roots	[28]
20	Malonylginsenoside Rd	$C_{51}H_{84}O_{21}$	A	1,033.20	1,032.5505	Roots	[28]
21	Malonylnotoginsenoside R4	$C_{62}H_{102}O_{30}$	A	1,327.46	1,326.6456	Roots	[29]
22	Protopanaxatriol	$C_{30}H_{52}O_4$	A	476.73	476.3866	(Hydrolysis)	[30]
23	Floralginsenoside M	$C_{53}H_{90}O_{22}$	A	1,079.27	1,078.5924	Flower buds	[31]
24	Floralginsenoside N	$C_{53}H_{90}O_{22}$	A	1,079.27	1,078.5924	Flower buds	[31]
25	Floralginsenoside P	$C_{53}H_{90}O_{23}$	A	1,095.27	1,094.5873	Flower buds	[31]
26	Ginsenoside F1	$C_{36}H_{62}O_9$	A	638.87	638.4394	Leaves	[16]
27	Ginsenoside F3	$C_{41}H_{70}O_{13}$	A	770.99	770.4816	Leaves	[16]
28	Ginsenoside Re	$C_{48}H_{82}O_{18}$	A	947.15	946.5501	Roots	[20,21,24,32]
29	Ginsenoside Rf	$C_{42}H_{72}O_{14}$	A	801.01	800.4922	Roots	[20,32]
30	Ginsenoside Rg1	$C_{42}H_{72}O_{14}$	A	801.01	800.4922	Roots	[20,21,33]
31	Ginsenoside Rg2	$C_{42}H_{72}O_{13}$	A	785.01	784.4973	Roots	[25,32,34,35]
32	Ginsenoside Rh1	$C_{36}H_{62}O_9$	A	638.87	638.4394	Steamed roots	[21,25,34]
33	20-Glucoginsenoside Rf	$C_{48}H_{82}O_{19}$	A	963.15	962.5450	Roots	[23]
34	Floralginsenoside H	$C_{50}H_{84}O_{21}$	B-(a)	1,021.19	1,020.5505	Flower buds	[36]
35	Floralginsenoside Tc	$C_{53}H_{90}O_{24}$	B-(a)	1,111.27	1,110.5822	Flower buds	[37]
36	Floralginsenoside Td	$C_{53}H_{90}O_{24}$	B-(a)	1,111.27	1,110.5822	Flower buds	[37]
37	Ginsenoside I	$C_{48}H_{82}O_{20}$	B-(a)	979.15	978.5400	Flower buds	[38]
38	Ginsenoside II	$C_{48}H_{82}O_{20}$	B-(a)	979.15	978.5400	Flower buds	[38]
39	Floralginsenoside A	$C_{42}H_{72}O_{16}$	B-(a)	833.01	832.4820	Flower buds	[39]
40	Floralginsenoside C	$C_{41}H_{70}O_{15}$	B-(a)	802.99	802.4715	Flower buds	[39]
41	Floralginsenoside J	$C_{48}H_{82}O_{20}$	B-(a)	979.15	978.5400	Flower buds	[36]
42	Floralginsenoside Ka	$C_{36}H_{62}O_{11}$	B-(a)	670.87	670.4292	Flower buds	[40]
43	Ginsenoside SL1	$C_{36}H_{62}O_{11}$	B-(a)	670.87	670.4292	Steamed leaves	[41]
44	Ginsenoside Rg7	$C_{36}H_{60}O_9$	B-(b)	636.86	636.4237	Leaves	[42]
45	Floralginsenoside La	$C_{48}H_{82}O_{19}$	B-(b)	963.15	962.5450	Flower buds	[36]
46	Floralginsenoside Lb	$C_{48}H_{82}O_{19}$	B-(b)	963.15	962.5450	Flower buds	[36]
47	Floralginsenoside Ta	$C_{36}H_{60}O_{10}$	B-(c)	652.86	652.4187	Flower buds	[37]
48	Floralginsenoside E	$C_{42}H_{72}O_{15}$	C-(a)	817.01	816.4871	Flower buds	[39]
49	Floralginsenoside F	$C_{42}H_{72}O_{15}$	C-(a)	817.01	816.4871	Flower buds	[39]
50	Floralginsenoside G	$C_{50}H_{84}O_{21}$	C-(a)	1,021.19	1,020.5505	Flower buds	[36]
51	Floralginsenoside K	$C_{48}H_{82}O_{21}$	C-(a)	995.15	994.5349	Flower buds	[36]
52	Floralginsenoside O	$C_{53}H_{90}O_{22}$	C-(a)	1,079.27	1,078.5924	Flower buds	[31]
53	Floralginsenoside B	$C_{42}H_{72}O_{16}$	C-(a)	833.01	832.4820	Flower buds	[39]
54	Floralginsenoside D	$C_{41}H_{70}O_{15}$	C-(a)	802.99	802.4715	Flower buds	[39]
55	Floralginsenoside I	$C_{48}H_{82}O_{20}$	C-(a)	979.15	978.5400	Flower buds	[36]
56	Ginsenoside Rh6	$C_{36}H_{62}O_{11}$	C-(a)	670.87	670.4292	Leaves	[42]
57	Ginsenoside ST2	$C_{36}H_{62}O_{10}$	C-(b)	654.87	654.4343	Steamed leaves	[43]
58	Ginsenoside Ki	$C_{36}H_{62}O_{10}$	C-(c)	654.87	654.4343	Leaves	[44]
59	Ginsenoside Km	$C_{36}H_{62}O_{10}$	C-(c)	654.87	654.4343	Leaves	[44]
60	Floralginsenoside Kb	$C_{45}H_{76}O_{19}$	D-(a)	921.07	920.4981	Flower buds	[40]
61	Floralginsenoside Kc	$C_{45}H_{76}O_{20}$	D-(a)	937.07	936.4930	Flower buds	[40]
62	Floralginsenoside Tb	$C_{35}H_{62}O_{11}$	D-(b)	658.86	658.4292	Flower buds	[37]
63	25-Hydroxyprotopanaxadiol	$C_{30}H_{54}O_4$	E	478.75	478.4022	Fruits	[45]
64	25-Hydroxyprotopanaxatriol	$C_{30}H_{54}O_5$	E	494.75	494.3971	Fruits	[45]
65	Dehydroprotopanaxadiol I	$C_{30}H_{50}O_2$	F-(a)	442.72	442.3811	Steamed roots	[46]
66	Ginsenoside Rg5	$C_{42}H_{70}O_{12}$	F-(a)	767.00	766.4867	Steamed roots	[47,48]
67	Ginsenoside Rh3	$C_{36}H_{60}O_7$	F-(a)	604.86	604.4339	Steamed roots	[47,49]
68	Ginsenoside Rs4	$C_{44}H_{72}O_{13}$	F-(a)	809.03	808.4973	Steamed roots	[46]
69	Dehydroprotopanaxatriol I	$C_{30}H_{50}O_3$	F-(a)	458.72	458.3760	Steamed roots	[46]
70	Ginsenoside F4	$C_{42}H_{70}O_{12}$	F-(a)	767.00	766.4867	Leaves	[50]
71	Ginsenoside Rh4	$C_{36}H_{60}O_8$	F-(a)	620.86	620.4288	Steamed roots	[47,51]
72	Ginsenoside Rs6	$C_{38}H_{62}O_9$	F-(a)	662.89	662.4394	Steamed roots	[46]

(*continued on next page*)

Table 2 (*continued*)

No.	Saponin	Formula	Backbone (Fig. 2)	Molecular mass (*u*) [1)]	Monoisotopic mass (u) [1)]	Plant part (process)	Refs
73	Ginsenoside Rz1	$C_{42}H_{70}O_{12}$	F-(b)	767.00	766.4867	Steamed roots	[52]
74	Dehydroprotopanaxadiol II	$C_{30}H_{50}O_2$	F-(c)	442.72	442.3811	Steamed roots	[46]
75	Ginsenoside Rk1	$C_{42}H_{70}O_{12}$	F-(c)	767.00	766.4867	Steamed roots	[47]
76	Ginsenoside Rk2	$C_{36}H_{60}O_7$	F-(c)	604.86	604.4339	Steamed roots	[47]
77	Ginsenoside Rs5	$C_{44}H_{72}O_{13}$	F-(c)	809.03	808.4973	Steamed roots	[46]
78	Dehydroprotopanaxatriol II	$C_{30}H_{50}O_3$	F-(c)	458.72	458.3760	Steamed roots	[46]
79	Ginsenoside Rg6	$C_{42}H_{70}O_{12}$	F-(c)	767.00	766.4867	Steamed roots	[53]
80	Ginsenoside Rk3	$C_{36}H_{60}O_8$	F-(c)	620.86	620.4288	Steamed roots	[47]
81	Ginsenoside Rs7	$C_{38}H_{62}O_9$	F-(c)	662.89	662.4394	Steamed roots	[46]
82	Panaxadiol	$C_{30}H_{52}O_3$	G-(a)	460.73	460.3916	(Hydrolysis)	[54,55]
83	Panaxatriol	$C_{30}H_{52}O_4$	G-(a)	476.73	476.3866	(Hydrolysis)	[30]
84	Ginsenoside Rh9	$C_{36}H_{60}O_9$	G-(b)	636.86	636.4237	Leaves	[42]
85	12,23-Epoxyginsenoside Rg1	$C_{42}H_{70}O_{14}$	G-(b)	799.00	798.4766	Leaves	[56]
86	Panaxadione	$C_{30}H_{48}O_5$	G-(c)	488.70	488.3502	Seeds	[57]
87	Ginsenoside Rh5	$C_{36}H_{60}O_9$	H-(a)	636.86	636.4237	Steamed roots	[42]
88	Ginsenoside Rh7	$C_{36}H_{60}O_9$	H-(b)	636.86	636.4237	Leaves	[42]
89	Ginsenoside Rh8	$C_{36}H_{60}O_9$	H-(c)	636.86	636.4237	Leaves	[42]
90	Ginsenoside Ro	$C_{48}H_{76}O_{19}$	H-(d)	957.11	656.4981	Roots	[19,22,58]
91	Ginsenoside SL2	$C_{42}H_{70}O_{14}$	I-(a)	799.00	798.4766	Steamed leaves	[41]
92	Ginsenoside ST1	$C_{36}H_{60}O_{10}$	I-(a)	652.86	652.4187	Steamed leaves	[43]
93	Ginsenoside SL3	$C_{42}H_{70}O_{14}$	I-(b)	799.00	798.4766	Steamed leaves	[41]
94	Hexanordammaran	$C_{24}H_{40}O_4$	I-(c)	392.57	392.2927	Leaves	[59]
95	Isoprotopanaxadiol	$C_{30}H_{52}O_3$	I-(d)	460.73	460.3916	(Hydrolysis)	[60]
	Synthetic saponins						
96	Ginsenoside DM1	$C_{48}H_{84}O_9$	J-(a)	805.18	804.6115	(Synthesis)	[61]
97	Ginsenoside PM1	$C_{52}H_{92}O_9$	J-(a)	861.28	860.6741	(Synthesis)	[61]
98	Ginsenoside SM1	$C_{54}H_{96}O_9$	J-(a)	889.33	888.7054	(Synthesis)	[61]
99	C-X1	$C_{53}H_{90}O_{23}$	J-(a)	1,095.27	1,094.5873	(Synthesis)	[62]
100	C-Y1	$C_{53}H_{90}O_{23}$	J-(a)	1,095.27	1,094.5873	(Synthesis)	[62]
101	C-Y2	$C_{42}H_{72}O_{14}$	J-(a)	801.01	800.4922	(Synthesis)	[62]
102	Ginsenoside ORh1	$C_{44}H_{76}O_{10}$	J-(a)	765.07	764.5439	(Synthesis)	[63]
103	Ocotillol derivative 3a	$C_{36}H_{62}O_{10}$	J-(b)	654.87	654.4343	(Synthesis)	[64]
104	Ocotillol derivative 3b	$C_{36}H_{62}O_{10}$	J-(b)	654.87	654.4343	(Synthesis)	[64]
105	Ginsenoside Rp1	$C_{42}H_{74}O_{12}$	J-(c)	771.03	770.5180	(Synthesis)	[65]
	Saponin metabolites						
106	M1 (Compound K)	$C_{36}H_{62}O_8$	K	622.87	622.4445	(Metabolization)	[66]
107	M2 (Compound Y)	$C_{41}H_{70}O_{12}$	K	754.99	754.4867	(Metabolization)	[66]
108	M3 (Ginsenoside Mc)	$C_{41}H_{70}O_{12}$	K	754.99	754.4867	(Metabolization)	[66]
109	M6	$C_{47}H_{80}O_{17}$	K	917.13	916.5396	(Metabolization)	[66]
110	M7 (Ginsenoside Mb)	$C_{47}H_{80}O_{17}$	K	917.13	916.5396	(Metabolization)	[66]
111	M9 (Gp-LXXV)	$C_{48}H_{82}O_{18}$	K	947.15	946.5501	(Metabolization)	[66]
112	M13 (Gp-XVII)	$C_{42}H_{72}O_{13}$	K	785.01	784.4973	(Metabolization)	[66]

[1)] The calculations are based upon the latest atomic mass data from the International Union of Pure and Applied Chemistry (IUPAC) [67].

In a similar fashion, Fig. 2C-(a,b) show the structures of ginseng saponins whose genin has a hydroperoxyl group and a hydroxyl group, respectively, at C-25 and a double bond between C-23 and C-24. While geometric isomerism is possible in compounds with a double bond between C-23 and C-24, most of those reported are the (*E*)-form isomers rather than the (*Z*)-form. In addition, Fig. 2C-(c) illustrates the structures of ginsenosides whose genin has a hydroxyl group either at C-26 or at C-27, which would be reduced from the hydroperoxyl group formed around the double bond between C-24 and C-25.

2.3. Cleavage products of PPD- and PPT-type saponins

The oxidative cleavage of the double bond of some saponins yields an aldehyde with three fewer carbon atoms, that is, 3β,12β,20-trihydroxy-25,26,27-trinordammar-24-al, and its derivatives, which are found mainly in the flower buds of ginseng.

Fig. 2D-(a) shows the structures of ginsenosides whose genin is considered to be formed by the oxidative cleavage of the double bond of PPD or 23-hydroxyprotopanaxadiol. Fig. 2D-(b) shows the structure of floralginsenoside Tb, whose genin is an acetal of 3β,6α,12β,20-tetrahydroxy-25,26,27-trinordammar-24-al, which appears to be formed from PPT.

2.4. Hydration and dehydration products of PPD- and PPT-type saponins

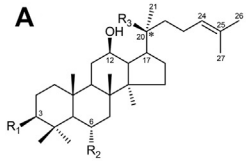
The hydration of the double bond of PPD or PPT yields a dammarane derivative with a hydroxyl group at C-25 and no double bond. Fig. 2E illustrates the structures of the saponins 25-hydroxyprotopanaxadiol and 25-hydroxyprotopanaxatriol.

Most PPD- and PPT-type ginsenosides tend to be deglycosylated and dehydrated at C-20 when steamed or heat processed. The resultant double bond is formed either between C-20 and C-21 or between C-20 and C-22. In the latter case, the (*E*)/(*Z*) geometric isomerism exists. Fig. 3 illustrates the probable pathways of the formation of artifactual saponins owing to heating. Fig. 2F shows the structures of saponins that are considered to be the dehydration products of the PPD- and PPT-type saponins shown in Fig. 2A.

2.5. Saponins with an epoxy group

The acid hydrolysis of a PPD-type and a PPT-type saponin leads to the formation of a six-membered ring containing oxygen, yielding panaxadiol, 3β,12β-dihydroxy-20,25-epoxydammarane, and panaxatriol, 3β,6α,12β-trihydroxy-20,25-epoxydammarane, respectively. Fig. 2G-(a) shows the structures of panaxadiol and panaxatriol. Moreover, some saponins are derivatives of 3β,6α,20-

A

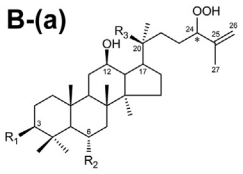


Glc: β-D-glucopyranosyl
Rha: α-L-rhamnopyranosyl
Ara(fur): α-L-arabinofuranosyl
Ara(pyr): α-L-arabinopyranosyl
Xyl: β-D-xylopyranosyl
Ac: acetyl
Ma: malonyl

		R_1	R_2	R_3
1*	protopanaxadiol	OH	H	OH
2	ginsenoside F2	OGlc	H	OGlc
3	ginsenoside Ra1	OGlc-(2 1)-Glc	H	OGlc-(6 1)-Ara(pyr)-(4 1)-Xyl
4	ginsenoside Ra2	OGlc-(2 1)-Glc	H	OGlc-(6 1)-Ara(fur)-(2 1)-Xyl
5	ginsenoside Ra3	OGlc-(2 1)-Glc	H	OGlc-(6 1)-Glc-(3 1)-Xyl
6	ginsenoside Rb1	OGlc-(2 1)-Glc	H	OGlc-(6 1)-Glc
7	ginsenoside Rb2	OGlc-(2 1)-Glc	H	OGlc-(6 1)-Ara(pyr)
8	ginsenoside Rb3	OGlc-(2 1)-Glc	H	OGlc-(6 1)-Xyl
9	ginsenoside Rc	OGlc-(2 1)-Glc	H	OGlc-(6 1)-Ara(fur)
10	ginsenoside Rd	OGlc-(2 1)-Glc	H	OGlc
11*	ginsenoside Rg3	OGlc-(2 1)-Glc	H	OH
12	ginsenoside Rh2	OGlc	H	OH
13	ginsenoside Rs1	OGlc-(2 1)-Glc(-6-Ac)	H	OGlc-(6 1)-Ara(pyr)
14	ginsenoside Rs2	OGlc-(2 1)-Glc(-6-Ac)	H	OGlc-(6 1)-Ara(fur)
15*	ginsenoside Rs3	OGlc-(2 1)-Glc(-6-Ac)	H	OH
16	malonylginsenoside Ra3	OGlc-(2 1)-Glc(-6-Ma)	H	OGlc-(6 1)-Glc-(3 1)-Xyl
17	malonylginsenoside Rb1	OGlc-(2 1)-Glc(-6-Ma)	H	OGlc-(6 1)-Glc
18	malonylginsenoside Rb2	OGlc-(2 1)-Glc(-6-Ma)	H	OGlc-(6 1)-Ara(pyr)
19	malonylginsenoside Rc	OGlc-(2 1)-Glc(-6-Ma)	H	OGlc-(6 1)-Ara(fur)
20	malonylginsenoside Rd	OGlc-(2 1)-Glc(-6-Ma)	H	OGlc
21	malonylnotoginsenoside R4	OGlc-(2 1)-Glc(-6-Ma)	H	OGlc-(6 1)-Glc-(6 1)-Xyl
22*	protopanaxatriol	OH	OH	OH
23	floralginsenoside M	OH	OGlc-(2 1)-Rha	OGlc-(6 1)-Ara(fur)
24	floralginsenoside N	OH	OGlc-(2 1)-Rha	OGlc-(6 1)-Ara(pyr)
25	floralginsenoside P	OGlc-(2 1)-Glc	OH	OGlc-(6 1)-Ara(pyr)
26	ginsenoside F1	OH	OH	OGlc
27	ginsenoside F3	OH	OH	OGlc-(6 1)-Ara(pyr)
28	ginsenoside Re	OH	OGlc-(2 1)-Rha	OGlc
29	ginsenoside Rf	OH	OGlc-(2 1)-Glc	OH
30	ginsenoside Rg1	OH	OGlc	OGlc
31*	ginsenoside Rg2	OH	OGlc-(2 1)-Rha	OH
32*	ginsenoside Rh1	OH	OGlc	OH
33	20-glucoginsenoside Rf	OH	OGlc-(2 1)-Glc	OGlc

* **1**, **11**, **15**, **22**, **31**, **32**: (*S*)- and (*R*)-configuration at C-20

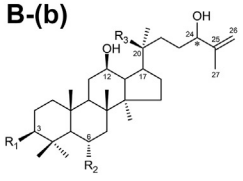
B-(a)



Glc: β-D-glucopyranosyl
Rha: α-L-rhamnopyranosyl
Ara(pyr): α-L-arabinopyranosyl
Ac: acetyl

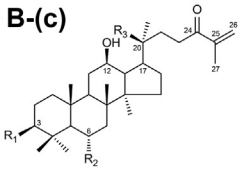
		R_1	R_2	R_3
34	floralginsenoside H	OGlc-(2 1)-Glc(-6-Ac)	H	OGlc
35*	floralginsenoside Tc	OGlc-(2 1)-Glc	H	OGlc-(6 1)-Ara(pyr)
36*	floralginsenoside Td	OGlc-(2 1)-Glc	H	OGlc-(6 1)-Ara(pyr)
37*	ginsenoside I	OGlc-(2 1)-Glc	H	OGlc
38*	ginsenoside II	OGlc-(2 1)-Glc	H	OGlc
39	floralginsenoside A	OH	OGlc	OGlc
40	floralginsenoside C	OH	OH	OGlc-(6 1)-Ara(pyr)
41	floralginsenoside J	OH	OGlc-(2 1)-Rha	OGlc
42	floralginsenoisde Ka	OH	OH	OGlc
43	ginsenoside SL1	OH	OGlc	OH

B-(b)



		R_1	R_2	R_3
44	ginsenoside Rg7	OGlc	H	OGlc
45*	floralginsenoside La	OH	OGlc-(2 1)-Rha	OGlc
46*	floralginsenoside Lb	OH	OGlc-(2 1)-Rha	OGlc

B-(c)

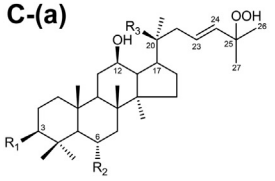


		R_1	R_2	R_3
47	floralginsenoside Ta	OH	OH	OGlc

* **35**, **36**: epimers at C-24, **37**, **38**: epimers at C-24, **45**, **46**: epimers at C-24

Fig. 2. Structures of ginseng saponins. A. Structures of ginseng saponins whose genin is 3β,12β,20-trihydroxydammar-24-ene (protopanaxadiol)/3β,6α,12β,20-tetrahydroxydammar-24-ene (protopanaxatriol); B. Structures of ginseng saponins whose genin is (a) 3β,12β,20-trihydroxy-24-hydroperoxydammar-25-ene/3β,6α,12β,20-tetrahydroxy-24-hydroperoxydammar-25-ene; (b) 3β,12β,20,24-tetrahydroxydammar-25-ene/3β,6α,12β,20,24-pentahydroxydammar-25-ene; (c) 3β,6α,12β,20-tetrahydroxydammar-24-one-25-ene; C. Structures of ginseng saponins whose genin is (a) (*E*)-3β,12β,20-trihydroxy-25-hydroperoxydammar-23-ene/(*E*)-3β,6α,12β,20-tetrahydroxy-25-hydroperoxydammar-23-ene; (b) (*E*)-3β,6α,12β,20,25-pentahydroxydammar-23-ene; (c) 3β,6α,12β,26-tetrahydroxydammar-24-ene/3β,6α,12β,27-tetrahydroxydammar-24-ene; D. Structures of ginseng saponins whose genin is (a) 3β,12β,20-trihydroxy-25,26,27-trinordammar-24-al/3β,12β,20,23-tetrahydroxy-25,26,27-trinordammar-24-al; (b) 3β,6α,12β,20-tetrahydroxy-24,24-dimethoxy-25,26,27-trinordammarane; E. Structures of ginseng saponins whose genin is 3β,12β,20,25-tetrahydroxydammarane/3β,6α,12β,20,25-pentahydroxydammarane; F. Structures of ginseng saponins whose genin is (a) (*E*)-3β,12β-dihydroxydammar-20(22),24-diene/(*E*)-3β,6α,12β-trihydroxydammar-20(22),24-diene; (b) (*Z*)-3β,12β-dihydroxydammar-20(22),24-diene; (c) 3β,12β-dihydroxydammar-20(21),24-diene/3β,6α,12β-trihydroxydammar-20(21),24-diene; G. Structures of ginseng saponins whose genin is (a) 3β,12β-dihydroxy-20,25-epoxydammarane (panaxadiol)/3β,6α,12β-trihydroxy-20,25-epoxydammarane (panaxatriol); (b) 3β,6α,20-trihydroxy-12,23-epoxydammar-24-ene; (3) 6α,25-dihydroxy-20,24-epoxydammar-3,12-dione; H. Structure of a ginseng saponin whose genin is (a) 3β,6α,12β,24-tetrahydroxydammar-20(22),25-diene; (b) 3β,7β,12β,20-tetrahydroxydammar-5,24-diene; (c) 3β,6α,20-trihydroxydammar-12-one-24-ene; (d) oleanolic acid; I. Structures of ginseng saponins whose genin is (a) 3β,6α,12β-trihydroxy-24-hydroperoxydammar-20(22),25-diene; (b) 3β,6α,12β-trihydroxy-23-hydroperoxydammar-20(21),24-diene; (c) 3β,6α,12β-trihydroxy-22,23,24,25,26,27-hexanordammar-20-one; (d) (*E*)-3β,12β,25-trihydroxydammar-20(22)-ene; J. Structures of synthesized saponins whose genin is (a) 3β,12β,20-trihydroxydammar-24-ene (protopanaxadiol)/3β,6α,12β,20-tetrahydroxydammar-24-ene (protopanaxatriol); (b) 3β,12β,25-trihydroxy-20,24-epoxydammarane/3β,6α,12β,25-tetrahydroxy-20,24-epoxydammarane; (c) 3β,12β-dihydroxydammarane; K. Structures of ginseng saponin metabolites whose genin is 3β,12β,20-trihydroxydammar-24-ene (protopanaxadiol)/3β,6α,12β,20-tetrahydroxydammar-24-ene (protopanaxatriol).

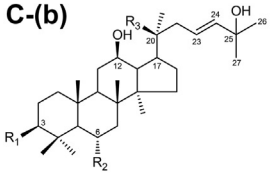
C-(a)



Glc: β-D-glucopyranosyl
Rha: α-L-rhamnopyranosyl
Ara(fur): α-L-arabinofuranosyl
Ara(pyr): α-L-arabinopyranosyl
Ac: acetyl

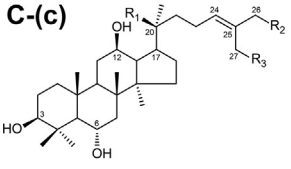
		R_1	R_2	R_3
48	floralginsenoside E	OGlc-(2 1)-Glc	H	OH
49	floralginsenoside F	OGlc	H	OGlc
50	floralginsenoside G	OGlc-(2 1)-Glc-(6)-Ac	H	OGlc
51	floralginsenoside K	OGlc-(2 1)-Glc	H	OGlc
52	floralginsenoside O	OGlc-(2 1)-Glc	H	OGlc-(6 1)-Ara(fur)
53	floralginsenoside B	OH	OGlc	OGlc
54	floralginsenoside D	OH	OH	OGlc-(6 1)-Ara(pyr)
55	floralginsenoside I	OH	OGlc-(2 1)-Rha	OGlc
56	ginsenoside Rh6	OH	OH	OGlc

C-(b)



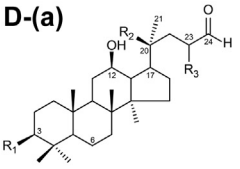
		R_1	R_2	R_3
57	ginsenoside ST2	OH	OGlc	OH

C-(c)



		R_1	R_2	R_3
58	ginsenoside Ki	OGlc	H	OH
59	ginsenoside Km	OGlc	OH	H

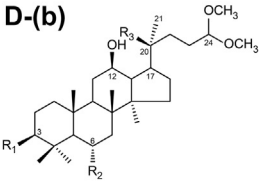
D-(a)



Glc: β-D-glucopyranosyl

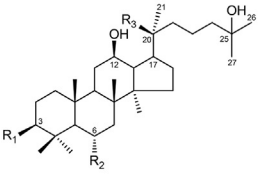
		R_1	R_2	R_3
60	floralginsenoside Kb	OGlc-(2 1)-Glc	OGlc	H
61	floralginsenoside Kc	OGlc-(2 1)-Glc	OGlc	OH

D-(b)



		R_1	R_2	R_3
62	floralginsenoside Tb	OH	OH	OGlc

E

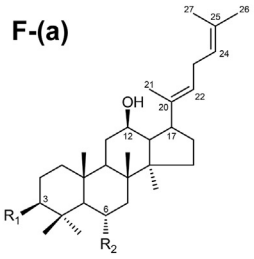


Glc: β-D-glucopyranosyl

		R_1	R_2	R_3
63	25-hydroxyprotopanaxadiol	OH	H	OH
64	25-hydroxyprotopanaxatriol	OH	OH	OH

Fig. 2. (*continued*).

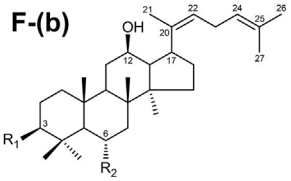
F-(a)



Glc: β-D-glucopyranosyl
Rha: α-L-rhamnopyranosyl
Ac: acetyl

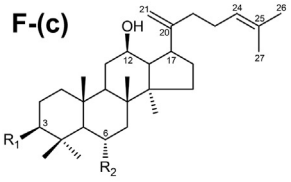
		R_1	R_2
65	**dehydroprotopanaxadiol I**	OH	H
66	**ginsenoside Rg5**	OGlc(2 1)Glc	H
67	**ginsenoside Rh3**	OGlc	H
68	**ginsenoside Rs4**	OGlc(2 1)Glc(6)Ac	H
69	**dehydroprotopanaxatriol I**	OH	OH
70	**ginsenoside F4**	OH	OGlc(2 1)Rha
71	**ginsenoside Rh4**	OH	OGlc
72	**ginsenoisde Rs6**	OH	OGlc(6)Ac

F-(b)



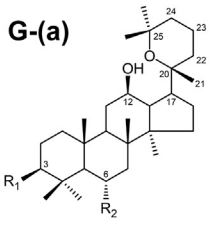
		R_1	R_2
73	**ginsenoside Rz1**	OGlc(2 1)Glc	H

F-(c)



		R_1	R_2
74	**dehydroprotopanaxadiol II**	OH	H
75	**ginsenoside Rk1**	OGlc(2 1)Glc	H
76	**ginsenoside Rk2**	OGlc	H
77	**ginsenoside Rs5**	OGlc(2 1)Glc(6)Ac	H
78	**dehydroprotopanaxatriol II**	OH	OH
79	**ginsenoside Rg6**	OH	OGlc(2 1)Rha
80	**ginsenoside Rk3**	OH	OGlc
81	**ginsenoside Rs7**	OH	OGlc(6)Ac

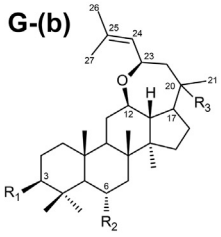
G-(a)



Glc: β-D-glucopyranosyl

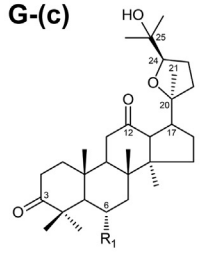
		R_1	R_2
82	**panaxadiol**	OH	H
83	**panaxatriol**	OH	OH

G-(b)



		R_1	R_2	R_3
84	**ginsenoside Rh9**	OH	OH	OGlc
85	**12,23-epoxyginsenoside Rg1**	OH	OGlc	OGlc

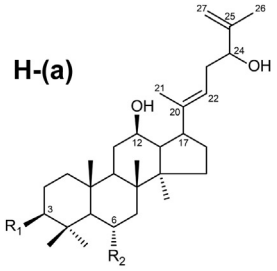
G-(c)



		R_1
86	**panaxadione**	OH

Fig. 2. (*continued*).

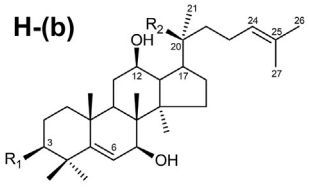
H-(a)



Glc: β-D-glucopyranosyl
Glcu: β-D-glucuronopyranosyl

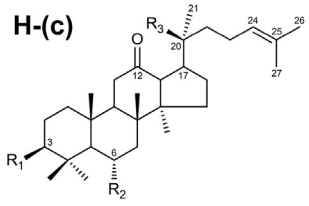
		R_1	R_2
87	ginsenoside Rh5	OH	OGlc

H-(b)



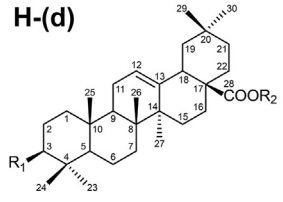
		R_1	R_2
88	ginsenoside Rh7	OH	OGlc

H-(c)



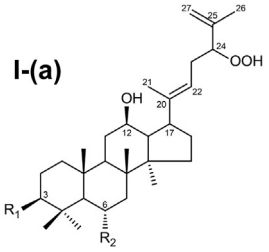
		R_1	R_2	R_3
89	ginsenoside Rh8	OH	OH	OGlc

H-(d)



		R_1	R_2
90	ginsenoside Ro	OGlcu(2→1)Glc	Glc

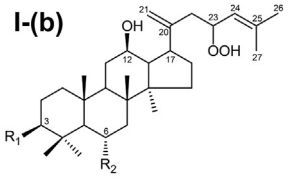
I-(a)



Glc: β-D-glucopyranosyl
Rha: α-L-rhamnopyranosyl

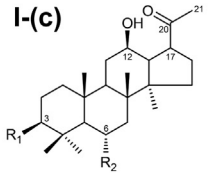
		R_1	R_2
91	ginsenoside SL2	OH	OGlc(2→1)Rha
92	ginsenoside ST1	OH	OGlc

I-(b)



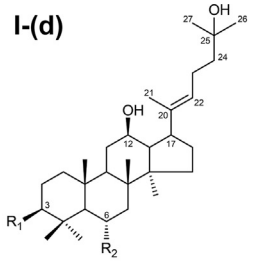
		R_1	R_2
93	ginsenoside SL3	OH	OGlc(2→1)Rha

I-(c)



		R_1	R_2
94	hexanordammaran	OH	OH

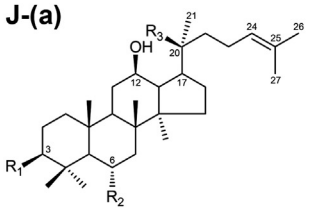
I-(d)



		R_1	R_2
95	isoprotopanaxadiol	OH	H

Fig. 2. (*continued*).

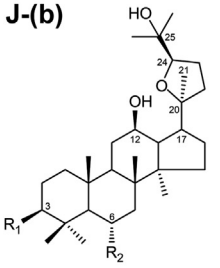
J-(a)



Glc: β-D-glucopyranosyl
Rha: α-L-rhamnopyranosyl
Xyl: β-D-xylopyranosyl

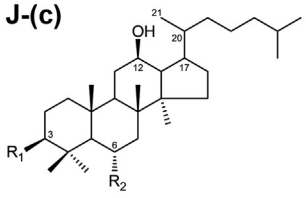
		R_1	R_2	R_3
96	**ginsenoside DM1**	OH	H	OGlc-(6)-dodecanoyl
97	**ginsenoside PM1**	OH	H	OGlc-(6)-palmitoyl
98	**ginsenoside SM1**	OH	H	OGlc-(6)-stearoyl
99	**C-X1**	OH	OGlc-(2,1)-Rha, -(4,1)-Xyl	OGlc
100	**C-Y1**	OH	OGlc-(2,1)-Rha, -(6,1)-Xyl	OGlc
101	**C-Y2**	OH	OGlc-(2,1)-Rha	OH
102	**ginsenoside ORh1**	OH	OGlc-(6)-octanoyl	OH

J-(b)



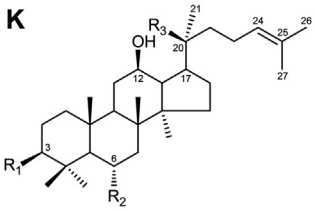
		R_1	R_2
103	**ocotillol derivative 3a**	OGlc	H
104	**ocotillol derivative 3b**	OH	OGlc

J-(c)



		R_1	R_2
105	**ginsenoside Rp1**	OGlc-(2,1)-Glc	H

K



Glc: β-D-glucopyranosyl
Ara(fur): α-L-arabinofuranosyl
Ara(pyr): α-L-arabinopyranosyl

		R_1	R_2	R_3
106	**M1 (compound K)**	OH	H	OGlc
107	**M2 (compound Y)**	OH	H	OGlc-(6,1)-Ara(pyr)
108	**M3 (ginsenoside Mc)**	OH	H	OGlc-(6,1)-Ara(fur)
109	**M6**	OGlc	H	OGlc-(6,1)-Ara(pyr)
110	**M7 (ginsenoside Mb)**	OGlc	H	OGlc-(6,1)-Ara(fur)
111	**M9 (Gp-XVII)**	OGlc	H	OGlc-(6,1)-Glc
112	**M13 (Gp-LXXV)**	OH	H	OGlc-(6,1)-Glc

Fig. 2. (*continued*).

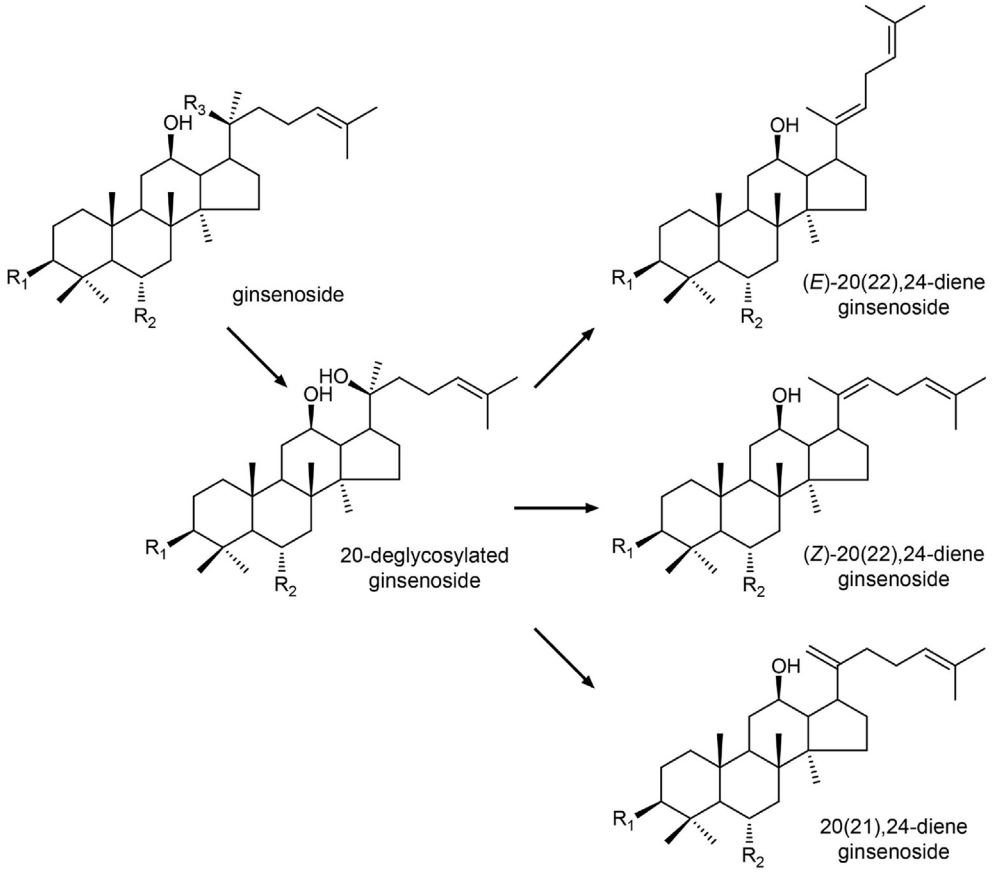


Fig. 3. Probable pathways of the formation of artifactual saponins owing to heating. Deglycosylation and dehydration may occur at C-20 when a PPD- or PPT-type ginsenoside is steamed or heat-processed. The resultant double bond is formed either between C-20 and C-21 or between C-20 and C-22, leading to positional and geometric isomerism. PPD, protopanaxadiol; PPT, protopanaxatriol.

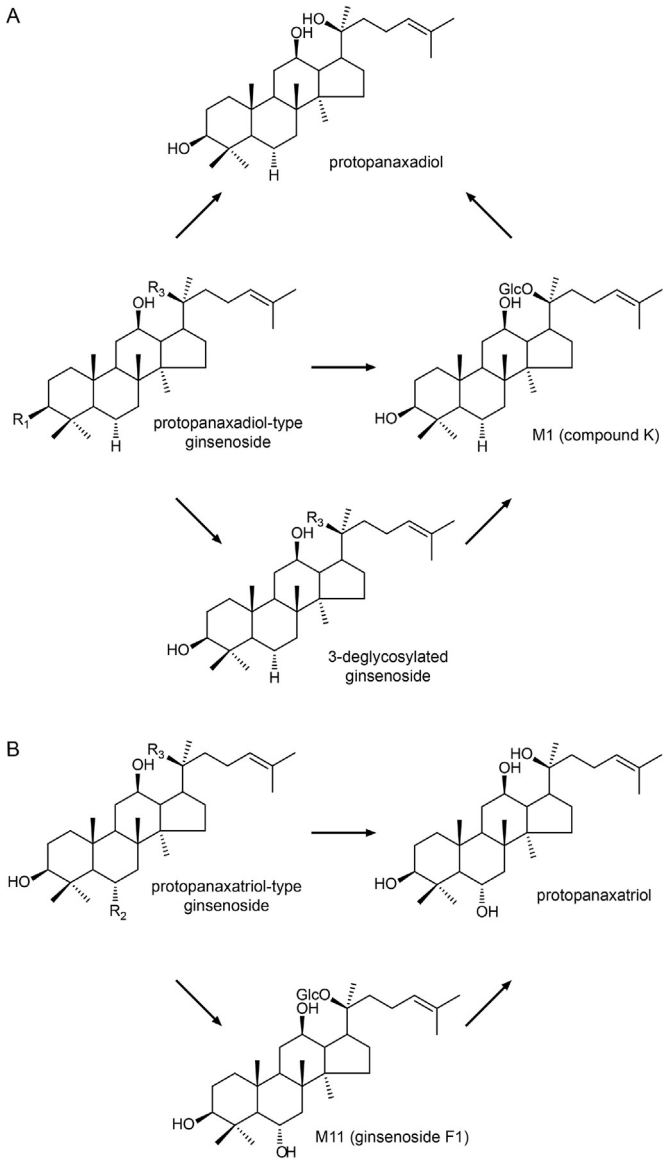


Fig. 4. Suggested metabolic pathways of PPD- and PPT-type ginsenosides. PPD-type ginsenosides tend to be deglycosylated at C-3, and M1 (compound K) may result. PPT-type ginsenosides are deglycosylated at C-6 and/or C-20. PPD, protopanaxadiol; PPT, protopanaxatriol.

dihydroxy-12,23-epoxydammar-24-ene or 6α,25-dihydroxy-20,24-epoxydammar-3,12-dione. Fig. 2G-(b,c) show the structures of saponins with an epoxy group between C-12 and C-23 and between C-20 and C-24, respectively.

2.6. Saponins isolated from P. ginseng with other aglycones

The genins of some saponins isolated from *P. ginseng* are different from those aforementioned. Fig. 2H, I illustrate the structures of ginsenosides with other backbones.

2.7. Synthetic saponins

Synthetic compounds whose structures are related to saponins isolated from *P. ginseng* have been reported. In most cases, derivatives of dammarane are synthesized from isolated ginsenosides to enhance biological activity. Indeed, several acylated saponins have been found to have antitumor activity [61,63]. In addition, some derivatives of ocotillol have shown myocardial ischemia protective effect [64]. Fig. 2J illustrates the structures of some synthetic saponins.

2.8. Saponin metabolites

Most ginsenosides are metabolized by intestinal bacteria. Fig. 4 shows the suggested metabolic pathways of PPD- and PPT-type ginsenosides. The former is deglycosylated at C-3 and transformed to either M1 (compound K) or PPD. By contrast, the latter is deglycosylated at C-6 and/or C-20, and eventually transformed to PPT. Fig. 2K shows the structures of the saponin metabolites that have not been reported as being present in raw or processed ginseng.

3. Concluding remarks

Ginseng is well known for its beneficial biological effects on the human body. While the plant contains various ingredients, ginsenosides play a more significant role in exerting pharmacological actions than any other constituents. Of the great number of ginsenosides present in *P. ginseng*, fewer than 10 account for most ginsenoside contents. In particular, ginsenosides Rb1, Rb2, Rc, Rd, Re, Rf, and Rg1 are most abundant in the roots of raw ginseng. Intriguingly, chemical reactions during the processing of ginseng, such as oxidation, hydrolysis, and/or dehydration, lead to the formation of artifactual compounds, which often have enhanced biological activities. Besides, orally administered ginsenosides undergo biotransformations in the gastrointestinal tract, and some metabolites produced by the action of bacteria have structures different from those of naturally occurring ginsenosides. Here, >100 ginsenosides have been classified according to their structural features.

Conflicts of interest

The authors declare no conflict of interest.

Acknowledgments

This study was supported by the Next-Generation BioGreen 21 Program (PJ008202) from the Rural Development Administration of Korea and the Bio-Synergy Research Project (NRF-2012M3A9C4048796) from the National Research Foundation funded by the Ministry of Science, ICT, and Future Planning.

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