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Review Article

Phytochemical analysis of *Panax* species: a review

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ABSTRACT

Panax species have gained numerous attentions because of their various biological effects on cardiovascular, kidney, reproductive diseases known for a long time. Recently, advanced analytical methods including thin layer chromatography, high-performance thin layer chromatography, gas chromatography, high-performance liquid chromatography, ultra-high performance liquid chromatography with tandem ultraviolet, diode array detector, evaporative light scattering detector, and mass detector, two-dimensional high-performance liquid chromatography, high speed counter-current chromatography, high speed centrifugal partition chromatography, micellar electrokinetic chromatography, high-performance anion-exchange chromatography, ambient ionization mass spectrometry, molecularly imprinted polymer, enzyme immunoassay, ^{1}H-NMR, and infrared spectroscopy have been used to identify and evaluate chemical constituents in *Panax* species. Moreover, Soxhlet extraction, heat reflux extraction, ultrasonic extraction, solid phase extraction, microwave-assisted extraction, pressurized liquid extraction, enzyme-assisted extraction, acceleration solvent extraction, matrix solid phase dispersion extraction, and pulsed electric field are discussed. In this review, a total of 219 articles published from 1980 to 2018 are investigated. *Panax* species including *P. notoginseng*, *P. quinquefolius*, sand *P. ginseng* in the raw and processed forms from different parts, geographical origins, and growing times are studied. Furthermore, the potential biomarkers are screened through the previous articles. It is expected that the review can provide a fundamental for further studies.

1. Introduction

Genus *Panax* belonging to Family Araliaceae contains eleven species (three varieties) namely *P. trifolius*, *P. notoginseng*, *P. quinquefolius*, *P. ginseng*, *P. pseudoginseng*, *P. zingiberensis*, *P. stipuleanatus*, *P. japonicus*, *P. japonicus* var. *angustifolius*, *P. japonicus* var. *major*, and *P. japonicus* var. *bipinnatifidus*, which are mainly distributed in the Eastern Asia and Northern America [1]. Among them, most of the investigations have been conducted on *P. notoginseng*, *P. quinquefolius*, and *P. ginseng* for their pharmacological activity. Their use to treat cardiovascular, kidney, and reproductive diseases has a long history [2]. Various bioactive constituents including ginsenosides, polysaccharides, alkaloids, glucosides, and phenolic acids have been identified in *P. ginseng* in a previous study [3]. The main ginsenosides isolated from *Panax* species are shown in Fig. 1. They contain protopanaxadiol, protopanaxatriol, ocotillol, oleanolic acid, and C-17 side chain type [4,5]. Protopanaxadiol has a glucose moiety attached to C-20 and C-3, and protopanaxatriol has glycosylation sites at C-20, C-3, and C-6. The cleavage of glucose bond at C-20 is hydrolyzed before bond at C-3 and C-6 in processed condition [6]. The amount of isomer pairs is detected, and 20(*S*)-ginsenosides are always eluted more easily than 20(*R*)-ginsenosides [6]. Moreover, Δ20(21) ginsenosides are eluted before their Δ20(22) derivatives. Ocotillol-type and oleanane-type have a side chain at C-20. Yao et al have identified 945 ginsenosides from *P. notoginseng* leaves and 662 potentially novel ginsenosides [7]. Various species, parts, processings, regions, and growing times have a great influence on the chemical compounds of herbal medicines.

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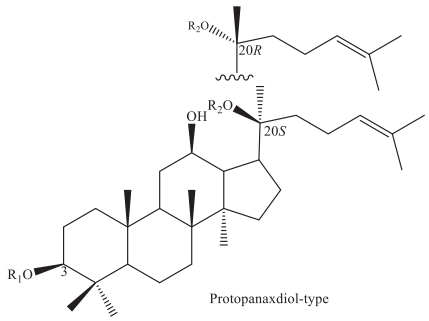
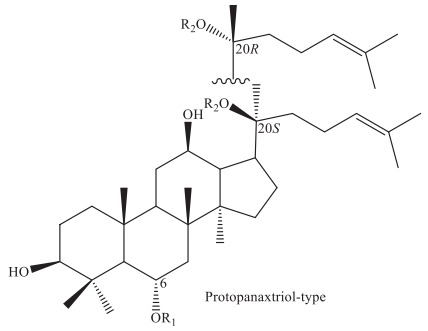
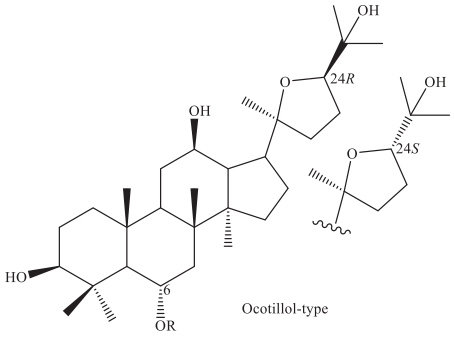
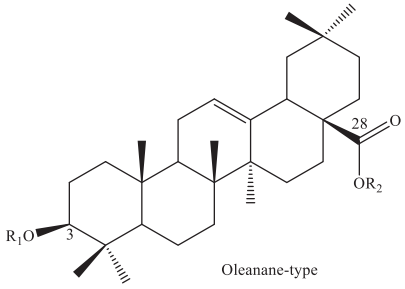




Ginsenoside Rb_1	R_1=-Glc(2→1)-Glc	R_2=-Glc(6→1)-Glc
Ginsenoside Rb_2	R_1=-Glc(2→1)-Glc	R_2=-Glc(6→1)-Ara(*p*)
Ginsenoside Rb_3	R_1=-Glc(2→1)-Glc	R_2=-Glc(6→1)-Xyl
Ginsenoside Rc	R_1=-Glc(2→1)-Glc	R_2=-Glc(6→1)-Ara(*f*)
Ginsenoside Rd	R_1=-Glc(2→1)-Glc	R_2=-Glc
Malonyl-ginsenoside Rb_1	R_1=-Glc(2→1)-Glc-6-malonyl	R_2=-Glc(6→1)-Glc
Malonyl-ginsenoside Rb_2	R_1=-Glc(2→1)-Glc-6-malonyl	R_2=-Glc(6→1)-Ara(*p*)
Malonyl-ginsenoside Rc	R_1=-Glc(2→1)-Glc-6-malonyl	R_2=-Glc(6→1)-Ara(*f*)
20(*R*/*S*)-Ginsenoside Rg_3	R_1=-Glc(2→1)-Glc	R_2=H
Ginsenoside F_2	R_1=-Glc	R_2=-Glc

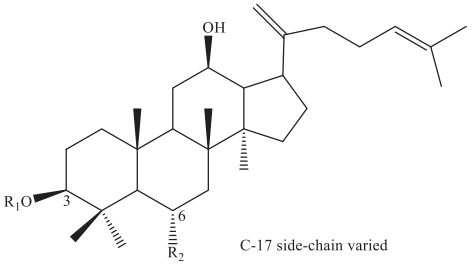
Ginsenoside Rg_1	R_1=-Glc	R_2=-Glc
Ginsenoside Re	R_1=-Glc(2→1)-Rha	R_2=-Glc
Ginsenoside Rf	R_1=-Glc(2→1)-Glc	R_2=-H
20(*R*/*S*)-Ginsenoside Rg_2	R_1=-Glc(2→1)-Rha	R_2=-H
20(*R*/*S*)-Ginsenoside Rh_1	R_1=Glc	R_2=-H
Notoginsenoside R_1	R_1=-Glc(2→1)-Xyl	R_2=-Glc
Notoginsenoside R_2	R_1=-Glc(2→1)-Xyl	R_2=-H
Notoginsenoside R_3	R_1=-Glc(2→1)-Rha	R_2=-Glc(6→1)-Ara(*f*)
Ginsenoside F_1	R_1=-H	R_2=-Glc
Ginsenoside F_3	R_1=-H	R_2=-Glc(6→1)-Ara(*p*)

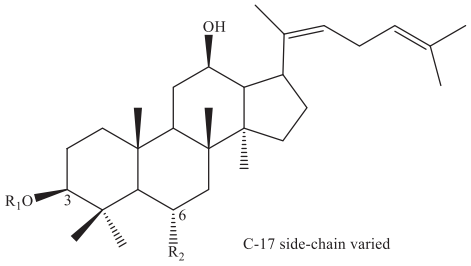




24(*R*)-Pseudoginsenoside F_{11}	R=-Glc(2→1)-Rha(24*R*)	
24(*S*)-Pseudoginsenoside F_{11}	R=-Glc(2→1)-Rha(24*S*)	

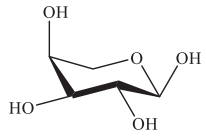
Ginsenoside Ro	R_1=-Glc-UAO(2→1)-Glc	R_2=-Glc
Chikusetsusaponin Iva	R_1=-Glc-UAO	R_2=-Glc



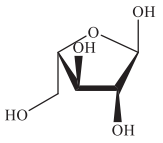


Ginsenoside Rk_1	R_1=-Glc(2→1)-Glc	R_2=-H
Ginsenoside Rk_2	R_1=-Glc	R_2=-H
Ginsenoside Rk_3	R_1=-H	R_2=-*O*-Glc

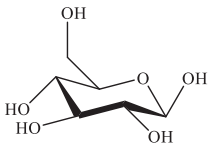
Ginsenoside Rg_5	R_1=-Glc(2→1)-Glc	R_2=-H
Ginsenoside Rh_3	R_1=-Glc	R_2=-H
Ginsenoside Rh_4	R_1=-H	R_2=-*O*-Glc



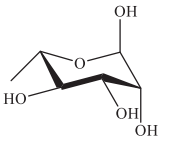
Ara(*p*): α-L-arabinopyronosyl



Ara(*f*): α-L-arabinofuranosyl



Glc: β-D-glucopyranosyl



Rha: α-L-rhamnopyranosyl

Fig. 1. The main ginsenosides of *Panax* species (protopanaxadiol, protopanaxatriol, ocotillol, oleanane, and C-17 side chain type).

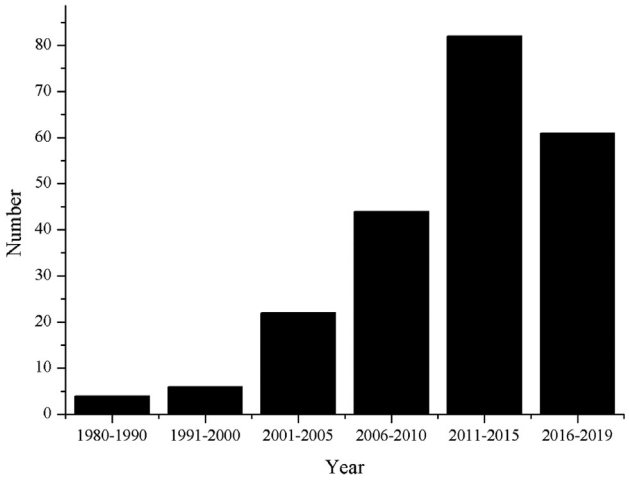


Fig. 2. The number of papers published during 1980 and 2019.

In the previous review, chemical and pharmacological diversity of ginsenosides of genus *Panax* L. was summarized [4,8,9]. Wang et al (2015) reviewed analytical techniques that were used in the evaluation of *P. quinquefolius*, while some advanced methods such as 2D-HPLC, micellar electrokinetic chromatography, and high-performance anion-exchange chromatography (HPAEC) were not investigated. In addition, *P. ginseng* and *P. notoginseng* with phenolic acids, dencichines, trilinoleins, flavonoids, and vitamins were not described [10]. Qi et al (2011) reviewed preparation, analytical advance, and applications of ginseng from January 2000 to September 2010 [11]. However, there are only few investigations in which analytical methods were applied to evaluate *Panax* species. Some advanced techniques such as ambient ionization mass spectrometry are hardly described in previous studies. In this review, we analyzed the published phytochemical analysis of *Panax* based on the keywords "*Panax*, ginseng" from Pubmed and Google Scholar. A total of 219 articles from 1980 to 2019 in the analytical methods of *Panax* species were investigated. As shown in Fig. 2, it is found that few researches are conducted during 1980 and 2000. The number of papers gradually grows with the time. It increased rapidly after 2011. Different sample preparations have significant influence on analysis of the bioactive compounds. The different analytical methods have different performances on the analysis of constituents of *Panax* species. Analytical methods including thin layer chromatography (TLC), high-performance thin layer chromatography (HPTLC), gas chromatography (GC), high-performance liquid chromatography (HPLC), ultra-high performance liquid chromatography (UHPLC) with tandem ultraviolet (UV) detector, diode array detector (DAD), evaporative light scattering detector (ELSD), and mass detector, two-dimensional high-performance liquid chromatography (2D-HPLC), ambient ionization mass spectrometry, high speed counter-current chromatography (HSCCC), and high speed centrifugal partition chromatography (HPCPC) are investigated. Furthermore, the methods have been applied to raw and processed ginseng of different species, from different parts, regions, growing ages, and biochemical analysis. The application in various fields is to screen the potential biomarkers for evaluating and quality control of *Panax* species. It is expected that the current review would have a solid fundamental for the future investigation.

2. Sample preparations

During isolation and purification of bioactive components from natural products, extraction is the first and essential step [12]. A method with short extraction time, less extraction solvent, simple operation, low cost, and high extraction efficiency could be accepted. Sometimes many of factors are not satisfied because of the chemical profile of medicinal plants. In this review, the factors of sample preparations for *Panax* species are discussed (Table 1). As a traditional method, heat reflux extraction is used to extract ginsenosides, while it has the disadvantages of chemical transformation, wasting extraction solvent, and complicate operation [13]. Owing to convenient, simple, and high-efficient extraction, various extraction solvents (different concentrations of ethanol and methanol) and times have been used to extract ginsenosides, polyacetylenes, phenolic acids, flavonoids, and so on [14–16]. The operation time of microwave-assisted extraction is 60 times more efficient than that of Soxhlet extraction and 20 times more efficient than that of ultrasonic extraction [17]. Moreover, malonyl-ginsenosides Rb_1, Rc, Rb_2, and Rd can transform into corresponding neutral ginsenosides Rb_1, Rc, Rb_2, and Rd under high pressure microwave-assisted extraction at 400 kPa in 70% ethanol–water and at 600 kPa in methanol [18]. Compared with Soxhlet extraction, heat reflux extraction, ultrasonic extraction, and microwave-assisted extraction, pressurized liquid extraction has the highest extraction efficiency in the shortest time for *P. quinquefolius*, *P. notoginseng*, and red ginseng [12,19,20]. The amount of total ginsenosides (Rb_1, Rb_2, Rc, Rd, Re, and Rg_1) increased with ultra-high-pressure extraction, whereas pressuring level and time have no influence on the content of ginsenosides [21]. The extraction time of pulsed electric field is less than 1 s, which is much less than that of the heat extraction method (6 h) [22]. In addition, matrix solid phase dispersion extraction has the advantages of short extraction time and less solvent usage, when compared with reflux extraction [23].

3. Analytical methods

In the previous study, chromatographic methods including TLC/HPTLC, GC, HPLC, UHPLC (UV detector, DAD, ELSD, and MS

Table 1
Various factors of sample preparation of *Panax* genus

Technology	Extraction Time	Extraction Solvent	Extraction Efficiency	Operation	Cost	Reference
Soxhlet extraction	Long	More	High	Moderate	Low	[13]
Heat reflux extraction	Long	More	High	Moderate	Low	[125]
Ultrasonic extraction	Moderate	Moderate	High	Simple	Moderate	[126]
Solid phase extraction	Long	Moderate	Moderate	Simple	Moderate	[127]
Microwave-assisted extraction	Short	Less	High	Simple	High	[17]
Pressurized liquid extraction	Short	Less	High	Simple	High	[128]
Enzyme-assisted extraction	Long	Less	Low	Complex	Low	[113]
Accelerated solvent extraction	Short	Less	High	Simple	High	[129]
Matrix solid phase dispersion extraction	Short	Less	High	Simple	Moderate	[23]
Pulsed electric field	Short	More	High	Simple	Moderate	[22]

Table 2
The advantages and shortcomings of technique analysis for *Panax* species

Technique		Advantages	Shortcomings	Reference
TLC/HPTLC		Rapid analysis Convenient operation High sensitivity and specificity Low cost	Bad efficiency in separation Bad stability Need volatile organic solvents Low accuracy in quantification	[24–26]
GC		Rapid analysis Less solvent consuming High sensitivity Less time analysis	Limited to volatile compounds Operation with the derivation High cost	[76,130]
HPLC/UHPLC	UV/DAD	Convenient operation High specificity High repeatability Low cost Combining with multiple detector	Long analysis time Large solvent consuming Analytes with ultraviolet absorption Low sensitivity	[131–133]
	ELSD	High specificity Low cost	Long analysis time Large solvent consuming Low sensitivity	[52,77,104]
	MS	Convenient operation High sensitivity Less solvent consuming High resolution	High cost Bad stability	[93,134,135]
2D-LC		Wide coverage Good orthogonality High efficiency in separation	Complicated operation Long analysis time Large solvent consuming	[55,56]
Ambient ionization mass spectrometry		Rapid analysis Convenient operation Less solvent consuming	Bad stability High cost Low sensitivity Some compound with the derivation	[59]
HSCCC/HPCCC		High efficiency in separation	More solvent consuming Low sensitivity	[62,136]
^{1}H NMR		Fast analysis Less solvent consuming Easy operation	High cost Low accuracy in quantification	[65,66]
Near infrared		Fast analysis No solvent consuming No sample preparation Low cost	Low accuracy in quantification Low specificity	[137,138]

Table 3
Chemical analysis of *Panax* species by TLC/HPTLC

Method	Species	Part	Analytes	Reference
HPTLC	*P. ginseng*	Root	Ginsenosides Rb_1, Rb_2, Rc, Rd, Re, Rg_1	[24]
HPTLC	*P. ginseng*, *P. quinquefolius*, *P. notoginseng*	Root	Glycome	[25]
2D-TLC	*P. trifolius*	Root	Ginsenosides Ro, Rb_1, Rb_2, Rc, Rd, Re, Rf, Rg_1, Rg_2	[26]

detector), 2D-HPLC, HSCCC/HPCPC, and spectroscopic analysis, e.g., near infrared (NIR) spectroscopy and NMR, have been used to evaluate *Panax* species. Moreover, some advanced techniques such as ambient ionization mass spectrometry are applied to *Panax*. It is obvious that different techniques show different advantages and shortcomings. Detailed comparisons are provided in Table 2.

3.1. TLC/HPTLC

As a rapid qualitative and quantitative analysis technology, TLC is recorded by Chinese Pharmacopoeia. Some scholars have applied TLC to evaluate *Panax* species (Table 3). In *P. ginseng*, ginsenosides Rb_1, Rb_2, Rc, Rd, Re, and Rg_1 are determined simultaneously by HPTLC at an absorption of 275 nm. The method consists of a quaternary-solvents system (1,2-dichloroethane–100% ethanol–methanol–water, 56.8:19.2:19.2:4.8) to have an efficient saponins recovery and selective separation [24]. Different species with free mono- and oligo-saccharides are identified by HPTLC [25]. Moreover, to determine ginsenosides in *P. trifolius*, 2D-TLC with eluent A (chloroform–methanol–ethyl acetate–butanol–water, 4:4:8:1:2), eluent B (chloroform–butanol–methanol–water, 4:8:3:4), and eluent C (chloroform–methanol–water, 13:7:2) were used [26].

Table 4
Chemical analysis of *Panax* species by GC–MS

Method	Species	Part	Analytes	Reference
GC–MS	*P. ginseng*	Root	Ginsenosides Rg_1, Re, Rd, Rc, Rb_2, Rb_1, F_1	[30]
GC–MS	*Panax* genus	Root	Panaxynol and panaxydol	[139]
GC–MS	*P. ginseng*	Root	Phenolic acids	[31]
GC–MS	*P. notoginseng*	Root	Dencichine	[32]
GC–MS	*P. ginseng*	Root	Volatile organic compounds	[76]
GC–MS	*P. ginseng*	Root	Volatile organic compounds	[130]
GC–MS	*P. ginseng*, *P. notoginseng*, *P. quinquefolius*	Root	Volatile organic compositions	[29]
GC–MS	*P. ginseng*, *P. quinquefolius*, *P. notoginseng*	Root	Volatile organic compounds	[140]

Table 5
Ginsenosides analysis of *Panax* species by HPLC-UV

Method	Species	Part	Analytes	Reference
HPLC-UV	*P. ginseng*	Root	Ginsenosides Rb_1, Rb_2, Rc, Rd, Rg_1, Re, Rf	[141]
HPLC-UV	*P. ginseng*	Different parts and ages	Ginsenosides Rg_1, Re, Rb_1, Rc, Rb_2, Rb_3, Rd	[102]
HPLC-UV	*P. ginseng*	Root	Ginsenosides Rg_1, Re, Rb_1, Rc, Rb_2, Rd	[22]
HPLC-UV	*P. ginseng*	Leaf	Ginsenosides F_1, F_2, F_3, Re, Rg_1, Rd, Rc, Rb_2	[23]
HPLC-UV	*P. ginseng*	Root	Ginsenosides Rg_2, Rg_3, Rg_5, Rg_6, Rh_1, Rh_4, Rk_1, Rk_3, F_1, R_4	[73]
HPLC-UV	*P. ginseng*	Root	Ginsenosides Rg_1, Re, Rb_1, Rd	[142]
HPLC-UV	*P. ginseng*	Root	Ginsenosides Rb_1, Rb_2, Rc, Rd, Rf, Rg_1, Rg_2, Rg_3, Rg_5, Rg_6, Rh_1, Rh_4, Rk_1, Rk_3, F_1, F_4	[131]
HPLC-UV	*P. ginseng*	Root	Ginsenosides Rg_1, Re, Ro	[143]
HPLC-UV	*P. ginseng*	Root	Malonyl ginsenosides	[144]
HPLC-UV	*P. ginseng*	Root	Ginsenosides and phenolic	[145]
HPLC-UV	*P. quinquefolius*	Root	Ginsenosides Rg_1, Re, Rb_1, Rc, Rb_2, Rd	[132]
HPLC-UV	*P. quinquefolius*	Leaf, stem, root	Ginsenosides Rg_1, Re, Rf, Rb_1, Rc, Rb_2, Rd	[125]
HPLC-UV	*P. quinquefolius*	Root	Ginsenosides Rb_1, Rc, Rd, Re, Rg_1 and F_2, gypenoside XVII	[43]
HPLC-UV	*P. quinquefolius*	Root	Ginsenosides Rb_1, Rc, Rd	[17]
HPLC-UV	*P. quinquefolius*	Root	Ginsenosides Rb_1, Rb_2, Rc, Rd, Re, Rf, Rg_1	[146]
HPLC-UV	*P. quinquefolius*	Root	Ginsenosides Rg_1, Re, Rb_1, Rc, Rd	[147]
HPLC-UV	*P. quinquefolius*	Root	Ginsenosides Rg_1, Re, Rb_1, Rb_2, Rc, Rd	[12]
HPLC-UV	*P. quinquefolius*	Root	Ginsenosides Rb_1, Rb_2, Rc, Rd, Rg_1, Rg_2	[113]
HPLC-UV	*P. quinquefolius*	Different parts and ages	Ginsenosides Rg_1, Re, Rb_1, Rc, Rb_2, Rb_3, Rd	[42]
HPLC-UV	*P. quinquefolius*	Root	Rare ginsenosides 20(*S*/*R*)-Rh_1, Rg_6, F_4, Rk_3, 20(*S*/*R*)-Rg_3, Rk_1, Rg_5	[148]
HPLC-UV	*P. notoginseng*	Root	Notoginsenoside R_1, ginsenosides Rg_1, Rb_1, Rd	[133]
HPLC-UV	*P. notoginseng*	Root	Notoginsenoside R_1, ginsenosides Rg_1, Rb_1, Rd,	[127]
HPLC-UV	*P. notoginseng*	Root	Notoginsenoside R_1, ginsenosides Rg_1, Rb_1, Rd,	[119]
HPLC-UV	*P. notoginseng*	Rat tissue	Ginsenosides Rg_1, Rb_1, Rd	[149]
HPLC-UV	*P. notoginseng*	Flower bud	Notoginsenoside R_1, ginsenosides Rg_1, Re, Rb_1, Rb_2, Rb_3, Rd, F_2	[150]
HPLC-UV	*P. notoginseng*	Different parts	Notoginsenoside R_1, ginsenosides Rb_1, Rb_2, Rd, Re, Rg_1, Rb_3, Rg_2, Rg_3, Rh_1	[110]
HPLC-UV	*P. notoginseng*	Root	Notoginsenoside R_1, ginsenosides Re, Rg_1, Rb_1, Rd	[151]
HPLC-UV	*P. notoginseng*	Root	Ginsenosides Rg_1, Re, Rb_1, 20(*S*/*R*)-Rh_1, Rk_3, Rh_4, 20(*S*/*R*)-Rg_3, notoginsenoside R_1	[152]
HPLC-UV	*P. notoginseng*	Root	Ginsenosides Rg_1, Re, Rb_1, Rd, notoginsenoside R_1	[153]
HPLC-UV	*P. notoginseng*	Root	Notoginsenoside R_1, ginsenosides Rg_1, Re, Rb_1, Rd	[154]
HPLC-UV	*P. notoginseng*	Root, leaf, stem	Ginsenosides Rg_1, Re, Rb_1, Rd, notoginsenoside R_1	[155]
HPLC-UV	*P. notoginseng*	Root, rhizome	Notoginsenoside R_1, R_2, R_3, ginsenosides Rg_1, Rg_2, Rg_3, Rb_1, Rd, Rh_1, Re, quercetin	[13,156]
HPLC-UV	*P. ginseng*, *P. quinquefolius,* and ginseng drug preparations	Different parts	Ginsenosides Rb_1, Rb_2, Rc, Rd, Re, Rf, Rg_1, Rg_2	[41]
HPLC-UV	*P. sokpayensis*, *P. bipinnatifidus*	Rhizomes	Ginsenosides Rg_1, Rg_2, Rf, Re, Rd, Rc, Rb_1, Rb_2	[95]

Table 6
Chemical analysis of *Panax* species by HPLC-UV

Method	Species	Part	Analytes	Reference
HPLC-UV	*P. ginseng*	Root	Ginsenosides and total phenolic	[157]
UHPLC-UV	*P. ginseng*	Fruit, leaf, root	Phenolic compounds	[38]
HPLC-UV	*P. ginseng*	Root	Phytosterols	[39]
HPLC-UV	*P. ginseng*	Main root, root hair, and leaf	Phenolic, flavonoid, vitamin	[14]
HPLC-UV	*P. ginseng*	Root, rhizome, and root hair	Trilinolein, 1,2-dilinoleoyl-3-oleoyl-glycerol	[45]
HPLC-UV	*P. pseudoginseng*	Root	Trilinolein	[45]
HPLC-UV	*P. ginseng*, *P. quinquefolius*, *P. japonicus*, *P. notoginseng*	Root	Polyacetylenes, ginsenosides	[37]
UHPLC-UV	*P. notoginseng*	Root	Fingerprinting analysis	[158]
HPLC-UV	*P. notoginseng*	Root	Fingerprinting analysis	[115]
HPLC-UV	*P. ginseng*, *P. quinquefolius*	Leaf	Metabolic profiling	[100]

The TLC technology has some advantages of rapid, convenient, and sensitive characteristics to target compounds, whereas it always needs standards and there is a lack of uniqueness for bioactive compounds. In recent years, HPTLC-MS with rapid and accurate profile will hope for evaluating *Panax* species [27]. Two-dimensional HPTLC showed an efficient performance and good isolation profiles for *Panax* species in another study [28].

3.2. Gas chromatography

Gas chromatography is employed to determine volatile organics, ginsenosides, and phenolic acids from *Panax* species (Table 4). Different derivatizations for chemical components were selected. For volatile organics, the GC–MS method can determine bioactive compounds of headspace without sample preparation for discriminating *Panax* species [29]. When determining ginsenosides in *P. ginseng*, it is applied to high-molecular-weight saponins after derivatization with trimethylsilylation [30]. Sample is subjected to trimethylsilane derivatization for evaluating phenolic acids in white and red ginsengs [31]. After derivatization with ethyl chloroformate, dencichine or other amino acids of *P. notoginseng* are determined [32]. GC–MS for volatile components can take some advantage with simple, fast, and effective characters, whereas for some non-volatile components, a complex operation is required. 2D-GC with high peak capacity, orthometric characteristic can be used to evaluate volatile components of samples, which is necessary to be discussed for the further study.

3.3. HPLC/UHPLC

HPLC/UHPLC is the most frequently used method for *Panax* species in the qualitative and quantitative analysis. In this review, it is found that stationary phases including C_{18} column (250 × 4.6 mm, 5 μm) with different brands are used for ginsenosides, OV-170 (500 × 0.25 mm), LiChrosorb for polyacetylenes, polymer C_{18} column (250 × 4 mm, 10 μm) for trilinoleins, Waters Atlantis HILIC (hydrophilic interaction liquid chromatography) silica (50 × 2.1 mm, 3 μm) [33] for dencichine, and Zorbax SB-Aq column (150 × 4.6 mm, 5 μm) for nucleobases and nucleosides. Moreover, the small particle size ACQUITY UHPLC BEH C_{18} (2.1 × 100 mm, 1.7 μm) is used in UHPLC. Two-phase solvent systems contain water or buffer solution in water (formic acid, acetic acid, phosphoric acid, ammonium formate, or ammonium acetate) and acetonitrile or methanol. Formic acid in water improves resolution and eliminates peak tailing [34–36]. The solvent range of 1% to 100% is changed to obtain the appropriate gradient elution grogram. Ginsenosides could be eluted by the solvent range of 30–50% as observed in the literature. UHPLC with less analytical time has the better performance than HPLC.

3.3.1. UV/DAD and ELSD detector

UV detector is the traditional detector for the qualitative and quantitative analysis of chemical compounds in the *Panax* species (Tables 5 and 6). The detector with its low cost and simple operation has become the most commonly used analytical method in the laboratory. Therefore, it has been widely employed to determine the ginsenosides (malonyl ginsenoside, protopanaxadiol, protopanaxatriol, ocotillol, and oleanane), trilinoleins, polyacetylenes [37], phenolics [38], phytosterols [39], flavonoids, and vitamins [40]. The detection wavelengths for different types of biochemical compounds are various. It is reported that ginsenosides Rb_1, Rb_2, Rc, Rd, Re, Rf, Rg_1, Rg_2, F_2, gypenoside XVII, and notoginsenoside R_1 could be detected in the wavelength of 203 and 198 nm [41–44]. The detection wavelength is set at 205 nm for trilinoleins [45], 254 nm for polyacetylenes [37], 260 nm for nucleobases and nucleosides [46], and 280 nm for phenolic compounds [38]. However, oleanane ginsenosides (ginsenoside Ro) are poor chromophores with weak UV absorption and are disturbed by solvents (the cut-off wavelength of methanol is 205 nm) that have low sensitivity with UV detection. DAD has the better recognition than conventional UV detection (Table 7). It is widely used to determine polar and nonpolar [47], neutral and malonyl ginsenosides [48] in *P. ginseng*, *P. quinquefolius,* and *P. notoginseng*. As a mass detection, ELSD is mainly used for analysis of biological compounds that lack appropriate chromophores (Table 8). It can be used to identify and quantify neutral and acidic ginsenosides Rg_1, Rg_2, Ro, Rb_1, Rb_2, Rc, and Rd in *P. ginseng*, while the sensitivity of ELSD is five times lower than that with UV detection [49].

3.3.2. MS detector

Modern analytical techniques based on MS with chromatographic separation have the sensitivity and specificity characteristic when compared with traditional detection analysis of *Panax* species (Table 9) [10]. Ion sources including atmospheric pressure chemical ionization (APCI) and electrospray ionization (ESI) are used. The APCI can be applied to low molecule and polar compounds, such as 24(*R*)-pseudoginsenoside F_{11}, ginsenoside Rf, and polyacetylenes [16,50,51]. The most of bioactive constituents of *Panax* species in the ESI mode has the better performance than that in the APCI mode, especially for the large and moderate polar compounds. Ginsenosides Rb_1, Rb_2, Rc, Rd, Re, Rf, Rg_1, and notoginsenoside R_1 have been analyzed with ESI mode in previous studies [52,53]. Dencichine, triterpenoid saponins, nucleobases, nucleosides, and polyacetylenes could be conducted by HPLC-MS as well (Table 10). In addition, MS hyphenations with Q-TOF, IT-TOF, Q-Trap, and Q-Orbitrap have been used to determine ginsenosides accurately and sensitively (Table 11). A total of 234 ginsenosides including 67 potential new ones were isolated tentatively by HPLC–QTOF-MS [54]. It is found that 646 ginsenosides were identified from stems and leaves of *P. ginseng* using linear ion-trap/Orbitrap mass spectrometry [55]. In the qualitative analysis, full

Table 7
Chemical analysis of *Panax* species by HPLC-DAD

Method	Species	Part	Analytes	Reference
HPLC-DAD	*P. ginseng*	Root	Polar and non-polar ginsenosides	[47]
UHPLC-DAD	*P. ginseng*	Root	Panaxfuraynes A and B	[101]
HPLC-DAD	*P. ginseng*	Root	Spectrum-efficacy relationship	[159]
HPLC-DAD	*P. quinquefolius*	Root	Ginsenosides Rb_1, Rb_2, Rc, Rd, Re, Rg_1, Ro, gypenoside XVII, pseudoginsenoside-F_{11}	[160]
HPLC-DAD	*P. quinquefolius*	Root	Neutral and malonyl ginsenosides	[48]
HPLC-DAD	*P. quinquefolius*	Root	Ginsenosides Rg_1, Re, Rb_1, Rc, Rb_2, Rd	[114]
HPLC-DAD	*P. quinquefolius*	Root	Ginsenosides Rb_1, Rb_2, Rc, Rd, Re, Rg_1	[126]
HPLC-DAD	*P. quinquefolius*	Fresh root	Ginsenosides and polyacetylenes	[161]
HPLC-DAD	*P. notoginseng*	Root	Notoginsenoside R_1, ginsenosides Rg_1, Re, Rf, Rb_1, Rc, Rb_2, Rb_3, Rd	[19]
HPLC-DAD	*P. notoginseng*	Root	Notoginsenoside R_1, ginsenosides Rg_1, Re, Rb_1, Rc, Rd	[44]
HPLC-DAD	*P. notoginseng*	Root	Ginsenosides Rb_1, Rc, Rd, Re, Rg_1, Rg_5, Rk_1, 20(*R*/*S*)-Rg_3, 20(*R*/*S*)-Rh_1, notoginsenosides R_1	[162]
HPLC-DAD	*P. notoginseng*	Root	Saponins	[79]
HPLC-DAD	*P. notoginseng*	Root	Ginsenosides Rb_1, Rb_2, Rc, Rd, Re, Rg_1	[21]
HPLC-DAD	*P. notoginseng*	Main root, rhizome, fibrous root	Notoginsenosides R_1, R_4, Fa, and K, ginsenosides Rg_1, Rb_1, Rd, Re, Rf, Rg_2, Rh_1	[107]
HPLC-DAD	*P. notoginseng*	Root	Notoginsensides R_1, ginsenosides Rg_1, Re, Rb_1, Rd	[163]
HPLC-DAD	*P. notoginseng*	Root	Notoginsenoside R_1, ginsenosides Rg_1, Rb_1, Rd, Re	[164]
UHPLC-DAD	*P. notoginseng*	Root	Notoginsenoside R_1, ginsenosides Rg_1, Re, Rf, Rb_1, Rg_2, Rb_3, Rd, Rg_3	[165]
UHPLC-DAD	*P. notoginseng*	Root	Notoginsenoside R_1, ginsenosides Rg_1, Re, Rb_1, Rd	[166]
HPLC-DAD	*P. notoginseng*	Different parts	Fingerprint analysis	[109]
HPLC-DAD	*P. notoginseng*	Flower	Fingerprint analysis	[167]
HPLC-DAD	*P. notoginseng*, *P. vietnamensis*, *P. stipuleanatus*	Root	Fingerprint analysis	[97]
UPLC-PDA	*P. ginseng*	Root	Ginsenosides Rg_1, Re, Rf, Rg_2, Rb_1, Rc, Rb_2, Rd, Ro	[168]

scan, parent scan, daughter scan, and neutral loss scan have been employed. Selective ion monitoring and multiple reaction monitoring have been used to quantify bioactive compounds.

3.3.3. 2D-HPLC

The traditional methods for comprehensive chemical analysis of *Panax* species are of low-efficiency and incomplete. Recently, two-dimensional liquid chromatography has been used to analyze the complicated bioactive constituents (Table 12). Online and offline systems are constructed to obtain a high orthogonality and peak capacity. On offline 2D LC system, the first dimensional HILIC analysis for separation of polar compounds and the second dimensional ACQUITY UPLC BEH C_{18} are used to determine ginsenosides in *P. notoginseng*; the results indicated that orthogonality could be up to 81%, and the peak capacity is found to be 10200 [56]. It is similar that two-dimensional liquid chromatography, hybrid linear ion-trap/Orbitrap mass spectrometry could discover the new natural molecules, and some even trace amount in *P. ginseng* [55]. Online 2D LC systems have a simpler operation than offline ones. For instance, a quick, reproducible, and fast method for separation of saponins from *P. notoginseng* is established by using an online two-dimensional chromatography [57].

3.4. Ambient ionization mass spectrometry

Recently, the developed ambient ionization mass spectrometry such as DART-MS and MALDI TOF-MSI are used to evaluate *Panax* (Table 13) [40,58]. For these methods, direct sampling and ionization are conducted in the open air with no or minimal sample preparation [59]. The most of ginsenosides need derivatization, whereas pseudoginsenoside F_{11}, compound K, protopanaxatriol, and protopanaxadiol are detected without derivatization [59]. In addition, notoginsenoside R_1, ginsenosides Rb_1, Rg_1, and Re from *P. ginseng*, and *P. notoginseng* are simultaneously determined by DART-MS [58,60].

3.5. HSCCC/HPCPC

As shown in Table 14, the similar techniques including HSCCC and HPCPC are liquid–liquid partition chromatography. The appropriate solvent systems composed of *n*-hexane, *n*-butanol, methylene chloride, methanol, isopropanol, ethyl acetate, and water are employed to isolate the bioactive compounds. In addition, ammonium acetate could reduce the separation time and eliminate emulsification [61]. Ginsenosides Rb_1, Re, Rg_1, Rb_2, Rd, Rf, Rh_1, and notoginsenoside R_1 could be isolated by HSCCC, and the purity of ginsenosides are more than 95% [62].

3.6. Others

Micellar electrokinetic chromatography could measure the ginsenosides Rg_1, Re, Rf, Rb_1, Rc, Rb_2, Rb_3, Rd, Rf, Rh_1, Rg_1, and notoginsenoside R_1 in high separation efficiency without any organic solvent and with shorter run time when compared to chromatographic analysis (Table 15) [63]. It can extract dencichine from *P. notoginseng* with a purity of 98.5% [64]. Moreover, NMR technique in the qualitative analysis is used to discriminate geographical origins of *P. ginseng* and to obtain the potential markers [65]. It also quantifies malonyl-ginsenosides Re, Rb_1, Rb_2, Rc, and Rd [66]. HPAEC-PAD could analyze amadori compounds in processed ginseng within 15 min of single chromatographic run and eliminate the complex derivatization [67]. Enzyme immunoassay by anti-Rf antiserum quantifies ginsenosides Rg_2 and Rf in *P. ginseng* [68]. Dencichine is measured by HPAEC for discrimination of *P. notoginseng*, *P. ginseng*, and *P. quinquefolius* [69]. In addition,

Table 8
Chemical analysis of *Panax* species by HPLC-ELSD

Method	Species	Part	Analytes	Reference
HPLC-ELSD	*P. ginseng*	Root	Ginsenosides Rg_1, Re, Rb_1, Rc, Rb_2, Rd	[49]
HPLC-ELSD	Red ginseng	Root	Ginsenosides Rg_1, Re, Rf, Rh_1, Rg_2, Rb_1, Rc, Rb_2, Rb_3, Rd, Rg_3, Rk_1, Rg_5, Rh_2	[77]
HPLC-ELSD	Black ginseng	Root	Less polar ginsenosides	[78]
HPLC-ELSD	*P. ginseng*	Root	Ginsenosides Rh_1, Rg_2, Rg_3, Rg_1, Rf, Re, Rd, Rb_2, Rc, Rd	[169]
HPLC-ELSD	*P. quinquefolius*	Different parts	Ginsenosides Rg_1, Re, F_{11}, Rf, Rg_2, Rh_1, Rb_1, Rc, Rb_2, Rb_3, Rd, Rh_2	[104]
HPLC-ELSD	*P. quinquefolius*	Different parts	20(*R*)-dammarane-3β,6α,12β,20,25-pentol, 25(*R*)-ocotillol, 20(*R*)-protopanaxatriol, 20(*S*)-panaxatriol and 20(*R*)-dammarane-3β,12β,20,25-tetrol	[105]
HPLC-ELSD	*P. ginseng*, *P. quinquefolius*	Root	Ginsenoside Rf, 24(*R*)-pseudoginsenoside F_{11}	[90]
HPLC-ELSD	*P. notoginseng*	Root	Ginsenosides Rg_1, Re, Rb_1, Rc, Rb_2, Rd	[170]
HPLC-ELSD	*P. notoginseng*	Different parts	Ginsenosides Rg_1, Re, Rf, Rb_1, Rc, Rb_2, Rb_3, Rd	[108]
HPLC-ELSD	*P. notoginseng*	Root	Ginsenosides Re, Rg_1, Rb_1, Rb_2, Rc, Rd, notoginsenoside R_1	[52]
HPLC-ELSD	*P. notoginseng*, *P. quinquefolius*, *P. ginseng*	Root	Notoginsenoside R_1, ginsenosides Rg_1, Re, Rf, Rg_2, Rc, Rb_2, Rb_3, Rd, Rg_3	[94,128]

Table 9
Ginsenosides analysis of *Panax* species using HPLC-MS

Method	Species	Part	Analytes	Reference
HPLC-MS	*P. ginseng*	Root	Ginsenosides Rb_1, Rb_2, Rc, Rd, Re, Rf, Rg_1, Rg_2	[118]
HPLC-ESI-MS	*P. ginseng*	Root	Ginsenosides Rg_1, Re, Rb_1, Rc, Rb_2, Rd	[18]
HPLC-FD-MS	*P. ginseng*	Ginseng extract	Ginsenosides Rb_1, Rb_2, Rc, Rd, Re, Rf, Rg_1 and Rg_2	[134]
HPLC-ESI-MS/MS^n	*P. ginseng*	Root	Ginsenosides Rg_1, 20(*S*)-Rg_2, Rb_1, Rc, Rh_2, malonyl-ginsenoside Rb_2 and Rc	[75]
HPLC-ESI-MS/MS	*P. ginseng*	Root	Low-polar ginsenosides	[80]
UHPLC-MS	*P. ginseng*	Root	Ginsenosides Rb_1, Rb_2, Rg_1, Rg_2, Rg_3, Rc, Rd, Re, Rf	[171]
HPLC-MS/MS	*P. ginseng*	Root	Ginsenosides Rg_1, Re, Rf, Rb_1, Rc, Rb_2, Rd, Rg_2, Rh_1, F_1, F_2, Rg_3, PPT	[122]
HPLC-MS/MS	*P. ginseng*	Fresh root	Ginsenosides Rg_1, Re, Rf, Rb_1, Rb_2, Rd, 20(*S*)-Rg_2, Rc, 20(*S*)-Rh_1, F_1, F_2, 20(*S*)-Rg_3, 20(*S*)-protopanaxatriol, compound K, 20(*S*)-Rh_2	[172]
HPLC-Qtrap-MS	*P. ginseng*	Root	Ginsenosides	[173]
HPLC-MS	*P. ginseng*	Root	Notoginsenoside R_1, ginsenoside Rb_2, Re, Rb_1, Rc, Rg_1, Rb_3, Rf, F_1, Rd, Rh_1, Rg_2, F_2, Rg_3, Rh_2, compound K	[174]
LC-MS/MS	*P. ginseng*	Root	15 ginsenosides	[175]
UHPLC-HRMS	*P. quinquefolius*	Root	Ginsenosides Rb_1, Rb_2, Rb_3, Rc, Rd, Re, Rf, Rg_1, Rg_2, Rg_3, Rh_1, Rh_2, Ro, F_1, F_2, F_3, pseudoginsenoside F_{11}, notoginsenosides R_1, R_2	[93]
HPLC-APCI-MS	*P. quinquefolius*	Root	24(*R*)-pseudoginsenoside F_{11}	[50]
UPLC-MS/MS	*P. quinquefolius*	Different parts	22 ginsenosides	[176]
HPLC-MS	*P. ginseng*, *P. quinquefolius*	Root	Ginsenosides Rb_1, Rb_2, Rc, Ro, Rd, Re, Rf, Rg_1, pseudoginsenoside F_{11}	[88]
HPLC-MS	*P. ginseng*, *P. quinquefolius*	Root	Ginsenoside Rf, 24(*R*)-pseudoginsenoside F_{11}	[89]
UHPLC-ESI-MS	*P. notoginseng*	Different parts	Metabolite profiling	[112]
HPLC-MS	*P. notoginseng*	extraction	Ginsenosides Rg_1, Rb_1, notoginsenoside R_1	[177,178]
UHPLC-MS/MS	*P. notoginseng*	Extract	Notoginsenoside R_1, ginsenosides Rg_1, Rb_1, Re, Rd	[120]
UPLC-MS/MS	*P. notoginseng*	Compounds	Notoginsenoside R_1, ginsenosides Rg_3, Rd, Rg_2, Rb_2, Rf, Rg_1, Rb_1, Re	[179]
HPLC-MS	*P. notoginseng*	Root	Notoginsenoside R_1, ginsenosides Rg_1, Rb_1, Rd, F_2, Re	[180]
LC-Q-Trap-MS	*P. notoginseng*	Extraction	Notoginseng total saponins	[181]
LC-MS/MS	*Steamed notoginseng*	Rat plasma	23 triterpenoids	[182]
UHPLC-MS	*P. japonicus*	Leaf	Chikusetsusaponins V, Ib, IV, IVa, IV ethyl ester	[183]
HPLC-MS	*P. ginseng*, *P. quinquefolius*, *P. notoginseng*	Root	Ginsenosides Ro, Ra_2, Ra_3, Rb_1, Rb_2, Rb_3, Rc, Rd, Re, Rg_1, Rg_2, 20(*S*)-Rg_3, Rf, notoginsenosides R_1, R_2, R_4 and 24(*R*)-pseudoginsenoside F_{11}	[91]
HPLC-APCI-MS	*P. quinquefolius*, *P. ginseng*, *P. notoginseng*	Root	Ginsenosides Rf, F_{11}, notoginsenoside R_1	[51]

MCI gel column chromatography combining with LC-MS could analyze metabolic profiling qualitatively [70]. To determine the various constituents of *Panax* species, multiple techniques have been used (Table 16). HPLC-UV coupled with GC-MS has been used to evaluate ginsenosides and volatile compounds [20]. Zhu et al using HPLC, CE, and NIR discriminated different parts of *P. notoginseng* [71].

4. Analytical methods applied to *Panax* species

As we all know, the different processing methods, species, parts, regions, and ages have different chemical information. To display the chemical markers of different conditions, we have reviewed the advanced techniques evaluating samples of *Panax*. In addition, the

Table 10
Other chemical constituents of *Panax* species using HPLC-MS

Method	Species	Part	Analytes	Reference
HPLC-MS	*Panax*	Root	Dencichine	[33]
HPLC-ESI-MS	*P. notoginseng*	Root	Triterpenoid saponins	[184]
HPLC-MS	*P. notoginseng*	Root	Nucleobases, nucleosides, and saponins	[46]
HPLC-APCI-MS	*P. ginseng*	Root	Polyacetylenes	[16]
NanoESI-MS	*P. ginseng*	Different parts	Lipidomics	[185]
UPLC-MS/MS	*P. quinquefolius*	Root	Zoxamide	[186]
LC-Q-TOF-MS	*P. ginseng*	Root	Malonyl ginsenoside, amino acids, polysaccharides	[187]

Table 11
Qualitative analysis of *Panax* species by HPLC-MS, HPLC-QTOF-MS, LC-IT-TOFMS

Method	Species	Part	Analytes	Reference
HPLC-ESI-MS/MS^n	*P. ginseng*	Root	Multicomponent quantification fingerprint	[188]
UHPLC-QTOF-MS	*P. ginseng*	Different parts	Qualitative analysis	[189]
LC-QTOF/MS	*P. ginseng*	Root	Fingerprint analysis	[190]
LC-QTOF-MS/MS	*P. ginseng*	Root	Ginsenosides Rc, Rb_2, Rb_3, malonyl-ginsenosides	[191]
UHPLC-QTOF MS	*P. ginseng*	Root	Metabolomics analysis	[117]
UHPLC-QTOF-MS	*P. ginseng*	Hairy root	Metabolomics analysis	[116]
LC-QTOF/MS	*P. ginseng*	Root	Metabolite profiling	[35]
UPLC-QTOF-MS	*P. ginseng*	Ginseng extract	22 ginsenosides	[6]
UPLC-QTOF-MS	*P. ginseng*	Rhizome and root	59 ginsenosides	[103]
UHPLC-QTOF-MS	*P. ginseng*	Root	Original neutral, malonyl, and chemically transformed ginsenosides	[192]
UPLC-DAD-QTOF-MS/MS	*P. ginseng*	Root	Qualitative and quantitative analysis	[193]
UPLC-QTOF-MS	*P. ginseng*	Root	Metabolomics analysis	[121]
UHPLC-Q-TOF MS	*P. ginseng*	Root	Metabolite profiling	[194]
UPLC-QTOF-MS	*P. ginseng*	Root	Metabolite profiling	[195]
UHPLC/QTOF-MS	*P. ginseng*	Leaf	Metabolite profiling	[196]
UPLC-QTOF-MS	*P. ginseng*	Root	Ginsenosides	[197]
UPLC-QTOF-MS	*P. ginseng*	Root	Metabolite profiling	[198]
UPLC-QTOF-MS	*Red ginseng*	Root	Metabolite profiling	[199]
UPLC-QTOF-MS	*P. ginseng*	Root	44 ginsenosides	[200]
UPLC-QTOF-MS	*P. ginseng*	Different parts	58 ginsenosides	[201]
UPLC-QTOF-MS	*P. ginseng*	Root	Cell-based neuroactivity screening	[202]
UPLC-QTOF-MS	*P. ginseng*	Flower	Transformation of ginsenosides	[203]
UPLC-QTOF-MS	*P. ginseng (different processed)*	Root	Metabolite profiling	[204]
UHPLC QTOF-MS	*P. ginseng* (different age)	Root	Metabolite profiling	[205]
UHPLC-QTOF-MS	White and red ginseng	Root	Fingerprint analysis	[206]
UPLC-QTOF-MS	*P. ginseng* (different age)	Root	Metabolomics analysis	[207]
LC-TOF-MS	*P. quinquefolius*	Root	Ginsenosides	[208]
UPLC-QTOF-MS	*P. quinquefolius*	Root	Metabolomics analysis	[209]
LC–MS	*P. quinquefolius*	Root	Fingerprint analysis	[210]
HPLC-ESI-MS	*P. quinquefolius*	Root	Metabolomics analysis	[211]
HPLC-MS^n	*P. quinquefolius*	Root	59 ginsenosides of protopanaxadiol, protopanaxatriol, oleanane and ocotillol types	[81]
UHPLC-QTOF-MS/MS	*P. quinquefolius*	Root	Metabolite profiling	[74]
UHPLC-QTOF-MS	*P. ginseng, P. quinquefolius*	Leaf	Metabolomics analysis	[36]
UHPLC-QTOF MS	*P. ginseng, P. quinquefolius*	Root	Metabolite profiling	[99]
HPLC-ESI-MS	*P. notoginseng*	Different parts	Metabolomics analysis	[111]
LC-MS	*P. notoginseng*	Root	Metabolite profiling	[15]
UHPLC-QTOF-MS	*P. notoginseng*	Root	Metabolite profiling	[53]
UHPLC-QTOF-MS	*P. notoginseng*	Root	Metabolite profiling	[72]
LC-QTOF-MS	*P. notoginseng*	Extract	Metabolomics analysis	[212]
LC-QTOF-MS	*P. notoginseng*	Leaf	Metabolite profiling	[34]
LC-IT-MS and UHPLC-QTOF-MS	*P. notoginseng*	Flower bud	Metabolite profiling	[70]
UPLC-ESI-QTOF-MS	*P. notoginseng*	Root	Fingerprint analysis	[213]
HPLC-QTOF-MS	*P. notoginseng*	Root	Metabolite profiling	[54]
LC-triple-TOF/MS	*P. notoginseng*	Extraction	Ginsenosides Rb_1, Rb_2, Rd, Re, Rf, Rg_1 and notoginsenoside R_1	[214]
UPLC/Q-TOF MS	*P. notoginseng*	Leaf	Ginsenosides Rb_1, Rc, Rb_2, Rb_3, notoginsenosides Fc, Fe, Fd	[215]
HPLC-QTOF-MS	*P. ginseng, P. notoginseng, P. japonicus, P. quinquefolius*	Root	Metabolite profiling	[98]
LC-MS-IT-QTOF	*P. ginseng, P. quinquefolius, P. notoginseng*	Root	Qualitative analysis	[87]
UHPLC-IMC-NLF	*P. ginseng, P. quinquefolius, P. notoginseng*	Root	Malonyl-ginsenosides	[216]
UPLC-LTQ-Qrbitrap-MS	*P. ginseng, P. quinquefolius, P. notoginseng*	Different parts	Malonyl-ginsenosides	[217]
UHPLC-QE-HRMS	*P. ginseng, P. quinquefolius, P. notoginseng*	Root	101 compounds	[135]

Table 12
2D-LC applied to *Panax* species

Method	Species	Part	Analytes	Reference
2D LC/LTQ-Orbitrap-MS/NMR	*P. ginseng*	Stems and leaves	A total of 646 ginsenosides were characterized, and 427 have not been isolated from the genus of *Panax* L.	[55]
2D LC-ESI	*P. ginseng*	Extraction	Triterpenoid saponins	[218]
2DLC-MS	*P. ginseng*	Extraction	Ginsenosides Rd, Rc, Rb_2, Rb_1, Re	[219]
2D chromatographic method	*P. notoginseng*	Root	Ginsenosides Rb_1, Rg_1, Rg_2, Rh_1, Rh_4, Rd, 20(*S*)-Rg_3, notoginsenosides R_1, T_5	[57]
HILIC × RPLC	*P. notoginseng*	Root	Metabolomics analysis	[56]
2D LC-QTOF-MS	*P. notoginseng*	Extraction	Total saponins	[220]

Table 13
Ambient ionization mass spectrometry applied to *Panax* species

Method	Species	Part	Analytes	Reference
DART-MS	*P. ginseng*	Root	Ginsenosides	[59]
DART-MS	*P. ginseng*	Root	Ginsenosides Rb_1, Re, Rg_1	[58]
DART-MS	*P. notoginseng*	Root	Notoginsenoside R_1, ginsenoside Rb_1, Rg_1	[60]
MALDI-TOF-MSI	*P. ginseng*	Root	Ginsenosides	[40]

Table 14
HPCCC and HSCCC applied to *Panax* species

Method	Species	Part	Analytes	Reference
HSCCC-ELSD	*P. ginseng*	Root	Ginsenosides Rg_3, Rk_1, Rg_5, F_4	[62]
HSCCC-DAD	*P. ginseng*	Leaf	Ginsenosides Rk_1, Rg_5, Rs_5, 20(*R*)-Rg_3, Rs_4	[129]
HPCCC-ESLD	*P. ginseng*	Root	Ginsenosides Rf, Rd, Re, Rb_1	[61]
HSCCC-ELSD	*P. ginseng*	Root	Ginsenosides Rg_1, Re, Rf, Rh_1, Rb_1, Rc, Rb_2, Rd	[221]
HPCCC	*P. ginseng*	Root	Ginsenosides Re, Rb_1, Rc, Rb_2	[222]
HSCCC-MCI gel column	*P. ginseng*	Root	Ginsenosides Re, Rg_1	[223]
CPC-ELSD	*P. notoginseng*	Root	Notoginsenoside R_1, ginsenosides Rg_1, Re, Rb_1	[224]
HSCCC	*P. ginseng*	Root	Ginsenosides Rg_1, Re, Rf, Rg_2, Rb_1, Rb_2, Rd, Rg_3, Rk_1, Rg_5, Rg_6, and F_4	[225]
HPCCC	*P. notoginseng*	Root	Notoginsenosides R_6, R_1, Spt_1, ginsenosides Rb_1, F_4, Rh_3, Rg_3, Rs_3, Rk_1	[136]
HSCCC	*P. notoginseng*	Root	Ginsenosides Rg_1, Rd, R_1, Re, Rb_1	[68]

mechanisms of chemical compounds changing for *Panax* are illustrated.

4.1. Raw and processed ginseng

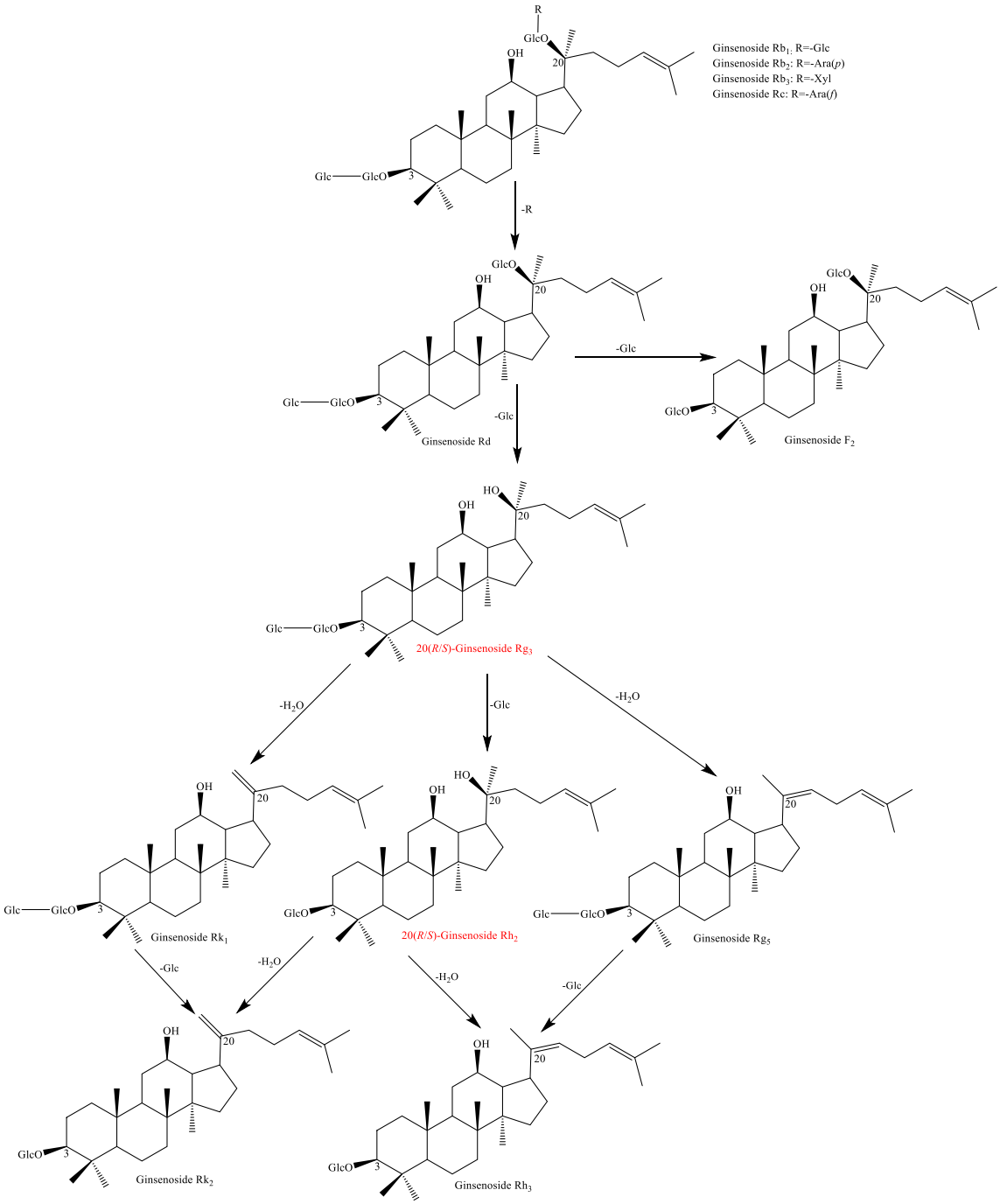
Processing *Panax* species leads to various bioactive characteristics, which have been used in the treatment of different diseases when compared to raw ginseng. In the Chinese medicine, “Sheng Da Shu Bu” and “Sheng Leng Shu Wen” with regard to raw *P. notoginseng* are used for hemostasis and cardiovascular diseases, whereas the steamed form is used to “nourish” blood [10]. Those theories suggested that raw and processing have the opposite effect on some illness. Different chemical profiles in the processing have been investigated in the previous study. As a formal method, from

Table 15
Other analysis of *Panax* species

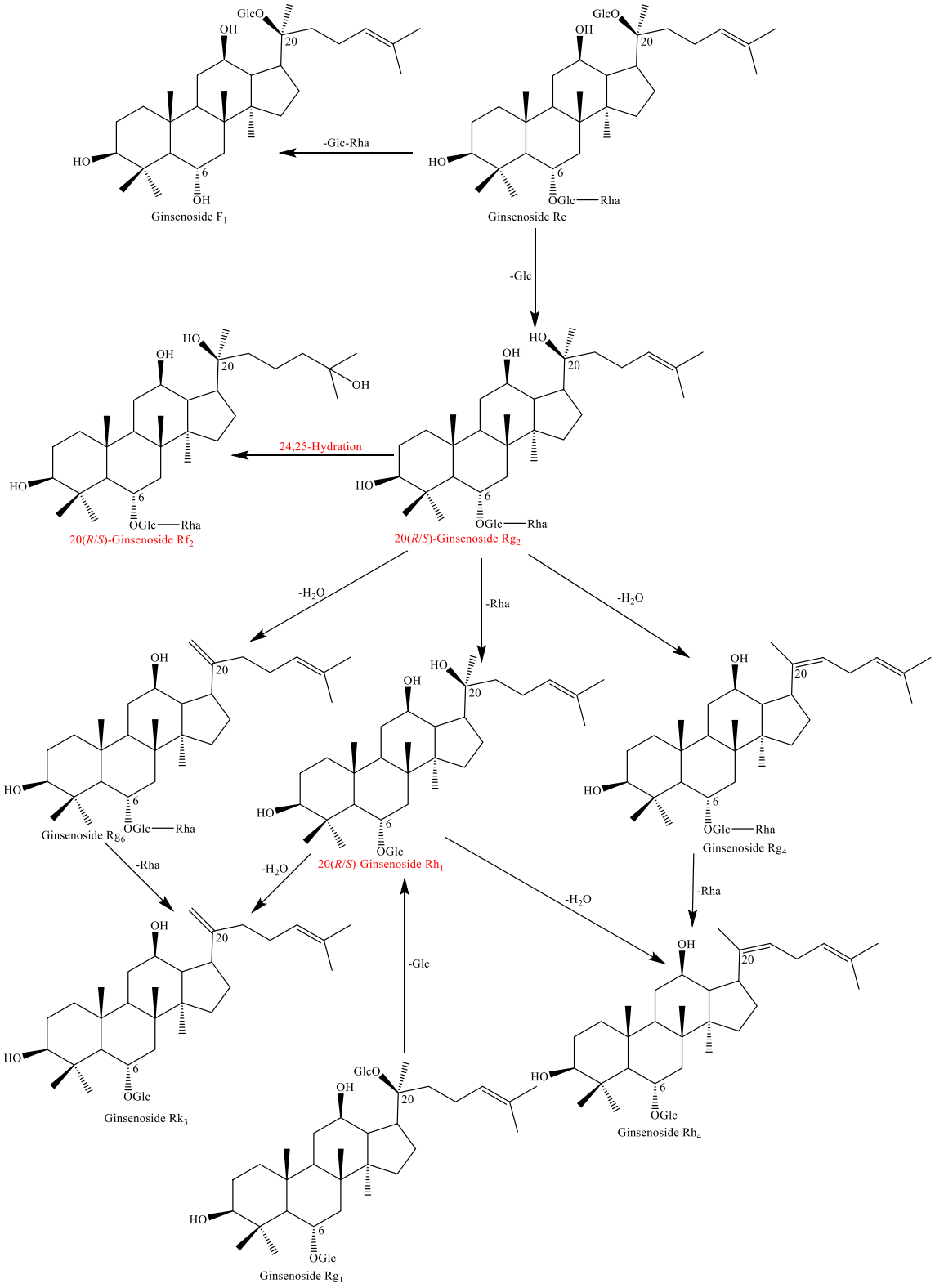
Method	Species	Part	Analytes	Reference
Micellar electrokinetic chromatography	*P. ginseng*	Root	Ginsenosides Rg_1, Re, Rf, Rb_1, Rc, Rb_2, Rd	[226]
Micellar electrokinetic chromatography	*P. notoginseng*	Root	Ginsenosides Rd, Rc, Rb_3, Rb_1, Rh_1, Rg_2, Rf, Rg_1, Re, notoginosides R_1	[227]
High-performance anion-exchange chromatography	*P. ginseng*	Extraction and rat plasma	Arginyl-fructose, arginyl-fructosyl-glucose	[67]
High-performance anion-exchange chromatography	*P. notoginseng*, *P. ginseng*, *P. quinquefolius*	Root	Dencichine	[69]
Molecularly imprinted polymer	*P. notoginseng*	Root	Dencichine	[64]
Enzyme immunoassay	*P. ginseng*	Root	Ginsenosides Rf and Rg_2	[63]
^{1}H NMR	*P. ginseng*	Root	Qualitative analysis	[65]
^{1}H NMR	*P. ginseng*	Flower bud	Malonyl-ginsenosides Re, Rb_1, Rb_2, Rc, Rd	[66]
^{1}H NMR	*P. quinquefolius*	Root	Qualitative analysis	[228]
SFC-MS	*P. ginseng*, *P. quinquefolius*	Root	Nucleobases, nucleosides, ginsenosides	[229]
UHPSFC-QTOF-MS	*P. ginseng*, *P. quinquefolius*, *P. notoginseng*		Lipids	[230]
FT-IR spectroscopy	*P. notoginseng*	Root	Protein	[231]
Near-infrared spectroscopy	*P. ginseng*	Root	Ginsenosides Rg_1, Rb_1, Re, Rf, Rc, Rb_2, Rg_2, Rb_3, Rd	[137]
Near-infrared spectroscopy	*P. notoginseng*	Root	Fingerprint analysis	[232]
Infrared and ultraviolet spectroscopy	*P. notoginseng*	Root	Notoginsenoside R_1, ginsenosides Rg_1, Re, Rb_1, Rd	[138]
FT-IR spectroscopy	*P. ginseng*	Different parts	Fingerprint analysis	[233]

Table 16
Multiple techniques applied to *Panax* species

Method	Species	Part	Analytes	Reference
HPLC-UV, UHPLC-PDA, CE-UV, IR	*P. notoginseng*	Main root, rhizome	Fingerprint analysis	[71]
HPLC-UV, GC-MS	*P. ginseng*	Root	Ginsenosides Rg_1, Re, Rf, Rh_1, Rg_2, Rb_1, Rc, Rb_2, Rg_3, F_2, compound K, Rk_1, Rg_5, Rh_2	[20]
HPLC-UV, HPLC-MS	*P. notoginseng*	Extract	Fingerprinting and quantitative analysis	[234]
HPLC-UV, HPLC-MS	*P. ginseng*	Rhizome	Ginsenosides Rb_1, Rb_2, Rc, Rd, Re, Rf, Rg_1, Rg_2	[235]
HPLC-DAD, LC-ESI-MS^n	*P. notoginseng*	Leaf	Chemical profiles and anticancer	[236]
GC–MS, LC–MS	*P. ginseng*, *P. quinquefolius*	Different parts	Primary and second metabolites	[106]
LC-ELSD, LC-Q-TOF-MS	*P. vietnamensis*	Radix and rhizome	Ginsenosides Rg_1, Re, Rb_1, Rc, Rb_2, Rd, majonoside R_1, R_2 and vina-ginsenoside R_2	[96]

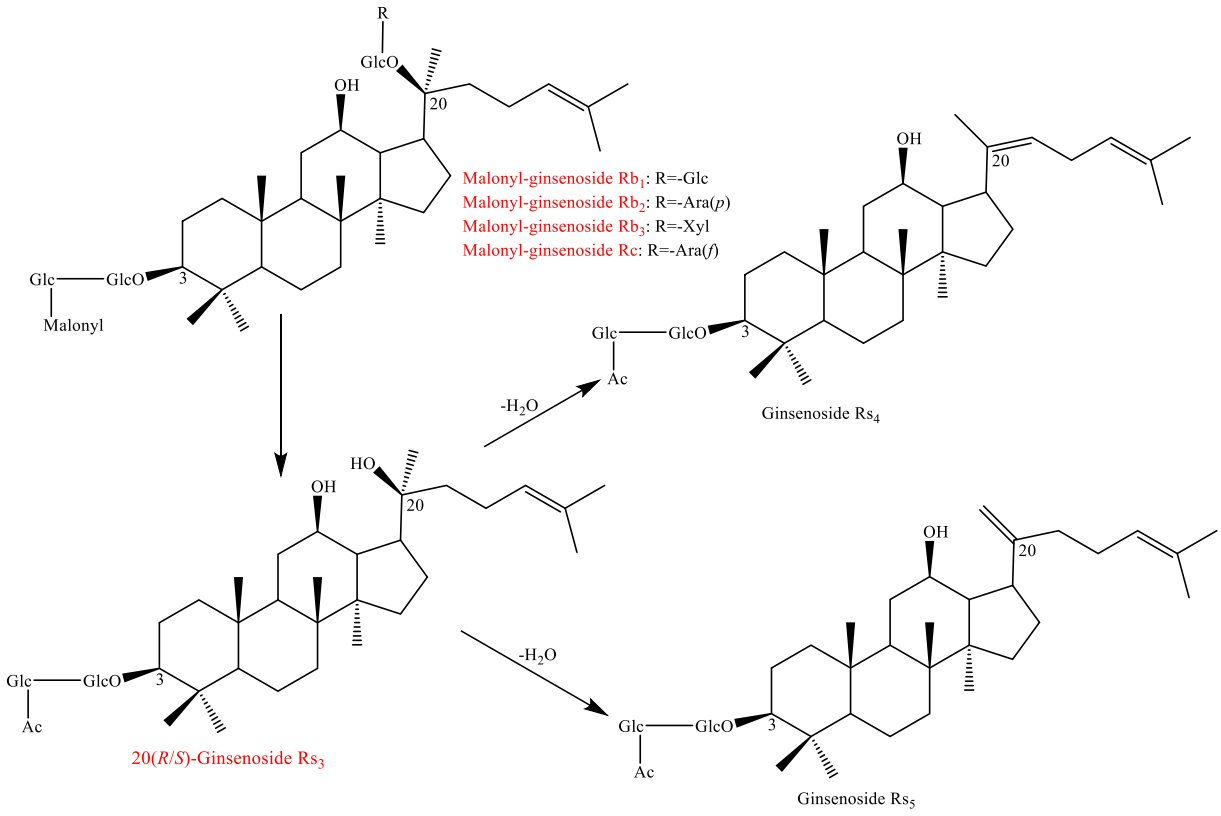


Scheme 1. The potential transformation pathway of protopanaxadiol ginsenosides after processing.



Scheme 2. The potential transformation pathway of protopanaxatriol ginsenosides after processing.

raw to processed material steaming with different temperatures and times has been used. *P. ginseng* is steamed at 98°C and 120°C at 2 h, 6 h, and 9 h, which shows the various bioactive constituents. Time-dependent profiling of raw and steamed *Panax* species is studied [72–74]. "Red ginseng" is formed at two- or three-time steaming and "black ginseng" is formed with cyclic nine-time steaming at 98°C for 3 h. Therefore, phytochemical components including saponins and volatile oils are reviewed in this



Scheme 3. The potential transformation pathway of malonyl and acetyl ginsenosides after processing.

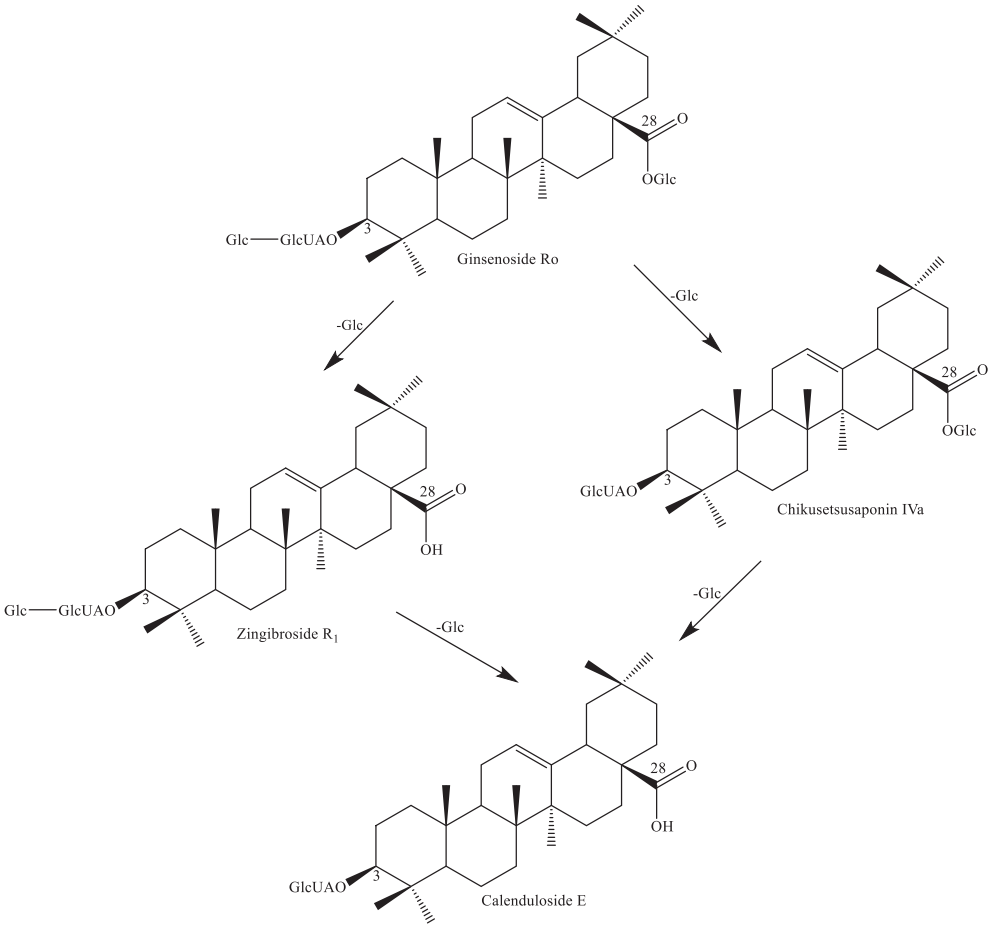
investigation. It is found that chemical constituents with polar ginsenosides can be transformed to low polar ginsenosides by hydrolysis, isomerization, and dehydration [75]. The concentration of polar ginsenosides, notoginsenoside R_1, ginsenosides Rg_1, Re, Rb_1, Rc, Rb_1, Rc, Rb_2, Rb_3, and Rd, decreased by steaming, wheras that of low polar ginsenosides, Rh_1, Rg_2, Rg_3, Rh_2, Rs_3, Rk_1, Rs_5, and Rs_4, increased, and ginsenosides Rg_3, Rg_5, and Rk_1 are the unique compounds from steamed ginseng [44,76–80].

Usually, the types of saponins in the *Panax* species are mainly protopanaxadiol, protopanaxatriol, ocotillol, and oleanane. As shown in Scheme 1, protopanaxadiol including ginsenosides Rb_1, Rb_2, Rb_3, and Rc converted to Rd by hydrolysis of a glycosylation moiety at C-20. Then, the loss of glycosylation moiety at C-20 and C-3 of Rd through hydrolysis generated ginsenosides 20(*R*/*S*)-Rg_3 and F_2. 20(*R*/*S*)-Rh_2, Rk_1, and Rg_5 under the reaction conditions gradually increased [44,74,75,77–81]. Interestingly, ginsenosides Rk_1 and Rg_5 were deduced to 20(*R*/*S*)-Rg_3 by Δ20(21) and Δ20(22) dehydration at C-20. Ginsenosides Rk_1 and Rg_5 are hydrolyzed to generate Rk_2 and Rh_3 by loss of a glycosylation moiety at C-20 [74,75,80,81]. Protopanaxatriol including ginsenosides Re and Rg_1 produced 20(*R*/*S*)-Rg_2, F_1, Rg_6, 20(*R*/*S*)-Rh_1, and Rg_4 through hydrolysis of a glycosylation moiety at C-20 and C-6 when the creaming with high-temperature and long-time shown in Scheme 2 [74,75,77,80,81]. Specifically, ginsenosides 20(*R*/*S*)-Rf_2 was deduced by C-24 and C-25 hydration of Rg_2 [81]. In addition, malonyl and acetyl ginsenosides could convert to the corresponding neutral ginsenosides through demalonylation and deacetylation reaction shown in Scheme 3 [74,75]. Such as acetyl-ginsenosides 20(*R*/*S*)-Rs_3, Rs_4, and Rs_5 were deduced to be generated from malonyl-ginsenosides Rb_1, Rb_2, and Rc through hydrolysis, decarboxylation, and dehydration [74,75]. For oleanane type, the chemical transformations have not been studied up to now. The possible transformation pathways deduced are shown in Scheme 4 [81].

4.2. Different species

Different species of *Panax* have different effects on diseases. *P. ginseng* is used for its anticancer effect [82]. While *P. quinquefolius* has a good performance on antidiabetic, anti-inflammatory, and neuroprotective effects [83–85], *P. notoginseng* always have effects on the cardiovascular system, hemostatic, and antioxidant activities [86]. *P. japonicus*, *P. vietnamensis*, *P. stipuleanatus*, *P. sokpayensis*, and *P. bipinnatifidus* are also used to protect and treat diseases all over the world. Usually, ginsenosides are the main bioactive components for the *Panax* species. Yao et al have reported that 623 ginsenosides in the ethanol extract of *P. ginseng*, *P. quinquefolius,* and *P. notoginseng* are discovered, and among those, 437 are potentially novel ginsenosides [87]. Polysaccharides, essential oils, phenolic acids, alkaloids, and others were also investigated in a previous study [3]. The similar morphological characteristics especially medicinal power and its extraction are hard to evaluate them in the markets. The fake and inferior goods may arise owing to price difference for *Panax* species largely. It is therefore necessary to select some quality markers for distinguishing *Panax*.

For saponins, ginsenoside Rf is only detected in *P. ginseng*, whereas 24(*R*)-pseudoginsenoside F_{11} is mainly detected in *P. quinquefolius* [88–90]. Ginsenoside Rs_1 is used to differentiate *P. ginseng* and *P. quinquefolius* also [91]. Furthermore, the higher amount of Rg_1 group (Rf, Rg_1) is in *P. ginseng* and that of the Rb_1 group is in the *P. quinquefolius* [92]. A higher protopanaxadiol/protopanaxatriol ratio for *P. quinquefolius* is about 3, while the value is between 1 and 3 for *P. ginseng* [93]. When *P. notoginseng* and *P. quinquefolius* are compared, the former has the highest



Scheme 4. The potential transformation pathway of oleanane ginsenosides after processing.

ginsenoside content (9.176%), and the latter has the highest polyacetylene content (0.08%) [37]. Notoginsenoside R_1 is detected in both *P. notoginseng* and *P. ginseng* [51], whereas ginsenoside Rg_3 is observed in the red ginseng [94]. Ginsenoside Rc was not detected in *P. sokpayensis*, and ginsenosides Rf, Rc, and Rb_2 are not detected in *P. bipinnatifidus* [95]. *P. vietnamensis* mainly has ocotillol type of ginsenosides [96]. To describe the more chemical information, metabolic components combined with multivariate statistical analysis, hierarchical clustering analysis, principal component analysis, and partial least squares discriminant analysis have been applied to evaluate different species and to select the appropriate chemomarkers [97]. The results indicated that ginsenoside Rf, 20(*S*)-pseudoginsenoside F_{11}, malonyl-ginsenoside Rb_1, and ginsenoside Rb_2 could be used to differentiate *P. ginseng*, *P. notoginseng*, *P. japonicus*, and *P. quinquefolius* [98]. 24(*R*)-Pseudoginsenoside F_{11}, ginsenoside Rf, Ra_1, F_2, and 20-glucoginsenoside Rf can differentiate processed *P. ginseng* and *P. quinquefolius* [99]. The metabolic constituents of leaves to avoid damaging the roots can separate *Panax* species [100]. Pseudoginsenoside F_{11}, Rb_3, malonyl-notoginsenoside Fd, malonyl-ginsenosides F_2, Rb_3, Re, F_3, R_2, and F_1 are selected as the chemical markers for leaves of *P. ginseng* and *P. quinquefolius* [36]. For essential oil, hexanal, 2-pyrrolidnone, (*E*)-2-heptenal, (*E*)-2-octenal, heptanal, isospathulenol, (*E*, *E*)-2,4-decadienal, 3-octen-2-one, benzaldehyde, 2-pentylfuran, and (*E*)-2-nonenal can discriminate *P. ginseng* and *P. notoginseng* [29]. Mono- and oligo-saccharide are similar in the different regions and *Panax* species [25]. However, dencichine varied in *Panax* species, the highest (0.36 ± 0.02%) is in *P. notoginseng*, then *P. ginseng* (0.31 ± 0.06%) and *P. quinquefolium* (0.1 ± 0.01%), and the lowest (0.03 ± 0.07%) was in steamed *P. ginseng*. The contents of panaxfuraynes A and B are less than 3 and 2 ng/g in the roots of *P. quinquefolius*, *P. japonicum*, *P. notoginseng*, and *P. ginseng*, whereas they were not found in *P. japonicum* [101].

4.3. Different parts

Different parts include aerial parts (flower, leaf, and stem) and underground parts (rhizome, main root, lateral root, and root hair) in *Panax* species, which have been used for medicinal purposes. As a medicinal tea, flower and leaf are used to prevent disease for the human in the eastern world, especially in China. An official herbal medicine, leaf of *P. ginseng* is recorded in Chinese Pharmacopoeia. Different parts of *Panax* species have long been used. For instance, rhizomes of *P. notoginseng* and *P. ginseng* are called as "Jinkou" and "Lutou" in the traditional medicine, respectively. Different parts have various pharmacological activities [86]. The chemical profile for different parts of *Panax* species is significant.

In *P. ginseng*, the content of ginsenosides is higher in the leaf and root hair and lower in stem and other parts. The content of ginsenosides in the root and root hair increases with age from one to five years [102]. More kinds of ginsenosides are found in cork than those in cortex, phloem, xylem, and resin canals; the content of ginsenosides of phloem, xylem, and resin canals from branch root is high than that from main root [103]. The content of total phenols in fruit and leaf is higher than in roots, including major phenolic compounds chlorogenic acid, gentisic acid, *p*- and *m*-coumaric acid, and rutin

[38]. Moreover, the order for triacylglycerol content is rhizome > main root > root hair. Ginsenosides in *P. quinquefolius* follow this order leaf > root hair > rhizome > stem [104]. Sapogenins are found more in stem and leaves than other parts of *P. quinquefolius* [105]. Both *P. ginseng* and *P. quinquefolius* mainly have ginsenosides Rg_1, Re, and Rd for leaves, and ginsenosides Re, Rb_1, and Rc for root hair [41]. The reason for ginsenosides accumulation in *P. ginseng* main root and *P. quinquefolius* lateral roots may be high rates of C assimilation to C accumulation [106]. In *P. notoginseng*, different parts can be identified based on saponin content difference [107]. The type of 20(*S*)-protopanaxatriol is mainly distributed in the underground parts, whereas 20(*S*)-protopanaxadiol is mainly distributed in the aerial parts [108,109]. Different parts could be identified by metabolomic combined with principal component analysis [71,110,111]. Notoginsenosides R_4, Fa, Q, S, Fc, R_1, H, A, B, ginsenosides Rb_1, Rb_2, Rb_3, Rc, Rd, F_2, Rh_2, Rg_1, Re, Rf, Rg_2, malonyl-ginsenoside-Rb_1, and 20-*O*-glucoginsenoside-Rf contribute to up- or down-regulation of different parts of *P. notoginseng* [112]. The main roots have 31% higher ginsenosides content than rhizome [96].

4.4. Different region and age

P. ginseng is mainly distributed in Korea, North Korea, and Northeastern China, *P. quinquefolius* in America and Canada, and *P. notoginseng* in Southwestern China. Geographical origin is a major influential factor for quality control [35]. Metabolomics combined with OPLS-DA could be used to discriminate *P. ginseng* of different regions [65]. The contents of 1,2-dilinoleoyl-3-oleoyl-glycerol of *P. ginseng* from Korea, Japan, and China are 0.41 ± 0.009 mg/g, 0.45 ± 0.01 mg/g, and 0.22 ± 0.008 mg/g, and those of trilinolein are 0.37 ± 0.009 mg/g, 0.39 ± 0.016 mg/g, and 0.27 ± 0.009 mg/g . Furthermore, *P. quinquefolius* roots cultivated in Jilin Province are similar to those cultivated in Canada in the compositions [113], whereas those grown in China and North America showed no major difference [93]. Ginsenosides Rb_1, Rc, Rb_2, Rg_1, and Rd are influenced by location [114]. The highest polyacetylene content is distributed in Nagano, Japan [37]. Chemical constituents of rhizome and main roots of *P. notoginseng* from Wenshan, Honghe, and Kunming have no significant difference [115]. Different growing years may lead to different chemical profiles. For *P. ginseng*, seven ginsenosides show age-dependent variations [116]. Metabolites combining with multivariate statistical methods could classify different ages, especially for 4, 5, and 6 years [117]. The total contents of ginsenosides for main root and fibrous root in four years are highest [118]. The highest concentrations of stigmasterol and β-sitosterol are found in 6-year-old *P. ginseng* cultivated in Jinan, Korea [39]. For notoginseng, different growth years can be identified by the saponin content, the content of most and total saponins in the order is 3 > 2>1-year-old in the main root samples [107]. The best season for harvesting is September to October [13].

4.5. Biochemical analysis

Metabolism of *Panax* species in the different tissues could obtain a better understanding of biological effects. Ginsenosides Rg_1, Rb_1, and Rd of *P. notoginseng* in rat tissues (kidney, liver, heart, spleen, and lung) are determined. The highest concentrations of three saponins were at 90 min except for spleen after oral dose, whereas after intravenous administration, they could not detect in all tissues after 8 h [119]. After nasal administration, notoginsenoside R_1, ginsenosides Rg_1, Rb_1, Rd, and Re from *P. notoginseng* have been determined in brain [120]. The metabolites in the urine after being administered orally ginseng decoction were used to distinguish normal control group, deficiency of vital energy model group, and ginseng treatment group and to find potential biomarkers [121]. Biotransformation of *P. ginseng* in the rat intestinal microflora indicated that protopanaxadiol-type ginsenosides were more easily metabolized than protopanaxatriol-type ginsenosides [122].

5. Conclusion

In this review, different sample preparations including Soxhlet extraction, heat reflux extraction, ultrasonic extraction, solid phase extraction, microwave-assisted extraction, pressurized liquid extraction, enzyme-assisted extraction, accelerated solvent extraction, matrix solid phase dispersion extraction, and pulsed electric field were compared. The TLC technique has been used to quantify and identify *Panax* species quickly, although it always needs standards and lacks uniqueness for bioactive compounds. GC–MS could be used to determine ginsenosides, phenolic acids, dencichine, pesticide residues, and volatile components, although for some non-volatile components complex operation is required. UHPLC with less analytical time has the better performance than HPLC, and DAD has the better recognition than conventional UV detection. HPLC tandem MS has the sensitivity and specificity characteristic when compared with traditional detection. In the liquid–liquid partition chromatography (HSCCC and HPCPC), ammonium acetate could reduce the separation time and eliminate emulsification. After processing ginseng, chemical constituents with polar ginsenosides can be transformed to low polar ginsenosides by hydrolysis, isomerization, and dehydration. Ginsenoside Rf is only detected in *P. ginseng*, whereas 24(*R*)-pseudoginsenoside F_{11} is mainly detected in *P. quinquefolius*. When *P. notoginseng* and *P. quinquefolius* are compared, the former has the highest ginsenoside content (9.176%) and the latter has the highest polyacetylene content (0.08%). The content of ginsenosides in the leaf and root hair is higher, and it is lower in stem and other parts of *P. ginseng*. In addition, the content of total phenols in fruit and leaf is higher than in roots. For *P. notoginseng*, the type of 20(*S*)-protopanaxatriol is mainly distributed in the underground parts, whereas 20(*S*)-protopanaxadiol is mainly distributed in the aerial parts. *P. ginseng* is mainly distributed in Korea, North Korea, and Northeastern China, *P. quinquefolius* in America and Canada, and *P. notoginseng* in Southwestern China. Protopanaxadiol-type ginsenosides were more easily metabolized than protopanaxatriol-type ginsenosides in the rat intestinal microflora.

From the current review, the present analysis of *Panax* species is not sufficient. The following aspects need to be investigated.

(1) According to previous studies, the different sample preparations and analytical methods have been used to evaluate ginsenosides of *Panax* species. It is necessary that the harmonious and practical standard criteria method is established for determining ginsenosides of different species, parts, and ages quickly and accurately.
(2) As we all know, ginseng has been widely used for prevention and treatment of diseases all over the world. Meanwhile, the criteria of Chinese Pharmacopoeia, United States Pharmacopeia, Japanese Pharmacopoeia, and South Korean Pharmacopoeia for *P. ginseng* have been developed. Different countries have different criteria. It is expected that the uniform criteria for ginseng should be established for development of the ginseng industry.
(3) As an oleanane type, ginsenoside Ro was only detected in the *P. ginseng* and *P. quinquefolius*, which could be used to inhibit testosterone 5α-reductase and for testosterone-treated disease [123]. Both Ro and its transformation products in red ginseng are the bioactive constituents [124]. The chemical transformation pathway and the metabolism *in vitro* and *in vivo* are the key research in the further investigation. Furthermore, in

Chinese Pharmacopoeia, quality markers for *P. ginseng* and red ginseng are ginsenosides Rg_1, Re, and Rb_1, although they have the various pharmacological effects. It is reported that red ginseng has the better performance biological activity than fresh ginseng [92]. What has not been investigated until now is the different bioactive components. The condition of ginseng from raw to processed, temperature, time, and pressure are necessary to be optimized for future studies.

(4) Notoginsenoside R_1 and ginsenoside Rg_3 are discovered in *P. notoginseng* and red ginseng, although they are not unique. Several biomarkers have been selected to discriminate *Panax* species by metabolite coupled to chemometrics. The possible biomarkers need to be verified through large number of samples. In Chinese Pharmacopoeia, Rg_1+Re + $Rb_1 \geq 2\%$ for *P. quinquefolius*, Rg_1+Re $\geq$ 0.3% and $Rb_1 \geq$ 0.2% for *P. ginseng*, Rg_1+Re $\geq$ 2.25% for leaves of *P. ginseng*, and Rg_1+Rb_1+$R_1 \geq$ 5% for *P. notoginseng* are quality control. Obviously, the biomarkers are unique for each one. The comprehensive evaluation of quality control for *Panax* species needs further investigation.

(5) Rhizome and main root of *Panax* species with different chemical profiles are recorded in official documents. Most of the time, main root is used and rhizome is not, such as “Qulu” (cutting out rhizome) in traditional medicine. Up to now, the differences between rhizome and main root have not been investigated. A comprehensive, accurate, and convenient method is necessary to establish in the further study.

Conflicts of interest

All authors declare that they have no conflict of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jgr.2019.12.009.

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