



Review article

Chemical diversity of ginseng saponins from *Panax ginseng*

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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.

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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*.

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Table 1
Scientific and common names of *panax* plants

Scientific name	Rank	Common name
<i>Panax bipinnatifidus</i> Seem	Species	
<i>Panax bipinnatifidus</i> var. <i>angustifolius</i>	Intraspecific taxon	
<i>Panax bipinnatifidus</i> var. <i>bipinnatifidus</i>	Intraspecific taxon	
<i>Panax ginseng</i> C. A. Mey.	Species	Korean ginseng, Ginseng
<i>Panax japonicus</i> (T. Nees) C. A. Mey.	Species	Japanese ginseng
<i>Panax notoginseng</i> (Burkill) F. H. Chen	Species	Chinese ginseng, sanchi
<i>Panax pseudoginseng</i> Wall.	Species	
<i>Panax quinquefolius</i> L.	Species	American ginseng
<i>Panax sokpayensis</i> Shiva K. Sharma & Pandit	Species	
<i>Panax stipuleanatus</i> H. T. Tsai & K. M. Feng	Species	
<i>Panax trifolius</i> L.	Species	
<i>Panax vietnamensis</i> Ha & Grushv.	Species	Vietnamese ginseng
<i>Panax wangianus</i> S. C. Sun	Species	
<i>Panax zingiberensis</i> 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), 3 β ,12 β ,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), 3 β ,6 α ,12 β ,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 3 β ,6 α ,12 β ,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).

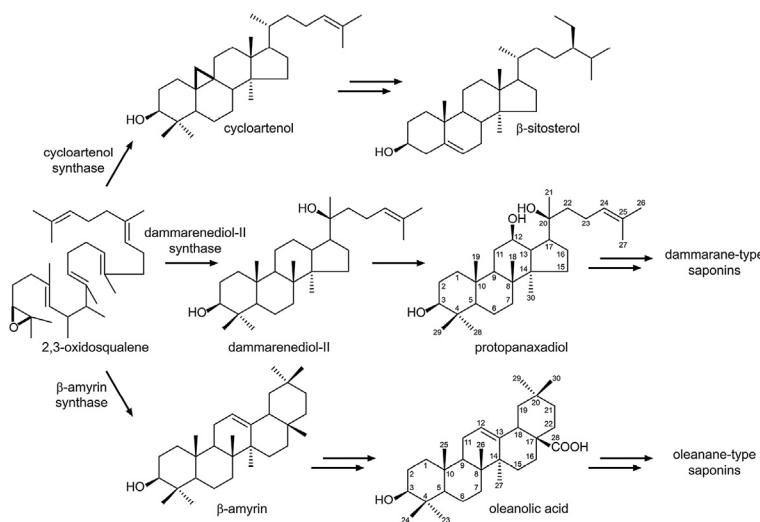


Fig. 1. Biosynthetic pathways of ginseng saponins. 2,3-Oxidosqualene may be cyclized into three different compounds, two of which are dammarenediol-II and β -amyrin, the precursor of dammarane-type saponins and oleanane-type saponins, respectively.

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
<i>Saponins from Panax ginseng</i>							
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 ₅₃ 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	Panaxadiolone	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]
<i>Synthetic saponins</i>							
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]
<i>Saponin metabolites</i>							
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-

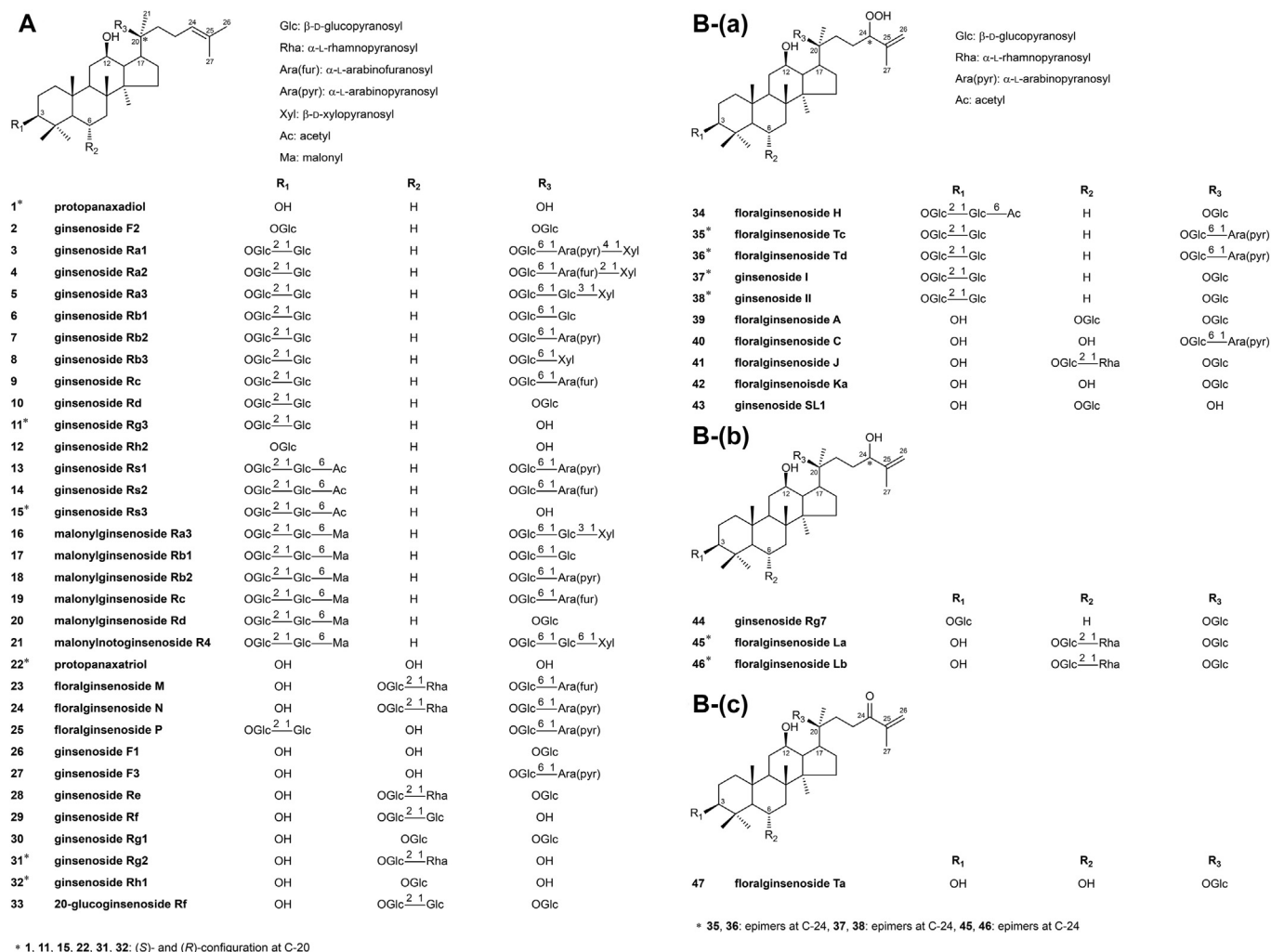
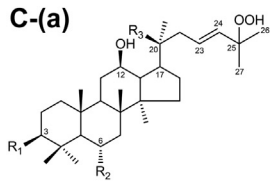


Fig. 2. Structures of ginseng saponins. A. Structures of ginseng saponins whose genin is $3\beta,12\beta,20$ -trihydroxydammar-24-ene (protopanaxadiol)/ $3\beta,6\alpha,12\beta,20$ -tetrahydroxydammar-24-ene (protopanaxatriol); B. Structures of ginseng saponins whose genin is (a) $3\beta,12\beta,20$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

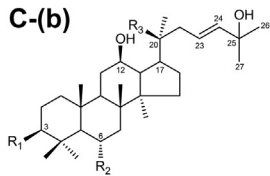
C-(a)



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

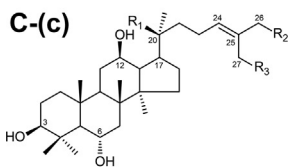
	R ₁	R ₂	R ₃
48 floralginsenoside E	OGlc ²⁻¹ Glc	H	OH
49 floralginsenoside F	OGlc	H	OGlc
50 floralginsenoside G	OGlc ²⁻¹ Glc-6-Ac	H	OGlc
51 floralginsenoside K	OGlc ²⁻¹ Glc	H	OGlc
52 floralginsenoside O	OGlc ²⁻¹ Glc	H	OGlc ⁶⁻¹ Ara(fur)
53 floralginsenoside B	OH	OGlc	OGlc
54 floralginsenoside D	OH	OH	OGlc ⁶⁻¹ Ara(pyr)
55 floralginsenoside I	OH	OGlc ²⁻¹ Rha	OGlc
56 ginsenoside Rh6	OH	OH	OGlc

C-(b)



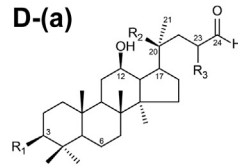
	R ₁	R ₂	R ₃
57 ginsenoside ST2	OH	OGlc	OH

C-(c)



	R ₁	R ₂	R ₃
58 ginsenoside Ki	OGlc	H	OH
59 ginsenoside Km	OGlc	OH	H

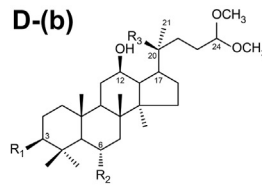
D-(a)



Glc: β -D-glucopyranosyl

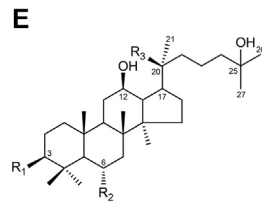
	R ₁	R ₂	R ₃
60 floralginsenoside Kb	OGlc ²⁻¹ Glc	OGlc	H
61 floralginsenoside Kc	OGlc ²⁻¹ Glc	OGlc	OH

D-(b)



	R ₁	R ₂	R ₃
62 floralginsenoside Tb	OH	OH	OGlc

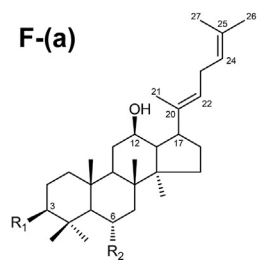
E



Glc: β -D-glucopyranosyl

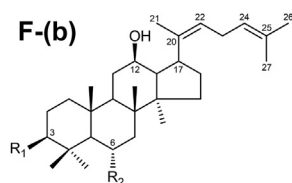
	R ₁	R ₂	R ₃
63 25-hydroxyprotopanaxadiol	OH	H	OH
64 25-hydroxyprotopanaxatriol	OH	OH	OH

Fig. 2. (continued).

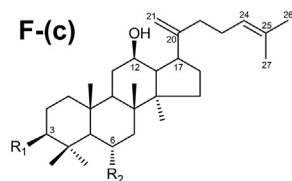


Glc: β -D-glucopyranosyl
 Rha: α -L-rhamnopyranosyl
 Ac: acetyl

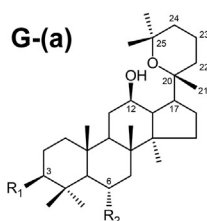
	R ₁	R ₂
65 dehydroprotopanaxadiol I	OH	H
66 ginsenoside Rg5	OGlc $\xrightarrow{2,1}$ Glc	H
67 ginsenoside Rh3	OGlc	H
68 ginsenoside Rs4	OGlc $\xrightarrow{2,1}$ Glc $\xrightarrow{6}$ Ac	H
69 dehydroprotopanaxatriol I	OH	OH
70 ginsenoside F4	OH	OGlc $\xrightarrow{2,1}$ Rha
71 ginsenoside Rh4	OH	OGlc
72 ginsenoside Rs6	OH	OGlc $\xrightarrow{6}$ Ac



	R ₁	R ₂
73 ginsenoside Rz1	OGlc $\xrightarrow{2,1}$ Glc	H

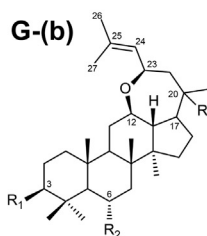


	R ₁	R ₂
74 dehydroprotopanaxadiol II	OH	H
75 ginsenoside Rk1	OGlc $\xrightarrow{2,1}$ Glc	H
76 ginsenoside Rk2	OGlc	H
77 ginsenoside Rs5	OGlc $\xrightarrow{2,1}$ Glc $\xrightarrow{6}$ Ac	H
78 dehydroprotopanaxatriol II	OH	OH
79 ginsenoside Rg6	OH	OGlc $\xrightarrow{2,1}$ Rha
80 ginsenoside Rk3	OH	OGlc
81 ginsenoside Rs7	OH	OGlc $\xrightarrow{6}$ Ac

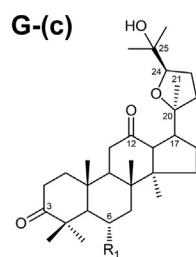


Glc: β -D-glucopyranosyl

	R ₁	R ₂
82 panaxadiol	OH	H
83 panaxatriol	OH	OH

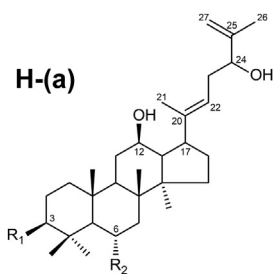


	R ₁	R ₂	R ₃
84 ginsenoside Rh9	OH	OH	OGlc
85 12,23-epoxyginsenoside Rg1	OH	OGlc	OGlc



	R ₁
86 panaxadiolone	OH

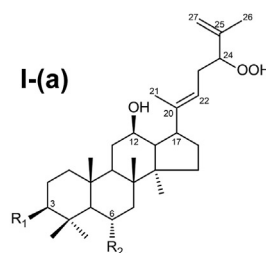
Fig. 2. (continued).



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

87 ginsenoside Rh5

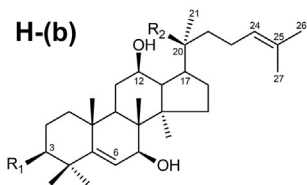
R_1 OH
 R_2 OGlc



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

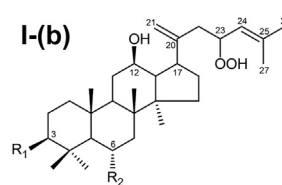
91 ginsenoside SL2
 92 ginsenoside ST1

R_1 OH
 R_2 OGlc $\xrightarrow{2,1}$ Rha
 OH OGlc



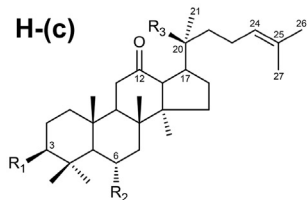
88 ginsenoside Rh7

R_1 OH
 R_2 OGlc



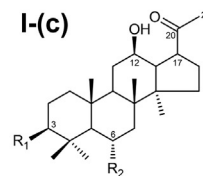
93 ginsenoside SL3

R_1 OH
 R_2 OGlc $\xrightarrow{2,1}$ Rha



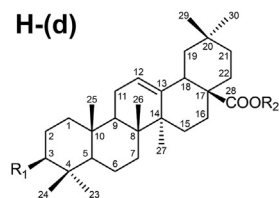
89 ginsenoside Rh8

R_1 OH
 R_2 OH
 R_3 OGlc



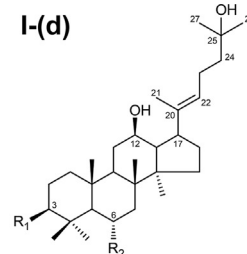
94 hexanordammaran

R_1 OH
 R_2 OH



90 ginsenoside Ro

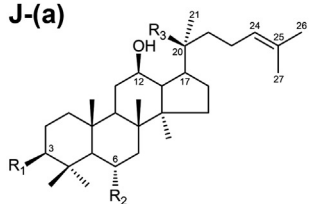
R_1 OGlc $\xrightarrow{2,1}$ Glc
 R_2 Glc



95 isoprotopanaxadiol

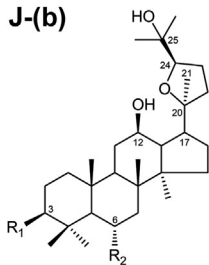
R_1 OH
 R_2 H

Fig. 2. (continued).

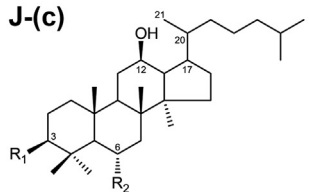
J-(a)

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

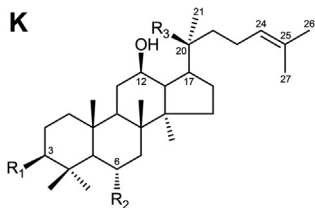
		R₁	R₂	R₃
96	ginsenoside DM1	OH	H	OGlc ⁶ -dodecanoyl
97	ginsenoside PM1	OH	H	OGlc ⁶ -palmitoyl
98	ginsenoside SM1	OH	H	OGlc ⁶ -stearoyl
99	C-X1	OH	OGlc ² ₁ ⁴ -Rha Xyl	OGlc
100	C-Y1	OH	OGlc ² ₁ ⁶ ₁ -Rha Xyl	OGlc
101	C-Y2	OH	OGlc ² ₁ -Rha	OH
102	ginsenoside ORh1	OH	OGlc ⁶ -octanoyl	OH

J-(b)

		R₁	R₂
103	ocotillol derivative 3a	OGlc	H
104	ocotillol derivative 3b	OH	OGlc

J-(c)

		R₁	R₂
105	ginsenoside Rp1	OGlc ² ₁ -Glc	H

K

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

		R₁	R₂	R₃
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).

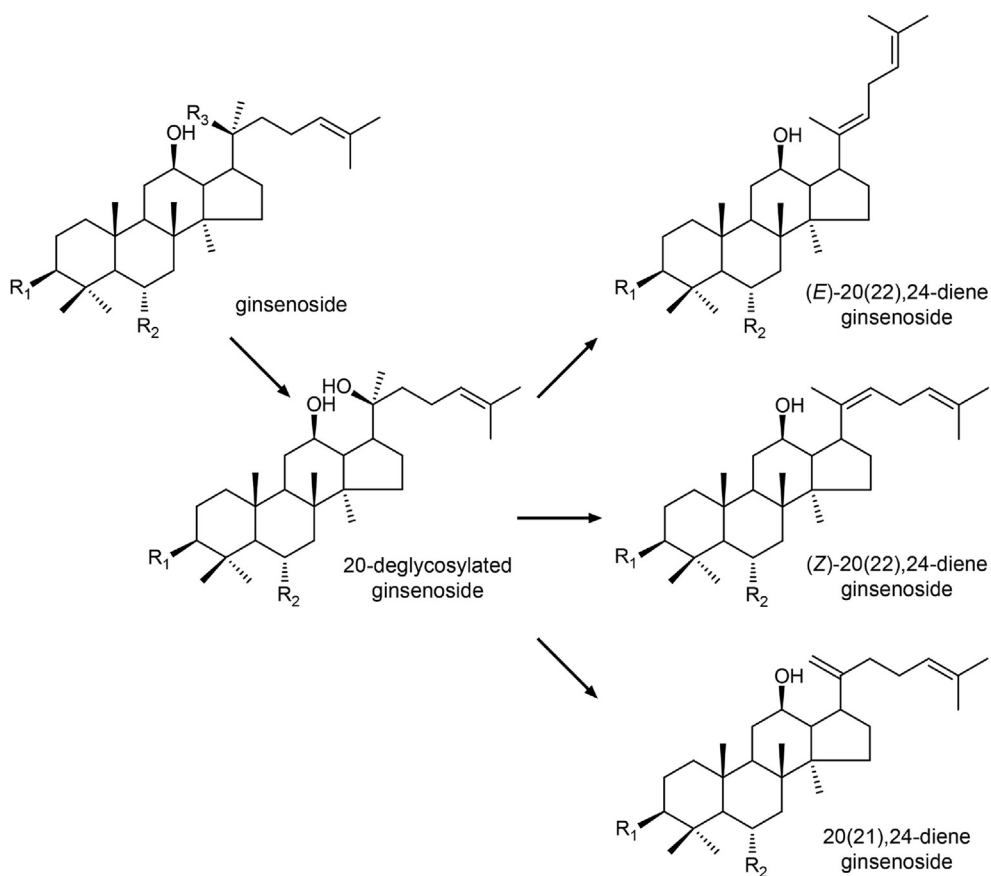


Fig. 3. Probable pathways of the formation of artifactual saponins owing to heating. Deglycosylation and dehydration may occur at C-20 when a PPD- or PPT-type ginsenoside is steamed or heat-processed. The resultant double bond is formed either between C-20 and C-21 or between C-20 and C-22, leading to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

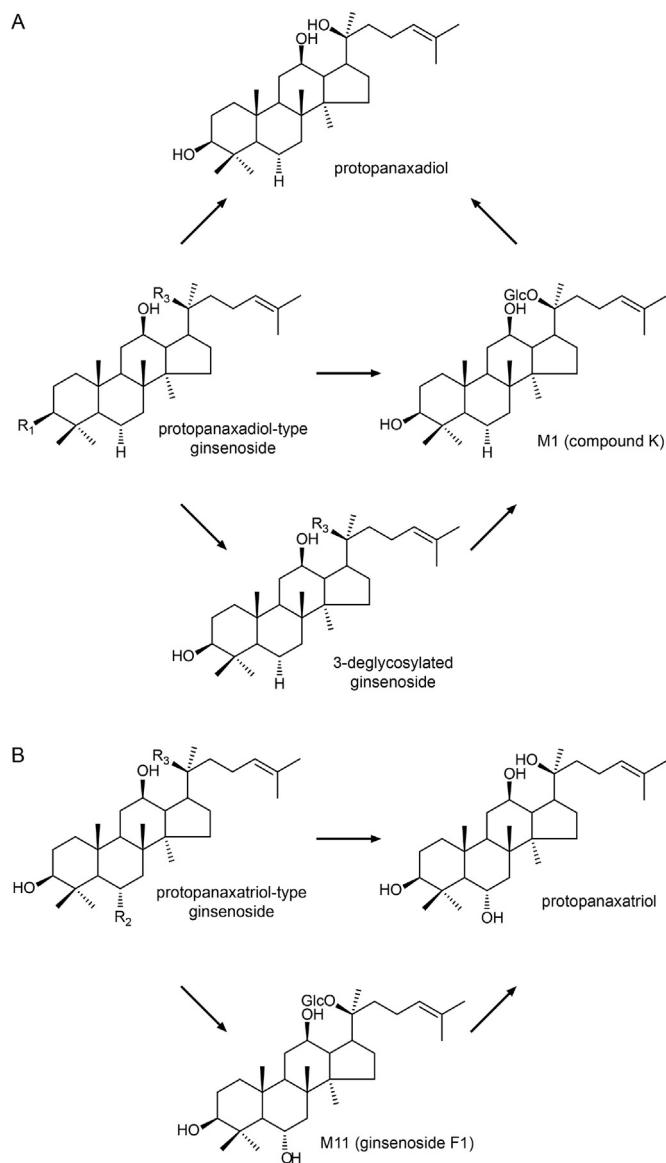


Fig. 4. Suggested metabolic pathways of PPD- and PPT-type ginsenosides. PPD-type ginsenosides tend to be deglycosylated at C-3, and M1 (compound K) may result. PPT-type ginsenosides are deglycosylated at C-6 and/or C-20. PPD, protopanaxadiol; PPT, protopanaxatriol.

dihydroxy-12,23-epoxydammar-24-ene or 6 α ,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 gens 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

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