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<Review>

Lipids in Ginseng (*Panax ginseng*) and Their Analysis

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Abstract – Ginseng (*Panax ginseng*) is recognized as one of the most valuable medicinal herbs in Asia and it contains diverse phytochemicals that contribute to its pharmacological effects. Although lipids represent a major component of ginseng, ginseng lipids are still far from being fully explored. This review is focused on ginseng lipid components and methodologies of their analysis. The ginseng lipid compounds were categorized according to the structural features of each lipid class. This basic information on ginseng lipid components and the analysis methods will be applicable to authentification or quality control of ginseng products, and development of lipid-based pharmaceuticals and nutraceuticals from ginseng.
Keywords – Ginseng, Lipids, Analysis

Introduction

Ginseng (*Panax ginseng*) is known to contain various phytochemicals, including ginseng saponins (ginsenosides), carbohydrates (e.g., monosaccharides, sugars, and polysaccharides), nitrogenous substances (e.g., amino acids, peptides, and alkaloids), fat-soluble substances (e.g., ginseng oils, phytosterols, and polyacetylenes), polyphenols, organic acid, vitamins, and minerals.[1,2] Among these compounds, ginsenosides were initially thought to be the principal active components of ginseng, and so many studies have predominantly focused on ginsenosides. Several reviews have been published describing the chemical structure and bioactivity of ginsenosides.[3-6] The biological activities of non-saponin compounds and non-polar ginseng extracts, however, have also been reported continuously for decades. It has been reported, for example, that the petroleum ether extract of ginseng inhibits the growth of mouse lymphocytic leukemia L1210, murine leukemia L5178Y, murine sarcoma 180 cells, human colon cancer cells (HRT-18, HCT-48, HT-29), and human renal cell carcinoma cell lines (A498, Caki-1, and CURC II).[7-11] More recently, it has been reported that lipid-soluble ginseng extracts show potent inhibitory activity on human hepatoma cells (HepG2), human breast cancer cells (MCF-7), and human lung cancer cells (NCI-H460).[12-14] Polyacetylenes, including panaxynol, panaxydol, and panaxytriol are considered responsible for the anticancer effects of these lipid-soluble extracts,[15,16] so the polyacetylenes of ginseng have been actively studied to elucidate their structures and bioactivities. As the techniques of lipid analysis have made remarkable advances, other lipid molecules such as glycerolipids, which were regarded at one-time simply as a cell membrane constituent, have been found to exhibit inhibitory effects on tumor growth and angiogenesis.[17,18] The comprehensive profiling of the lipid constituents of ginseng is therefore important not only to expand the range of phytochemicals known from this plant, but also to develop pharmacologically active lipid compounds.

To date, numerous lipid compounds have been reported from ginseng. Among these, the lipid species registered in the LIPID Metabolites and Pathways Strategy (LIPID MAPS) (www.lipidmaps.org) are discussed here. The LIPID MAPS has proposed eight lipid classes: fatty acyls [FA], glycerolipids [GL], glycerophospholipids [GP], sphingolipids [SP], sterol lipids [ST], prenol lipids [PR], saccharolipids [SL], and polyketides [PK].[19,20] In this review, the lipid components of ginseng were summarized according to the LIPID MAPS lipid classification system. The purpose of this review is to provide a comprehensive overview of ginseng lipid components and the analysis methods for these lipids.

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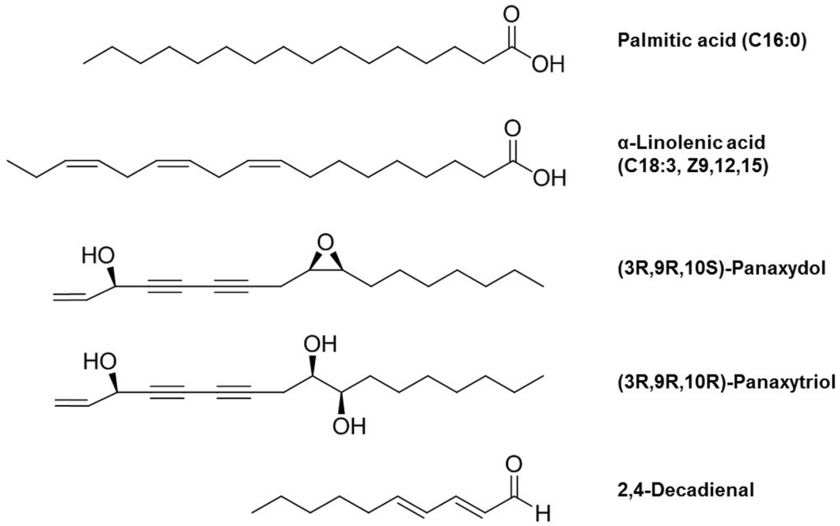

Fig. 1. Representative chemical structures of fatty acyls (palmitic acid, α-linolenic acid, (3R,9R,10S)-panaxydol, (3R,9R,10R)-panaxytriol, 2,4-decadienal) in ginseng.

Ginseng lipid components and their analysis

Fatty acyls – The fatty acyl structure is considered a fundamental building block of complex lipids. Many of these fatty acyls, generally referred to as fatty acids, belong to fatty acids and conjugates class. These lipid molecules are characterized by a repeating series of methylene groups that either straight chain form or unsaturated form possessed a *cis*-unsaturated double bond (Fig. 1).[19] Major fatty acids include palmitic acid (C16:0), palmitoleic acid (C16:1), stearic acid (C18:0), oleic acid (C18:1), linoleic acid (C18:2), and linolenic acid (C18:3) [21] and these major fatty acids have been found in ginseng root (Table 1).

Cho *et al.* [22] identified short chain saturated fatty acids (e.g., C6:0, C7:0, and C8:0) as volatile compounds. A dried white *P. ginseng* sample was directly extracted with dichloromethane and the dried extract was analyzed by gas chromatography-mass spectrometry (GC-MS) equipped with DB-5ms column. Shin and Lee[23] fractionated the total lipid extract of fresh and dried ginseng into neutral lipids, glycolipids, and phospholipids by silicic acid column chromatography (SCC), and then saponified the fatty acids using 0.5N sodium hydroxide and methylated with trifluoride-methanol reagent. The resulting free fatty acid methyl esters were analyzed with a gas liquid chromatography-flame ionization detector (GLC-FID). Fatty acids with 12-24 atoms of carbon were identified, with C18:2 as the predominant component, followed by C16:0, C18:1, and C18:3. Zhang *et al.* [24] also detected C16:0 and C18:2 from 70% ethanol extract of *P. ginseng* by GC-MS equipped with HP-5ms.

Another main class of fatty acyls is the fatty alcohols. The polyacetylenes of *P. ginseng* including panaxydol, panaxynol, panaxytriol, ginsenoyne A-K, and 10,12-octadecadiynoic acid, belong to this class (Table 1). Polyacetylenes are organic polymers that consist of at least two, usually conjugated, triple carbon-carbon bonds. They are mainly produced by higher plants in the families Araliaceae and Apiaceae, and they are recognized as bioactive phytochemicals.[25]

Takahashi and Yoshikura[26] were the first to isolate a polyacetylene compound, panaxynol, from an ether extract of *P. ginseng* roots using the silica-column chromatography and the chemical structure was determined with infrared spectroscopy (IR). The first isolation of panaxydol from *P. ginseng* roots was reported by Poplawski *et al.*[27] The extract of 50% ethanol was fractionated with petrol, and then purified by column chromatography with petrol/acetone/wet diethyl ether (40:1:1) on silica gel. The chemical structure was identified with ^{1}H-nuclear magnetic resonance spectroscopy (NMR), IR, and MS. Another polyacetylenic compound, panaxytriol, was isolated from fresh *P. ginseng* root.[28] The crushed ginseng root sample was extracted with methanol and partitioned using petrol. This petrol layer was washed several times with 5% sodium hydroxide solution and dried. The polyacetylene fraction was obtained by column chromatography with gradient elution of petrol/diethyl ether (from 5:1 to 2:1) from crude oily residue. The fraction of interest was separated by high-performance chromatography with μ-Bondapak CN column and the mobile phase of *n*-hexane/

Table 1. Lipid compounds of *P. ginseng* registered in LIPID MAPS

No.	Compounds	Category	Main Class	Sub Class	LM ID	Typical Class	Analytical Tool [a]	Sample
1	Hexanoic acid (C6:0)	Fatty Acyls [FA]	Fatty Acids and Conjugates [FA01]	Straight chain fatty acids [FA0101]	LMFA01010006	Fatty acids	GC-MS(22)	Root (white ginseng) (22)
2	Heptanoic acid (C7:0)	Fatty Acyls [FA]	Fatty Acids and Conjugates [FA01]	Straight chain fatty acids [FA0101]	LMFA01010007	Fatty acids	GC-MS(22)	Root (white ginseng) (22)
3	Octanoic acid (C8:0)	Fatty Acyls [FA]	Fatty Acids and Conjugates [FA01]	Straight chain fatty acids [FA0101]	LMFA01010008	Fatty acids	GC-MS [22]	Root (white ginseng) (22)
4	Lauric acid (C12:0)	Fatty Acyls [FA]	Fatty Acids and Conjugates [FA01]	Straight chain fatty acids [FA0101]	LMFA01010012	Fatty acids	GLC-FID (23)	Root (fresh and dried ginseng) (23)
5	Myristic acid (C14:0)	Fatty Acyls [FA]	Fatty Acids and Conjugates [FA01]	Straight chain fatty acids [FA0101]	LMFA01010014	Fatty acids	GLC-FID (23)	Root (fresh and dried ginseng) (23)
6	Pentadecylic acid (C15:0)	Fatty Acyls [FA]	Fatty Acids and Conjugates [FA01]	Straight chain fatty acids [FA0101]	LMFA01010015	Fatty acids	GLC-FID (23)	Root (fresh and dried ginseng) (23)
7	Palmitic acid (C16:0)	Fatty Acyls [FA]	Fatty Acids and Conjugates [FA01]	Straight chain fatty acids [FA0101]	LMFA01010001	Fatty acids	GLC-FID (23), GC-MS (24)	Root (fresh and dried ginseng) (23); Root (dried ginseng) (24)
8	Margaric acid (C17:0)	Fatty Acyls [FA]	Fatty Acids and Conjugates [FA01]	Straight chain fatty acids [FA0101]	LMFA01010017	Fatty acids	GLC-FID (23)	Root (fresh and dried ginseng) (23)
9	Stearic acid (C18:0)	Fatty Acyls [FA]	Fatty Acids and Conjugates [FA01]	Straight chain fatty acids [FA0101]	LMFA01010018	Fatty acids	GLC-FID (23)	Root (fresh and dried ginseng) (23)
10	Arachidic acid (C20:0)	Fatty Acyls [FA]	Fatty Acids and Conjugates [FA01]	Straight chain fatty acids [FA0101]	LMFA01010020	Fatty acids	GLC-FID (23)	Root (fresh and dried ginseng) (23)
11	Behenic acid (C22:0)	Fatty Acyls [FA]	Fatty Acids and Conjugates [FA01]	Straight chain fatty acids [FA0101]	LMFA01010022	Fatty acids	GLC-FID (23)	Root (fresh and dried ginseng) (23)
12	Lignoceric acid (C24:0)	Fatty Acyls [FA]	Fatty Acids and Conjugates [FA01]	Straight chain fatty acids [FA0101]	LMFA01010024	Fatty acids	GLC-FID (23)	Root (fresh and dried ginseng) (23)
13	Pentadecenoic acid (C15:1)	Fatty Acyls [FA]	Fatty Acids and Conjugates [FA01]	Unsaturated fatty acids [FA0103]	LMFA01030259	Fatty acids	GLC-FID (23)	Root (fresh and dried ginseng) (23)
14	*cis*-9-Palmitoleic acid (C16:1)	Fatty Acyls [FA]	Fatty Acids and Conjugates [FA01]	Unsaturated fatty acids [FA0103]	LMFA01030056	Fatty acids	GLC-FID (23)	Root (fresh and dried ginseng) (23)
15	Oleic acid (C18:1)	Fatty Acyls [FA]	Fatty Acids and Conjugates [FA01]	Unsaturated fatty acids [FA0103]	LMFA01030002	Fatty acids	GLC-FID (23)	Root (fresh and dried ginseng) (23)
16	Linoleic acid (C18:2)	Fatty Acyls [FA]	Fatty Acids and Conjugates [FA01]	Unsaturated fatty acids [FA0103]	LMFA01030120	Fatty acids	GLC-FID (23), GC-MS (24)	Root (fresh and dried ginseng) (23); Root (dried ginseng) (24)
17	α-Linolenic acid (C18:3)	Fatty Acyls [FA]	Fatty Acids and Conjugates [FA01]	Unsaturated fatty acids [FA0103]	LMFA01030152	Fatty acids	GLC-FID (23)	Root (fresh and dried ginseng) (23)
18	*cis*-Gondoic acid (C20:1)	Fatty Acyls [FA]	Fatty Acids and Conjugates [FA01]	Unsaturated fatty acids [FA0103]	LMFA01030085	Fatty acids	GLC-FID (23)	Root (fresh and dried ginseng) (23)
19	*cis*-Erucic acid (C22:1)	Fatty Acyls [FA]	Fatty Acids and Conjugates [FA01]	Unsaturated fatty acids [FA0103]	LMFA01030089	Fatty acids	GLC-FID (23)	Root (fresh and dried ginseng) (23)

Table 1. continued

No.	Compounds	Category	Main Class	Sub Class	LM ID	Typical Class	Analytical Tool [a]	Sample
20	Nervonic acid (C24:1)	Fatty Acyls [FA]	Fatty Acids and Conjugates [FA01]	Unsaturated fatty acids [FA0103]	LMFA01030092	Fatty acids	GLC-FID (23)	Root (fresh and dried ginseng) (23)
21	Panaxydol	Fatty Acyls [FA]	Fatty alcohols [FA05]	-	LMFA05000028	Polyacetylenes	HPLC-UV, NMR (27)	Root (dried ginseng) (27)
22	Panaxynol	Fatty Acyls [FA]	Fatty alcohols [FA05]	-	LMFA05000689	Polyacetylenes	IR, UV, NMR (26)	Root (dried ginseng) (26)
23	Panaxytriol	Fatty Acyls [FA]	Fatty alcohols [FA05]	-	LMFA05000027	Polyacetylenes	HPLC-UV, IR, NMR (28)	Root (fresh ginseng) (28)
24	Ginsenoyne A - K	Fatty Acyls [FA]	Fatty alcohols [FA05]	-	LMFA05000661	Polyacetylenes	UV, IR, NMR, HR-EIMS (30,31)	Root (white ginseng) (30,31)
25	10,12-Octadecadiynoic acid	Fatty Acyls [FA]	Fatty Acids and Conjugates [FA01]	Unsaturated fatty acids [FA0103]	LMFA01030542	Polyacetylenes	GC-MS (24)	Root (dried ginseng) (24)
26	Hexanal	Fatty Acyls [FA]	Fatty aldehydes [FA06]		LMFA06000109	Fatty aldehydes	GC-MS (22)	Root (white ginseng) (22)
27	Heptanal	Fatty Acyls [FA]	Fatty aldehydes [FA06]		LMFA06000001	Fatty aldehydes	GC-MS (22)	Root (white ginseng) (22)
28	Octanal	Fatty Acyls [FA]	Fatty aldehydes [FA06]		LMFA06000028	Fatty aldehydes	GC-MS (22)	Root (white ginseng) (22)
29	2,4-Decadienal	Fatty Acyls [FA]	Fatty aldehydes [FA06]		LMFA06000057	Fatty aldehydes	GC-MS (22)	Root (white ginseng) (22)
30	Oleamide	Fatty Acyls [FA]	Fatty amides [FA08]	Primary amides [FA0801]	LMFA08010004		GC-MS (24)	Root (white ginseng) (24)
31	Monoacylglycerols	Glycerolipids [GL]	Monoradylglycer-ols [GL01]	Monoacylglycerols [GL0101]	LMGL01010000	Neutral lipids; storage lipids	TLC (23)	Root (fresh and white ginseng) (23)
32	Diacylglycerols	Glycerolipids [GL]	Diradylglycerols [GL02]	Diacylglycerols [GL0201]	LMGL02010000	Neutral lipids; storage lipids	TLC (23)	Root (fresh and white ginseng) (23)
33	Triacylglycerols	Glycerolipids [GL]	Triradylglycerols [GL03]	Triacylglycerols [GL0301]	LMGL03010000	Neutral lipids; storage lipids	TLC (23); nano-EIS-MS (35)	Root (fresh and white ginseng) (23); Root, rhizome (fresh ginseng) (35)
34	Monogalactosyldia-cylglycerols (MGDG)	Glycerolipids [GL]	Glycosyldiradylg-lycerols [GL05]	Glycosyldiacylglyc-erols [GL0501]	LMGL0501AA00	Galactolipids	TLC (23); nano-EIS-MS (35)	Root (fresh and white ginseng) (23); Root, rhizome (fresh ginseng) (35)
35	Digalactosyldiacyl-glycerols (DGDG)	Glycerolipids [GL]	Glycosyldiradylg-lycerols [GL05]	Glycosyldiacylglyc-erols [GL0501]	LMGL0501AD00	Galactolipids	TLC (23)	Root (fresh and white ginseng) (23)
36	Phosphatidic acid (PA)	Glycerophospholipid s [GP]	Glycerophosphates [GP10]	Diacylglycerophosph ates [GP1001]	LMGP10010000	Phospholipids	nano-ESI-MS (35)	Root, rhizome (fresh ginseng) (35)

Table 1. continued

No.	Compounds	Category	Main Class	Sub Class	LM ID	Typical Class	Analytical Tool [a]	Sample
37	Phosphatidylcholine (PC)	Glycerophospholipids [GP]	Glycerophosphocholines [GP01]	Diacylglycerophosphocholines [GP0101]	LMGP01010000	Phospholipids	TLC (23); nano-ESI-MS (35)	Root (fresh and white ginseng) (23); Root, rhizome (fresh ginseng) (35)
38	Phosphatidylethanolamine (PE)	Glycerophospholipids [GP]	Glycerophosphoethanolamines [GP02]	Diacylglycerophosphoethanolamines [GP0201]	LMGP02010000	Phospholipids	TLC (23); nano-ESI-MS (35)	Root (fresh and white ginseng) (23); Root, rhizome (fresh ginseng) (35)
39	Phosphatidylglycerol (PG)	Glycerophospholipids [GP]	Glycerophosphoglycerols [GP04]	Diacylglycerophosphoglycerols [GP0401]	LMGP04010000	Phospholipids	TLC (23); nano-ESI-MS (35)	Root (fresh and white ginseng) (23); Root, rhizome (fresh ginseng) (35)
40	Phosphatidylinositol (PI)	Glycerophospholipids [GP]	Glycerophosphoinositols [GP06]	Diacylglycerophosphoinositols [GP0601]	LMGP06010000	Phospholipids	nano-ESI-MS (35)	Root, rhizome (fresh ginseng) (35)
41	Cholesterol	Sterol Lipids [ST]	Sterols [ST01]	Cholesterol and derivatives [ST0101]	LMST01010001	Sterols	TLC, GC-MS (44)	Seed oil (44)
42	Campesterol	Sterol Lipids [ST]	Sterols [ST01]	Ergosterols and C24-methyl derivatives [ST0103]	LMST01030097	Phytosterols	TLC, GC-MS (45)	Root (white ginseng) (45)
43	Obtusifoliol	Sterol Lipids [ST]	Sterols [ST01]	Ergosterols and C24-methyl derivatives [ST0103]	LMST01030101	4α-Methylsterols	TLC, GC-MS (44)	Seed oil (44)
44	β-Sitosterol	Sterol Lipids [ST]	Sterols [ST01]	Stigmasterols and C24-ethyl derivatives [ST0104]	LMST01040250	Phytosterols	TLC, GC-MS (45); GC-MS (24)	Root (white ginseng) (24)
45	Stigmasterol	Sterol Lipids [ST]	Sterols [ST01]	Stigmasterols and C24-ethyl derivatives [ST0104]	LMST01040123	Phytosterols	GC-MS (45)	Root (white ginseng) (45)
46	Isofucosterol	Sterol Lipids [ST]	Sterols [ST01]	Stigmasterols and C24-ethyl derivatives [ST0104]	LMST01040145	Sterols	TLC, GC-MS (44)	Seed oil (44)
47	δ7-Avenasterol	Sterol Lipids [ST]	Sterols [ST01]	Stigmasterols and C24-ethyl derivatives [ST0104]	LMST01040154	Sterols	TLC, GC-MS (44)	Seed oil (44)
48	Cycloartenol	Sterol Lipids [ST]	Sterols [ST01]	Cycloartanols and derivatives [ST0110]	LMST01100008	Triterpene alcohols	TLC, GC-MS (44)	Seed oil (44)
49	24-Methylene-cycloartanol	Sterol Lipids [ST]	Sterols [ST01]	Cycloartanols and derivatives [ST0110]	LMST01100001	Triterpene alcohols	TLC, GC-MS (44)	Seed oil (44)
50	Cycloeucalenol	Sterol Lipids [ST]	Sterols [ST01]	Cycloartanols and derivatives [ST0110]	LMST01100011	4α-Methylsterols	TLC, GC-MS (44)	Seed oil (44)

Table 1. continued

No.	Compounds	Category	Main Class	Sub Class	LM ID	Typical Class	Analytical Tool [a]	Sample
51	Myrcene	Prenol Lipids [PR]	Isoprenoids [PR01]	C10 isoprenoids (monoterpenes) [PR0102]	LMPR0102010005	Monoterpenes	GC-MS (22)	Root (white ginseng) (22)
52	Terpinolene	Prenol Lipids [PR]	Isoprenoids [PR01]	C10 isoprenoids (monoterpenes) [PR0102]	LMPR0102090062	Monoterpenes	GC-MS (22)	Root (white ginseng) (22)
53	α-Pinene	Prenol Lipids [PR]	Isoprenoids [PR01]	C10 isoprenoids (monoterpenes) [PR0102]	LMPR0102120012	Monoterpenes	GC-MS (22)	Root (white ginseng) (22)
54	β-Pinene	Prenol Lipids [PR]	Isoprenoids [PR01]	C10 isoprenoids (monoterpenes) [PR0102]	LMPR0102120013	Monoterpenes	GC-MS (22)	Root (white ginseng) (22)
55	Bicyclogermacrene	Prenol Lipids [PR]	Isoprenoids [PR01]	C15 isoprenoids (sesquiterpenes) [PR0103]	LMPR0103100001	Sesquiterpenes	GC-MS (22)	Root (white ginseng) (22)
56	Humulene	Prenol Lipids [PR]	Isoprenoids [PR01]	C15 isoprenoids (sesquiterpenes) [PR0103]	LMPR0103110001	Sesquiterpenes	GC-MS (22)	Root (white ginseng) (22)
57	Nerolidol	Prenol Lipids [PR]	Isoprenoids [PR01]	C15 isoprenoids (sesquiterpenes) [PR0103]	LMPR0103010005	Sesquiterpenes	GC-MS (22)	Root (white ginseng) (22)
58	Zingiberene	Prenol Lipids [PR]	Isoprenoids [PR01]	C15 isoprenoids (sesquiterpenes) [PR0103]	LMPR0103060002	Sesquiterpenes	GC-MS (22)	Root (white ginseng) (22)
59	β-Bisabolene	Prenol Lipids [PR]	Isoprenoids [PR01]	C15 isoprenoids (sesquiterpenes) [PR0103]	LMPR0103060013	Sesquiterpenes	GC-MS (22)	Root (white ginseng) (22)
60	β-Caryophyllene	Prenol Lipids [PR]	Isoprenoids [PR01]	C15 isoprenoids (sesquiterpenes) [PR0103]	LMPR0103120001	Sesquiterpenes	GC-MS (22)	Root (white ginseng) (22)
61	β-Selinene	Prenol Lipids [PR]	Isoprenoids [PR01]	C15 isoprenoids (sesquiterpenes) [PR0103]	LMPR0103190010	Sesquiterpenes	GC-MS (22)	Root (white ginseng) (22)
62	δ-Cadinene	Prenol Lipids [PR]	Isoprenoids [PR01]	C15 isoprenoids (sesquiterpenes) [PR0103]	LMPR0103330001	Sesquiterpenes	GC-MS (22)	Root (white ginseng) (22)
63	Squalene	Prenol Lipids [PR]	Isoprenoids [PR01]	C30 isoprenoids (triterpenes) [PR0106]	LMPR0106010002	Triterpenes	TLC, GC-MS (44)	Seed oil (44)
64	β-Amyrin	Prenol Lipids [PR]	Isoprenoids [PR01]	C30 isoprenoids (triterpenes) [PR0106]	LMPR0106150015	Triterpene alcohols	TLC, GC-MS (44)	Seed oil (44)

Table 1. continued

No.	Compounds	Category	Main Class	Sub Class	LM ID	Typical Class	Analytical Tool [a]	Sample
65	Lupeol	Prenol Lipids [PR]	Isoprenoids [PR01]	C30 isoprenoids (triterpenes) [PR0106]	LMPR0106130001	Triterpene alcohols	TLC, GC-MS (44)	Seed oil (44)
66	Catechin	Polyketides [PK]	Flavonoids [PK12]	Flavans, Flavanols and Leucoanthocyanidi-ns [PK1202]	LMPK12020001	Phenolic acids	UPLC-UV (48)	Fruit, leaves, roots (48)
67	Formononetin	Polyketides [PK]	Flavonoids [PK12]	Isoflavonoids [PK1205]	LMPK12050037	Phenolic acids	UPLC-UV (48)	Fruit, leaves, roots (48)
68	Kaempferol	Polyketides [PK]	Flavonoids [PK12]	Flavones and Flavonols [PK1211]	LMPK12110003	Phenolic acids	UPLC-UV (48)	Fruit, leaves, roots (48)
69	Quercetin	Polyketides [PK]	Flavonoids [PK12]	Flavones and Flavonols [PK1211]	LMPK12110004	Phenolic acids	UPLC-UV [48	Fruit, leaves, roots (48)
70	Rutin	Polyketides [PK]	Flavonoids [PK12]	Flavones and Flavonols [PK1211]	LMPK12112098	Phenolic acids	UPLC-UV (48)	Fruit, leaves, roots (48)
71	Hesperetin	Polyketides [PK]	Flavonoids [PK12]	Flavanones [PK1214]	LMPK12140003	Phenolic acids	UPLC-UV (48)	Fruit, leaves, roots (48)
72	Naringenin	Polyketides [PK]	Flavonoids [PK12]	Flavanones [PK1214]	LMPK12140001	Phenolic acids	UPLC-UV (48)	Fruit, leaves, roots (48)
73	Naringin	Polyketides [PK]	Flavonoids [PK12]	Flavanones [PK1214]	LMPK12140235	Phenolic acids	UPLC-UV (48)	Fruit, leaves, roots (48)
74	Resveratrol	Polyketides [PK]	Flavonoids [PK12]	Diphenyl ethers, biphenyls, dibenzyls and stilbenes [PK1309]	LMPK13090005	Phenolic acids	UPLC-UV (48)	Fruit, leaves, roots (48)

[a]GC-FID, gas chromatography-flame ionization detection; HLPC-UV, high-performance liquid chromatography-ultra violet detector; HR-EIMS, high resolution-electron impact mass spectrometry; IR, infrared spectroscopy; GC-MS, gas chromatography-mass spectrometry; GLC-FID, gas liquid chromatography-flame ionization detection; NMR, nuclear magnetic resonance spectroscopy; TLC, thin layer chromatograph

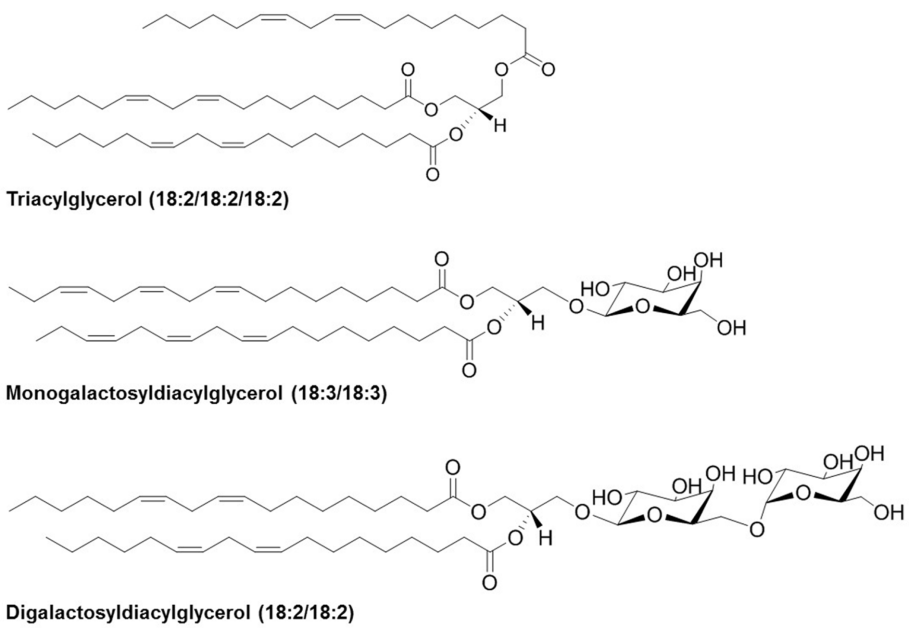

Fig. 2. Representative chemical structures of glycerolipids (triacylglycerol (18:2/18:2/18:2), monogalactosyldiacylglycerol (18:3/18:3), digalactosyldiacylglycerol (18:2/18:2)) in ginseng.

diethyl ether (20:1). Finally, the panaxytriol fraction was isolated using semi-prep HPLC and its chemical structure was determined with ultra violet spectroscopy (UV), IR, ^{1}H-, ^{13}C-NMR.

Hirakura *et al.*[29-31] purified ginsenoynes A-K from a hexane extract of dried *P. ginseng* root. The hexane extract was loaded to a silica gel column, eluted and fractionated using hexane, hexane-ethyl acetate, ethyl acetate, and methanol. The chemical structure was determined by UV-, and IR, ^{1}H-, ^{13}C-NMR, and high resolution-electron impact mass spectrometry (HR-EIMS). Zhang *et al.* [24] identified 10,12-octadecdiynoic acid in *P. ginseng* roots by GC-MS analysis.

In addition, fatty aldehydes and fatty amides have been found in ginseng. The fatty aldehydes were analyzed Cho *et al.* [22] with same method used for short chain fatty acid analysis. For the fatty amide analysis, dried ginseng powder was soaked with 70% ethanol, and then dried extract was partitioned with distilled water and chloroform.[24] The chloroform extract was analyzed by using GC-MS equipped with HP-5ms column.

Glycerolipids – The term glycerolipids is generally used to refer to the fatty acid esters of glycerol (Fig. 2).[19] As shown in Table 1, there are two main types: glycerols substituted with mono-, di-, and tri-fatty acyls, and diglycerides attached to one or more galactose residues via a glycosidic linkage. Among these, the galactoglycerolipids [e.g., monogalactosyldiacylglycerol (MGDG) and digalactosyldiacylglycerol (DGDG)] are the primary constituent of photosynthetic thylakoid membranes in plants. Glycerolipids can contain various fatty acyl structures with different chain lengths and numbers and positions of double bonds, and each species with different combination of fatty acyls has a different biological function. For instance, glycerolipids containing polyunsaturated fatty acids play an important role in *Synechocystis* sp. PCC 6803 cell growth, respiration, and photosynthesis, whereas mutated cells containing monounsaturated fatty acids showed growth suppression and photoinhibitory damage.[32]

Neutral lipids, including monoacylglycerols, diacylglycerols, triacylglycerols (TAGs), have been found in ginseng root, and the total amount of these neutral lipids in fresh ginseng lipid extracts was reported to be 45.28%.[23] Two galactoglycerolipids, MGDG and DGDG, have also been identified, and they represent 18.12% of the total lipid extract. These glycerolipid compounds were extracted by the method of Bligh and Dyer[33] with chloroform/methanol (2:1, v/v). Using the SCC system, the individual fractions of neutral lipids, glycolipids, and glycerophospholipids were obtained with elution solvents of ethyl ether, acetone, and methanol, respectively. Each species was then separated and identified by thin-layer chromatography (TLC). The neutral lipid fraction was developed on silica gel HR 60 TLC plate using a solvent system of petrol ether-ethyl ether-acetic acid (80:20:1, v/

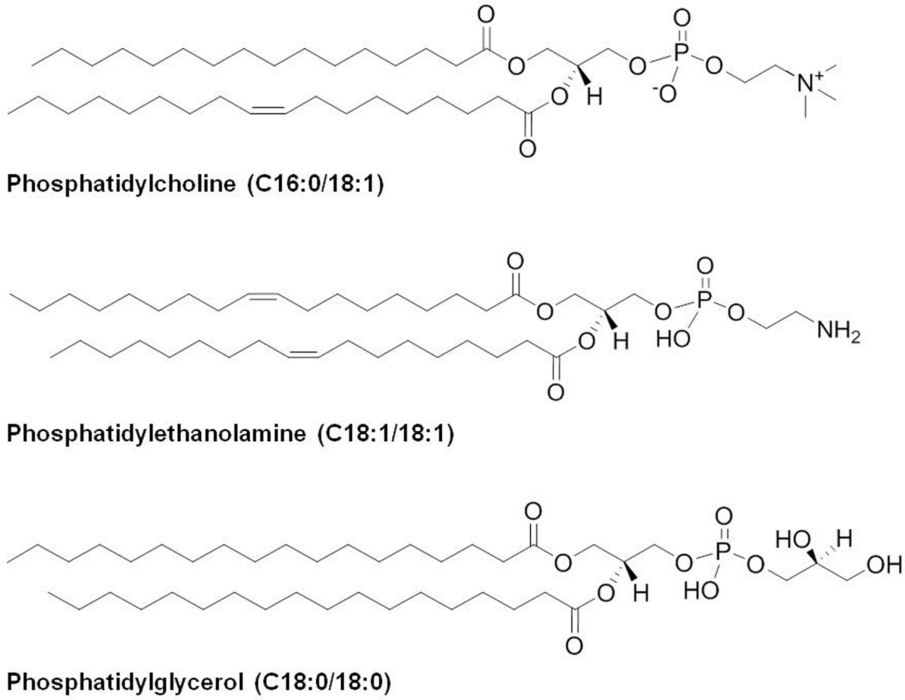

Fig. 3. Representative chemical structures of glycerophospholipids (phosphatidylcholine (C16:0/18:1), phosphatidylethanolamine (C18:1/18:1), phosphatidylglycerol (C18:0/18:0)) in ginseng.

v). Visualization was achieved by spraying with 40% sulfuric acid, and identification was conducted by comparison with commercial standards. The glycolipid fraction was developed using a solvent system of chloroform-acetone-methanol-acetic acid-water (65:20:10:10:3, v/v), and the presence of sugar was determined using anthrone reagent.[34]

More recently, Kim *et al*. [35] extracted lipids using Matyash *et al*.'s method[36] with methyl-*tert*-butyl ether/methanol/water (10:3:2.5, v/v/v). The intact species of TAGs and MGDG from ginseng lipid extract were analyzed using direct infusion (DI)-MS by untargeted approach. Han and Gross were the pioneers in the field of DI-MS.[37]

Glycerophospholipids – The glycerophospholipids are universal in nature and are major components of cell membranes.[19] Fatty acyls are esterified to the glycerol backbone in the *sn*-1 and *sn*-2 positions, and the characteristic polar head groups are esterified via a phosphate group in the *sn*-3 position (Fig. 3). The polar head group contains a phosphate group that determines the nature of the lipid molecules. Like glycerolipids, glycerophospholipids possess numerous combinations of fatty acyls.

Ginseng glycerophospholipids include phosphatidylinositol (PI), phosphatidylcholine (PC), phosphatidylglycerol (PG), and phosphatidylethanolamine (PE), which together make up 36.60% of lipid extract.[23] The glycerophospholipids were separated and identified using TLC, and the glycerophospholipid fraction was developed using a solvent system of chloroform-acetone-methanol-acetic acid-water (65:20:10:10:3, v/v). The presence of amino groups, choline groups, and phosphate groups was determined using ninhydrin,[38] Dragendorff,[39] and Zinzdze reagents,[40] respectively. In addition to the identification of PI, PC, PG, and PE species, phosphatidic acid and lyso-PE species have also been found in ginseng lipid extract using nano-ESI-MS.[35]

Sterol lipids – More than 250 different types of phytosterols are known to occur in plant.[21] These lipid molecules contain a common fused four-ring core structure and have different biological roles as hormones and signaling molecules in plant (Fig. 4). It is known that stigmasterol, sitosterol, and two 24-ethyl sterols are major sterols in plant.[41] Plant sterols have been in the spotlight for their pharmacological effects, which include lowering cholesterol levels, preventing coronary heart disease, and exhibiting antitumor activity.[42,43]

Matsumoto *et al.* [44] identified sterol lipids from ginseng seed oil. They obtained three sterolic fractions including triterpene alcohol, 4α-methylsterol, and sterol using TLC on silica gel with *n*-hexane/ethyl acetate (6:1, v/v). Each

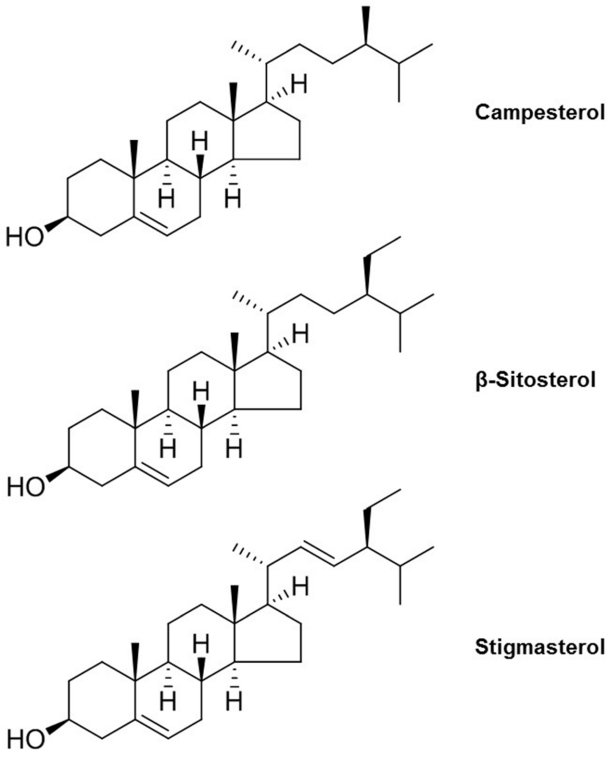

Fig. 4. Representative chemical structures of sterol lipids (campesterol, β-sitosterol, stigmasterol) in ginseng.

fraction was separated into subfractions using argentic (silver nitrate/silica gel, 1:4) preparative TLC with a carbon tetrachloride/dichloromethane (5:1, v/v) solvent system. The lipid compounds were identified from these fractions by GLC, MS, and GC-MS. A total of 18 sterol lipids were reported and seven of these compounds were registered in LIPID MAPS as shown in Table 1. Among these compounds, 28-isofucosterol is the most predominant sterol component of *P. ginseng* seed oil.

Phytosterols including campesterol, β-sitosterol, and stigmasterol, have been detected from ethyl acetate extract of *P. ginseng* root by GC-MS analysis with an HP-1 column.[45] Zhang *et al.* [24] reported that the highest sitosterol content was observed in 6-year-old ginseng, but the levels dramatically decreased in older ginseng.

Prenol lipids – Prenol lipids represent the lipid molecules synthesized from the five-carbon precursors isopentenyl diphosphate and dimethylallyl diphosphate that are the end-product of the mevalonic acid pathway (Fig. 5).[19] In particular, terpenes derived biosynthetically from units of isoprene (C_5) are a representative class of prenol lipids. Monoterpene (two isoprene units, C_{10}) and sesquiterpene (three isoprene units, C_{15}) are major constituents of essential oils and are known to be closely relate to the aroma of the plants.[46]

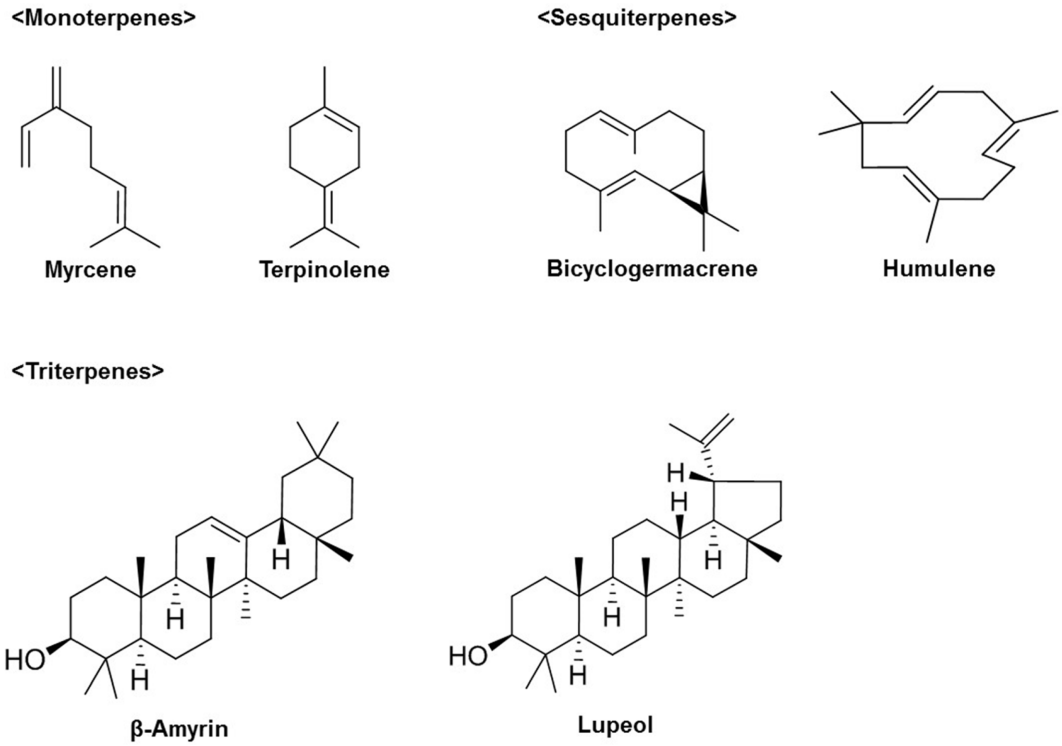

Fig. 5. Representative chemical structures of prenol lipids (myrcene, terpinolene, bicyclogermacrene, humulene, β-amyrin, lupeol) in ginseng.

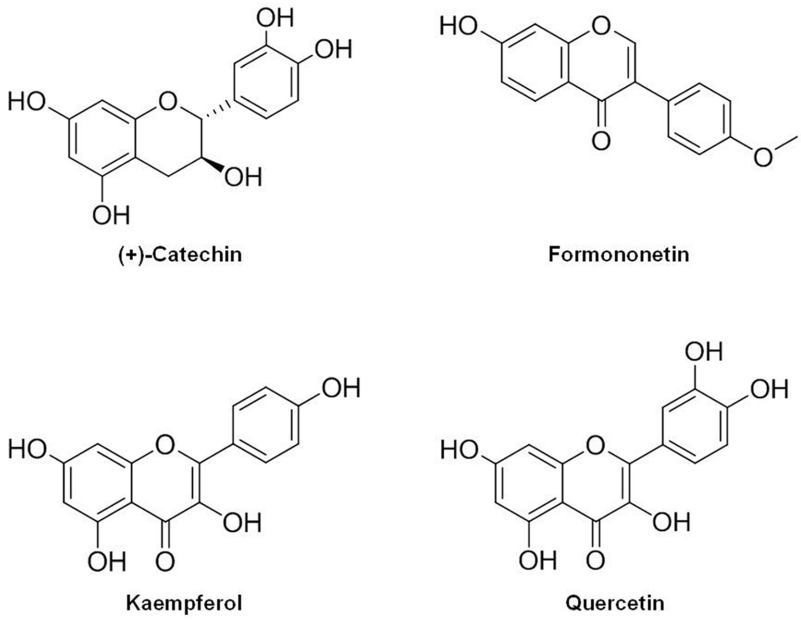

Fig. 6. Representative chemical structures of polyketides ((+)-catechin, formononetin, kaempferol, quercetin) in ginseng.

Cho *et al.*[22] analyzed 27 terpenes by GC-MS and reported that the main volatile compounds of ginseng were sesquiterpenes, such as bicyclogermacrene and humulene. Matsumoto *et al.* [44] reported squalene as the most abundant component of the lipid fraction of *P. ginseng* seed oil and identified β-amyrin and lupeol from a triterpene alcohol fraction.

Polyketides – Interestingly, flavonoids belong to the class of lipid molecules known as polyketides (Fig. 6). Polyketides include a diverse group of natural products that have highly bioactive properties and display antimicrobial, anticancer, and anticholesterol acitivity.[47] They are synthesized by three types of polyketide synthases (PKSs). Among these synthetic enzymes, chalcone synthase, a type III PKS, is involved in the first step of flavonoid biosynthesis.[47] In addition to the flavonoids listed in Table 1, a total 23 phenolic compounds have been identified in *P. ginseng* fruit, leaves, and roots.[48] Ginseng powder (1 g) was extracted with 10 mL of acetonitrile and 2 mL of 0.1 N hydrochloric acid solution using a shaker. The filtrate of the crude ginseng extract was dried and reconstituted with 5 mL of 80% aqueous methanol. The phenolic compounds were separated using ultra performance liquid chromatography with a two-solvent system (solvent A: 0.1% glacial acetic acid in distilled water; solvent B: 0.1% glacial acetic acid in acetonitrile) on a C_{18} reverse phase column. The identification of phenolic compounds was carried out by comparing the retention times to authentic standards.

Conclusion

In this review, various lipid components in ginseng have been summarized as like follows: fatty acyls, glycerolipids, glycerophospholipids, sterol lipids, prenol lipids, and polyketides. As ginseng lipids have diverse chemical structures, extract methods and analysis techniques differ according to their chemical properties. Initially, the lipid components in ginseng were revealed by traditional analytical techniques such as TLC and spectroscopy including UV, IR and NMR. However, more recently, GC-, LC-, and DI-MS are more often applied to simultaneous analysis of ginseng lipids from various classes. In particular, intact lipid species that have not gone through the saponification process can be directly analyzed using DI-MS.

This review provides fundamental information about the lipid components in ginseng. This information will be useful to screening novel ginseng lipids and their bioactivities as well as for authentification or quality control of ginseng products, and it will assist with the development of lipid-based pharmaceuticals and nutraceuticals from ginseng.

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