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Panacis majoris Rhizoma: A Comprehensive Review of Phytochemistry, Pharmacology and Clinical Applications

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Abstract: *Panacis majoris* Rhizoma (PMR) is a traditional Chinese medicine with tonic, hemostatic, and pain-relieving properties, classified under the genus Panax in the family Araliaceae. With a lengthy history of folk usage, PMR holds considerable potential for further development and exploration. Modern research indicates that saponins are the main active constituents. To date, a total of 122 compounds have been isolated from PMR, with the vast majority being triterpenoid saponins. In addition, there are small amounts of flavonoids, aromatic hydrocarbons, alkynes, and volatile oils. Pharmacological studies have demonstrated that compounds and extracts from PMR exhibit notable activities, including hepatoprotective, anti-cancer, cardioprotective, anti-ischemic brain injury, antioxidant, anti-inflammatory, analgesic, and anticoagulant effects. These compounds, serving as precursor molecules for drug development, are of significant value. This article provides a comprehensive review of PMR's botany, phytochemistry, pharmacology, and clinical applications, offering valuable insights for its subsequent development and resource utilization.

Keywords: *Panacis majoris*; phytochemistry; pharmacology; Clinical Applications.

1. Introduction

China has a rich history of herbal medicine usage, abundant with natural medicinal resources. PMR stands out as a natural treasure among medicinal plants, consisting of the dried roots and rhizomes of *Panax japonicus* C. A. Mey. var. *major* (Burk.) C. Y. Wu & K. M. Feng or

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Panax japonicus C. A. Mey. var. *bipinnatifidus* (Seem.) C. Y. Wu & K. M. Feng. PMR is characterized by a bitter and sweet taste, and mild coldness in nature, and is known for functions such as lung nourishment, Yin replenishment, blood stasis elimination, pain relief, and hemostasis [1]. Folk medicine commonly employs PMR for treating injuries, contusions, and external bleeding. Since the 1970s, scholars have systematically researched PMR, isolating over a hundred compounds to date. Modern pharmacological studies have demonstrated the outstanding activity of its saponin constituents, including the protection of the cardiovascular and cerebrovascular systems, hepatoprotection, and anti-cancer properties [2]. Therefore, conducting a systematic review is essential for an in-depth exploration and enhanced development of PMR. In this paper, we provide a thorough overview of its botany, phytochemistry, pharmacology, and clinical applications. These findings contribute to a deeper understanding of PMR, exploration of its potential bioactive compounds, and offer reference points for its future development and resource utilization.

2. Botany, Description and Distribution

PMR is a widely used tonic, pain reliever, and hemostatic Chinese medicine, and is one of the *Taibai Qi yao*, a specialty Chinese medicine of Shaanxi Province [3]. The original plant is a variant of *Panax japonicus* (T.Nees) C.A.Mey. According to scholars, the history of the use of PMR is as long as 500 years, and it was first recorded in the *Dian nan ben cao* in 1443. Due to its distribution at high altitudes, it has long been poorly understood. Some sources confuse the Genera *Codonopsis* plant *Zhuzishen* with the PMR, at the same time, the research content of PMR has not been well separated from which of the PJR (*Panacis japonici* rhizoma) [4]. The modern Chinese Pharmacopoeia specifies two plant sources, *Panax japonicus* C. A. Mey. var. *major* (Burk.) C. Y. Wu et K. M. Feng and *Panax japonicus* C. A. Mey. var. *bipinnatifidus* (Seem.) C. Y. Wu C. Y. Wu et K. M. Feng.

As per the Flora of China, *P. japonicus* typically exhibits common botanical features, appearing as herbaceous plants ranging from 50 to 100 cm in height with a horizontal rootstock. The stems are straight and glabrous, often flagellate or moniliform. At the apex of the stem, there is a verticillate arrangement of 3-5 leaves that are palmately compound. The petiole lacks stipules or stipule-like appendages at its base. The leaflets, numbering 5, are obovate-elliptic to narrowly elliptic, measuring 5-18 × 2-6.5 cm. They are membranous with sparse setae on veins on both surfaces. The leaf base is broadly cuneate to subrounded, exhibiting a serrulate or biserrate margin, while the apex is acuminate or long acuminate. The inflorescence consists of a solitary terminal umbel, bearing 50-80 (or more) flowers, with a glabrous or slightly pubescent peduncle measuring 12-21 cm and pedicels 7-12 mm in length. Filaments are shorter than petals. The ovary is 2-5-carpellate, and the styles, numbering 2-5, are united to the middle. The fruit is red and subglobose, measuring 5-7 mm in diameter, containing 2-5 white seeds that are triangular-ovoid, measuring 3-5 × 2-4 mm [5]. The local name, distribution, and morphological features of PMR are shown in Table 1. Different plant sources and traditional medicinal parts of PMR are shown in Figure 1.

Table 1. The local name, distribution, and morphological features of PMR

Species name	Local name	Distribution	Morphological features
Panax japonicus C. A. Mey. var. *major* (Burk.) C. Y. Wu et K. M. Feng	Zhu zi shen, Zhu er shen, Kou zi qi, Niu zi qi.	China (Guizhou, Gansu, Shanxi, Henan, Hubei, Sichuan, Xizang, Yunnan), Nepal, N Myanmar, N Vietnam.	Rootstock moniliform. Leaflets not 2-pinnatifid, obovate-elliptic to elliptic, apex acuminate, rarely long acuminate [5].
Panax japonicus C. A. Mey. var. *bipinnatifidus* (Seem.) C. Y. Wu et K. M. Feng	Ge da qi, Fu yu lie shen.	China (Gansu, Shaanxi, Hubei, Xizang, Sichuan, Yunnan), Myanmar, Bhutan, N India, Nepal.	Rootstock moniliform-mounded, rarely like a knot of bamboo. Leaflets 2-pinnatifid [5].

Figure 1. Different plant sources and traditional medicinal parts of PMR

3. Phytochemistry

Up to now, a total of 123 different chemical components have been isolated and identified from PMR. The primary types include triterpene saponins, along with small amounts of flavonoids, aromatic hydrocarbons, steroids, and acetylenic alcohols. Among them, triterpene saponins are recognized as the primary active components in PMR, and this group of compounds can be categorized into Oleanane-type (**1-28**), Dammarane-type (**29-90**), and Ocotillol-type (**91-100**) according to their structures, with the highest number of Dammarane-types being **62**. In addition to this, there are 23 other compounds (**101-123**). The names and sources of the compounds and their specific structures are shown in Table 2 and Figures 2~6.

Table 2. Constituents isolated and identified from PMR

No.	Compounds	Source	Part	Ref
Oleanane-type				
1	Chikusetsusaponin V methyl ester	P1	rhizomes	[6]
2	Zingibroside R_1	P1	rhizomes	[7]
		P2	rhizomes	[8]
3	Ginsenoside Ro	P1	rhizomes	[9]
		P1	roots	[10]
		P2	rhizomes	[8]
4	3-*O*-[*β*-*D*-glucopyranosyl-(1→2)-*β*-*D*-(6′-*O*-ethyl)-glucuronopyranosyl]-oleanolic acid 28-*O*-*β*-*D*-glucopyranoside	P1	rhizomes	[11]
5	Taibaienoside I	P1	rhizomes	[9]
		P1	roots	[12]
6	Oleanicacid	P1	rhizomes	[13]
		P1	roots	[12]
7	Oleanolic acid-28-*O*-*β*-*D*-glucopyranoside	P1	rhizomes	[14]
		P1	roots	[10]
8	Calenduloside E (Deglucose chikusetsusaponin IVa)	P1	rhizomes	[9]
9	Chikusetsusaponin IVa	P1	rhizomes	[6]
		P1	roots	[10]
		P2	rhizomes	[8]
10	Taibaienoside IV	P1	rhizomes	[9]
		P1	roots	[12]
11	Pseudoginsenoside RT1	P1	roots	[12]
		P1	rhizomes	[7]
		P2	rhizomes	[15]
12	Pseudoginsenoside RT1 butyl ester	P1	roots	[12]
13	Pseudoginsenoside RP_1	P1	rhizomes	[7]
		P2	rhizomes	[15]
14	Pseudoginsenoside RT1 methyl ester	P1	roots	[12]
		P1	rhizomes	[7]
15	Oleanolic acid-3-*O*-[*α*-*L*-arabinofuranosyl-(1→4)]-*β*-*D*-glucopyranoside	P1	rhizomes	[16]
16	Oleanolic acid-3-*O*-*β*-*D*-glucuronopyranosyl-6-*O*-n-butyl ester	P1	rhizomes	[14]
17	Oleanolic acid-3-*O*-*β*-*D*-(6'-methyl ester)-glucuronopyranoside	P1	rhizomes	[6]
18	Chikusetsusaponin IV	P1	rhizomes	[7]
		P1	roots	[10]
		P2	rhizomes	[8]

19	Oleanolic acid-3-*O*-*α*-*L*-arabinofuranosyl-(1→4)-*β*-*D*-glucuronopyranoside	P1	rhizomes	[7]
20	Chikusetsusaponin-IV methyl ester	P1	roots	[12]
		P1	rhizomes	[7]
21	Chikusetsusaponin-IVa methyl ester	P1	roots	[12]
		P1	rhizomes	[7]
22	Oleanolic acid-3-*O*-*β*-*D*-glucuronopyranosyl-6-*O*-methyl ester	P1	rhizomes	[17]
23	Stipuleanoside R_2	P1	roots	[12]
		P1	rhizomes	[7]
24	Chikusetsusaponin-Ib	P1	roots	[12]
25	Oleanolic acid-3-*O*-*β*-*D*-glucopyranoside	P1	rhizomes	[14]
26	oleanolic acid-3-*O*-*β*-*D*-glucopyranosyl-(1→2)-[*α*-*L*-arabinofuranosyl-(1→4)]-*β*-*D*-glucuronopyranoside	P1	rhizomes	[7]
27	3-*O*-[*β*-*D*-glucopyranosyl-(1→2)-*β*-*D*-glucopyranosyl]-oleanolic acid 28-*O*-*β*-*D*-glucopyranoside	P1	rhizomes	[17]
28	Oleanolic acid-3-*O*-*β*-*D*-glucopyranoside-(1→2)-*β*-*D*-glucorunopyranosy-6′-*O*-butyl ester	P1	rhizomes	[13]
Dammarane-type				
29	Vinaginsenoside R_4	P1	rhizomes	[7]
30	20(*S*)-dammarane-24-ene-3*β*,12*β*,20-triol	P1	rhizomes	[14]
31	6-*O*-[*β*-*D*-glucopyranosyl-(1→2)-*β*-*D*-glucopyranosyl]-20-*O*-[*β*-*D*-glucopyranosyl-(1→4)-*β*-*D*-glucopyranosyl]-20(*S*)-protopanaxatriol	P1	rhizomes	[18]
32	6″-acetyl-ginsenoside Rd	P1	rhizomes	[19]
33	(20*S*)-ginsenoside Rg_3	P1	roots	[12]
34	Notoginsenoside R_2	P1	rhizomes	[9]
		P1	roots	[10]
35	notoginsenoside R_1	P1	rhizomes	[7]
36	20-glucoginsenoside-Rf	P1	rhizomes	[20]
37	Ginsenoside F_3	P2	leaves	[21]
38	Ginsenoside F_1	P2	leaves	[21]
39	Ginsenoside Rb_3	P1	leaves	[22]
		P1	rhizomes	[14]
		P2	leaves	[21]
40	Ginsenoside Rc	P1	leaves	[22]
		P1	rhizomes	[16]
41	Ginsenoside Rb_1	P1	leaves	[22]
		P1	rhizomes	[7]
		P1	roots	[12]
		P2	rhizomes	[8]
		P2	leaves	[21]

42	Ginsenoside Rb_2	P1	leaves	[22]
		P2	rhizomes	[15]
43	Gypenosiden IX	P1	leaves	[23]
44	Ginsenoside Rd	P1	leaves	[24]
		P1	rhizomes	[20]
		P1	roots	[12]
		P2	rhizomes	[8]
		P2	leaves	[21]
45	Ginsenoside Re	P1	leaves	[24]
		P1	rhizomes	[6]
		P1	roots	[10]
		P2	rhizomes	[8]
		P2	leaves	[21]
46	Ginsenoside Rg_1	P1	leaves	[24]
		P1	rhizomes	[6]
		P1	roots	[12]
		P2	rhizomes	[8]
47	Ginsenoside Rg_2	P1	leaves	[24]
		P1	rhizomes	[16]
		P1	roots	[10]
		P2	rhizomes	[8]
		P2	leaves	[21]
48	Ginsenoside F_2	P1	leaves	[24]
		P2	leaves	[21]
49	6‴-*O*-acetylginsenoside Re	P1	rhizomes	[11]
50	Notoginsenoside Fe	P1	leaves	[23]
51	Ginsenoside Rd_2	P1	leaves	[23]
52	Ginsenoside Rs_2	P1	leaves	[23]
53	Ginsenoside Rs_1	P1	leaves	[23]
54	Ginsenoside Rf	P1	rhizomes	[25]
		P1	roots	[12]
55	6″-*O*-acetylginsenoside Rb_1	P1	rhizomes	[11]
56	Quinquenoside R_1	P1	leaves	[23]
57	(20*R*)-ginsenoside Rg_3	P1	roots	[12]
58	20(*R*)-dammarane-24-ene-3β,6α,12β,20-tetrol	P1	rhizomes	[14]
59	20(*R*)-dammarane-24-ene-3β,12β,20-triol	P1	rhizomes	[14]
60	Majoroside F_1	P1	leaves	[24]
		P2	leaves	[21]
61	Majoroside F_2	P1	leaves	[24]
62	Bipinnatifidusoside F_1	P2	leaves	[21]

63	6-*O*-[*β*-*D*-glucopyranosyl-(1→2)-*β*-*D*-glucopyranosyl]-dammar-25(26)-ene-3*β*,6*α*,12*β*,20*S*,24*R*-pentaol	P1	rhizomes	[25]
64	Vinaginsenoside R_9	P1	rhizomes	[7]
65	Ginsenoside I	P1	rhizomes	[7]
66	Quinquenoside L_{11}	P1	rhizomes	[7]
67	ginsenoside Re_5	P1	rhizomes	[25]
			roots	[12]
68	Yesanchinoside R_2	P1	rhizomes	[11]
69	Ginsenjilinol	P1	rhizomes	[7]
70	Bipinnatifidusoside F_2	P2	leaves	[21]
71	Majoroside F_3	P1	leaves	[21]
72	Majoroside F_5	P1	leaves	[26]
73	20(*R*)-dammarane-25-methoxyl-3*β*,12*β*,20-triol	P1	rhizomes	[14]
74	20(*R*)-dammarane-3*β*,12*β*,20,25-tetrol	P1	rhizomes	[14]
75	20(*R*)-dammarane-25-methoxyl-3*β*,6α,12*β*,20-tetrol	P1	rhizomes	[14]
76	Majoroside F_4	P1	leaves	[24]
77	Majoroside F_6	P1	leaves	[26]
78	Vinaginsenoside R_8	P1	rhizomes	[11]
79	Notoginsenoside E	P1	rhizomes	[11]
80	6-*O*-[*β*-*D*-glucopyranosyl-(1→2)-*β*-*D*-glucopyranosyl]-dammar-3*β*,6*α*,12*β*,20*S*,24*R*,25-hexaol	P1	rhizomes	[25]
81	vinaginsenoside R_{13}	P1	rhizomes	[11]
82	Ginsenoside Rk_3	P1	rhizomes	[16]
83	Dammar-20(21),24-diene-3*β*,6*α*,12*β*-triol	P1	leaves	[27]
84	Ginsenoside Rg_5	P1	roots	[12]
85	Dammar-20(22)*E*, 24-diene-3*β*,6*α*,12*β*-triol	P1	leaves	[22]
86	Dammar-20(22)*Z*,24-diene-3*β*,6*α*,12*β*-triol	P1	leaves	[27]
87	Majoroside Z	P1	leaves	[27]
88	20(*S*)-dammarane-20,25-epoxy-3*β*,6*α*-12*β*-triol	P1	rhizomes	[14]
89	20(*S*)-dammarane-20,25-epoxy-3*β*,12*β*-diol	P1	rhizomes	[14]
90	(20*S*)-6-*O*-[*β*-*D*-glucopyranosyl-(1→2)-*β*-*D*-glucopyranosyl]-dammar-20,25-epoxy-3*β*,6*α*,12*β*,24*α*-tetraol	P1	rhizomes	[25]
Ocotillol-type				
91	(20*S*,24*R*,25*R*)-6-*O*-[*β*-*D*-glucopyranosyl-(1→2)-*β*-*D*-glucopyranosyl]-dammar-20,24-epoxy-3*β*,6*α*,12*β*,25,26-pentaol	P1	rhizomes	[25]
92	Majonoside R_1	P1	rhizomes	[20]
		P1	roots	[12]
93	Majonoside R_2	P1	rhizomes	[20]
94	24(*R*)-majoroside R_1	P1	rhizomes	[18]
95	Pseudoginsenoside RT_2	P1	rhizomes	[11]

96	(20*S*,24*S*,25*R**)-6-*O*-[*β*-*D*-glucopyranosyl-(1→2)-*β*-*D*-glucopyranosyl]-dammar-20,24-epoxy-3*β*,6*α*,12*β*,25,26-pentaol	P1	rhizomes	[25]
97	Pseudoginsenoside F_{11}	P1	rhizomes	[7]
		P2	rhizomes	[15]
98	24(*S*)-pseudoginsenoside F_{11}	P2	rhizomes	[8]
		P2	leaves	[21]
99	20*S*,24*S*,dammarane-20,24-epoxy-3*β*,6*α*,12*β*,25-tetrol	P1	rhizomes	[14]
100	20*S*,24*R*,dammarane-20,24-epoxy-3*β*,6*α*,12*β*,25-tetrol	P1	rhizomes	[14]
Others				
101	Panasenoside	P2	leaves	[21]
102	5,7-dihydroxy-8-methoxyl flavone	P1	leaves	[23]
103	*β*-sitosteryl	P1	rhizomes	[14]
104	*β*-sitosteryl *β*-*D*-glucoside	P1	roots	[28]
		P1	rhizomes	[17]
105	Stigmasterol	P1	rhizomes	[13]
106	Daucosterol	P1	rhizomes	[13]
107	Benzoin acid	P1	rhizomes	[13]
108	Vanillin	P1	roots	[12]
109	Syringaldehyde	P1	roots	[12]
110	3,4,5-trimethoxy benzoic acid	P1	roots	[12]
111	2,6-dimethoxyphenol	P1	roots	[12]
112	Docosyl *trans*-ferulate	P1	roots	[28]
113	1*β*,6*α*-dihydroxy-4(14)-eudesmene	P1	roots	[28]
114	Succinic acid	P1	rhizomes	[14]
115	Panajaponin	P1	roots	[10]
116	Adenosine	P1	roots	[10]
117	Panaxjapyne A	P1	roots	[28]
118	(3*R*)-(–)-falcarinol	P1	roots	[28]
119	Panaxjapyne B	P1	roots	[28]
120	(3*S*,10*S*)-panaxydiol	P1	roots	[28]
121	Panaxjapyne C	P1	roots	[28]
122	(3*S*,9*R*,10*R*)-panaxytriol	P1	roots	[28]
123	(3*S*,9*R*,10*R*)-gensenoyne C	P1	roots	[28]

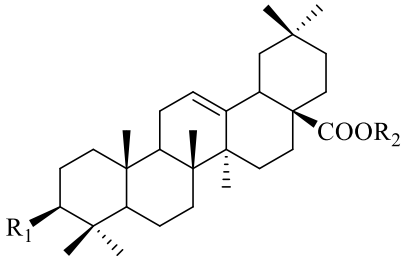
P1: *Panax japonicus* C. A. Mey. var. *major* (Burk.) C. Y. Wu et K. M. Feng

P2: *Panax japonicus* C. A. Mey. var. *bipinnatifidus* (Seem.) C. Y. Wu et K. M. Feng

3.1. Oleanane-Type Triterpenoids

Oleanane-type triterpenoid saponins are pentacyclic triterpenes, constituting the predominant structural type in PMR. In PMR, there are a total of 28 saponins of this type, exclusively isolated from roots or rhizomes. They frequently form saponins by connecting sugar-containing groups at C-3 and C-28. Notably, the carboxyl group at C-28 is predominantly linked to glucose, forming a

glycosidic bond. Conversely, sugars attached at the C-3 position exhibit structural variability and complexity, involving a broad spectrum of sugar substituents from monosaccharides to trisaccharides. Similar to compound **26**, a glycoside is derived from a trisaccharide at the C-3 position. The sugar substituent composition primarily comprises xylose, arabinose, and glucose. Among these, glucose is directly linked to the C-3 position of the parent nucleus, while esters (or acids) with varying carbon chain lengths are frequently formed at its C-6′ position. The specific structure is illustrated in Figure 2.



1 R_1=S_{23}, R_2=Glc	**8** R_1=S_1, R_2=H	**15** R_1=S_{19}, R_2=H	**22** R_1=S_3, R_2=H
2 R_1=S_{10}, R_2=H	**9** R_1=S_1, R_2=Glc	**16** R_1=S_4, R_2=H	**23** R_1=S_{29}, R_2=Glc
3 R_1=S_{10}, R_2=Glc	**10** R_1=S_4, R_2=Glc	**17** R_1=S_3, R_2=H	**24** R_1=S_{11}, R_2=Glc
4 R_1=S_{25}, R_2=Glc	**11** R_1=S_{12}, R_2=Glc	**18** R_1=S_{20}, R_2=Glc	**25** R_1=OGlc, R_2=H
5 R_1=S_{27}, R_2=Glc	**12** R_1=S_{28}, R_2=Glc	**19** R_1=S_{20}, R_2=H	**26** R_1=S_{29}, R_2=H
6 R_1=OH, R_2=H	**13** R_1=S_{12}, R_2=H	**20** R_1=S_{21}, R_2=Glc	**27** R_1=S_6, R_2=Glc
7 R_1=OH, R_2=Glc	**14** R_1=S_{22}, R_2=Glc	**21** R_1=S_3, R_2=Glc	**28** R_1=S_{26}, R_2=H

Figure 2. The structures of Oleanane-type triterpenoid glycosides (**1-28**) isolated from PMR

3.2. Dammarane-type Triterpenoids

Dammarane-type triterpenoid saponins, the most prevalent type in PMR, are tetracyclic triterpenoids with β-methyl groups at C-8 and C-10. The C-20 configuration is classified as either R or S, and C-17 possesses a β side chain. A total of 62 compounds of this type, constituting more than half of all PMR compounds, were isolated. The C-20 configuration of these compounds is predominantly in the S configuration, with a few exceptions in the R configuration, exemplified by **57-59**. Double bonds are present in C-17 side chains, with $\Delta^{24,25}$ being more frequent. Recently, scholars have isolated and identified compound **87**, exhibiting novel structures with C-23 and C-25 conjugation. Substitution of hydroxyl groups often occurs on the C-17 side chain, mainly at positions C-24~27, with **65** and **79** having peroxy groups at C-24 and C-25, respectively, which are less common. These compounds undergo glycosidization at the C-3, C-6, and C-20 positions. Glycosidization at the C-3 position is primarily linked to glucose or two glucose (1→2)-linked disaccharides. In addition to glycosides with glucose at the C-6 position, these compounds primarily form glycosides with three disaccharides: xyl(1→2) glc, glc(1→2)glc, rha(1→2) glc. At the C-20 position, besides attachment to glucose, glycosidization mainly occurs with three disaccharides: ara(1→6)glc, xyl(1→6)glc, and glc(1→6)glc. Furthermore, **88-90** are ginsenotriol-type saponins, a less frequently isolated type in PMR. The specific structures of these compounds are illustrated in Figure 3.

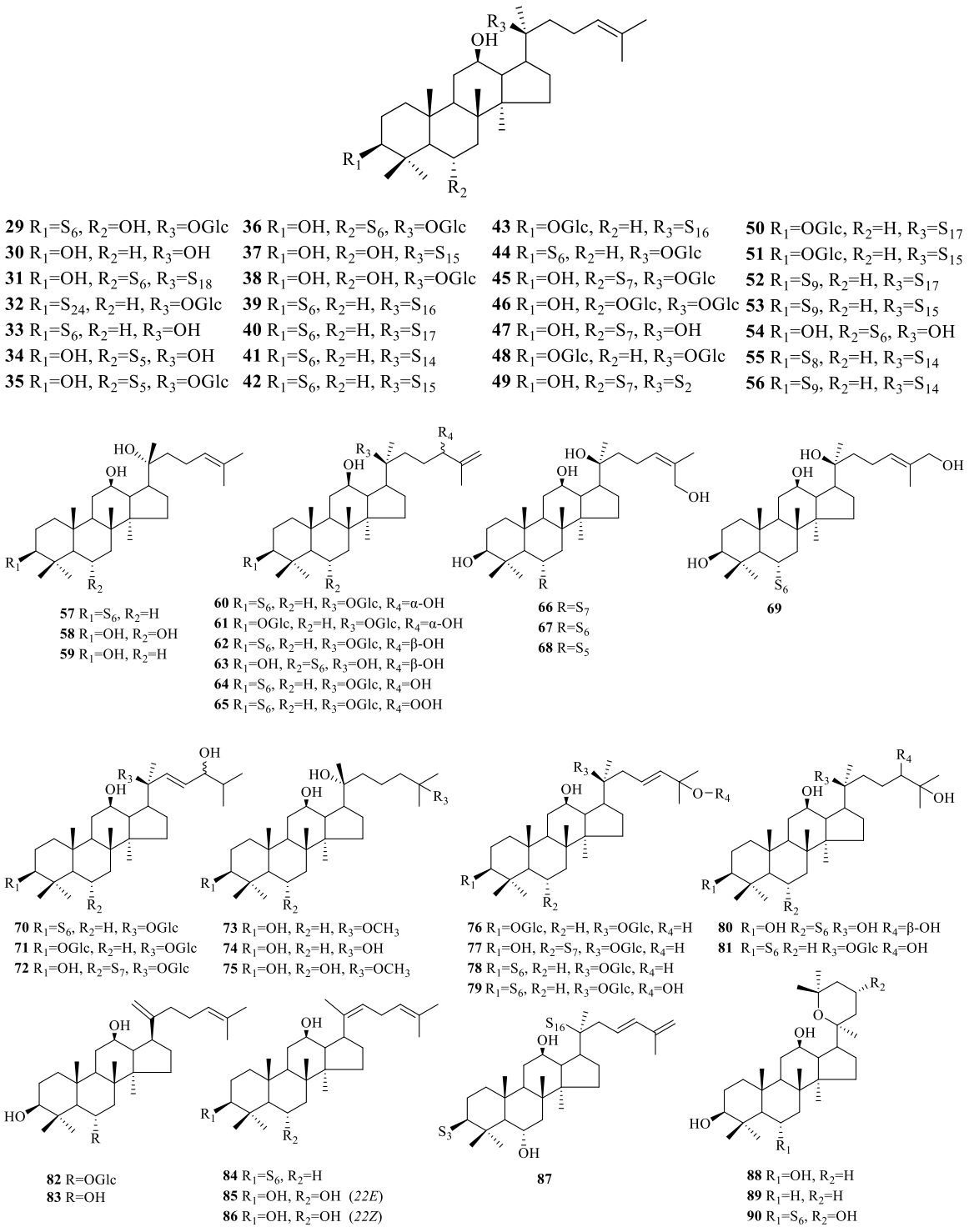
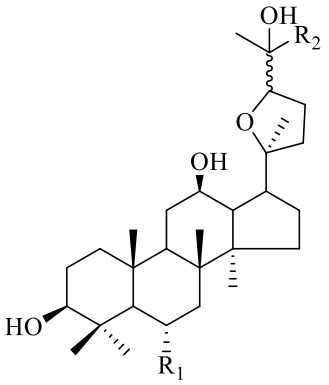


Figure 3. The structures of Dammarane-type triterpenoid glycosides (**29-90**) isolated from PMR

3.3. Ocotillol-Type Triterpenoids

Ocotillol-type saponin is less abundant in PMR, which is a tetracyclic triterpene with a furan ring in the C-17 side chain. Both C-20 and C-24 have R and S configurations, and a total of 10 compounds of this type were isolated from PMR. The C-20 conformations are all S, and the C-24R/S conformations are equally distributed. Ocotillol-type saponins predominantly form glycosides at the C-6 position, with attached sugar substituents primarily being disaccharides,

mainly xyl(1→2) glc, glc(1→2) glc, rha(1→2) glc. The specific structure is illustrated in Figure 4.



91 R_1=S_6, R_2=CH_2OH (*24R*)
92 R_1=S_6, R_2=CH_3 (*24S*)
93 R_1=S_5, R_2=CH_3 (*24S*)
94 R_1=S_6, R_2=CH_3 (*24R*)
95 R_1=S_5, R_2=CH_3 (*24R*)
96 R_1=S_6, R_2=CH_2OH (*24S*)
97 R_1=S_7, R_2=CH_3 (*24R*)
98 R_1=S_7, R_2=CH_3 (*24S*)
99 R_1=OH, R_2=CH_3 (*24S*)
100 R_1=OH, R_2=CH_3 (*24R*)

Figure 4. The structures of Ocotillol-type triterpenoid glycosides (**91-100**) isolated from PMR

3.4. Others

A total of 23 other compounds were isolated from PMR, including 2 flavonoids (**101-102**), 4 steroids (**103-106**), 6 aromatic hydrocarbons (**107-112**), 2 aliphatic hydrocarbons (**113-114**), 1 new glycosphingolipid (**115**), 1 nucleoside (**116**), and 7 acetylenic alcohols (**117-123**), and interestingly, this type of acetylenic alcohol showed relatively good biological activity. The specific structure is shown in Figure 5.

In addition, some scholars have analyzed the polysaccharides, volatile oils, and trace elements in PMR. Zhang *et al*. extracted the polysaccharides from PMR using distilled water as a solvent with a yield of 17.16%, and it was found that the solvent PH did not affect the yield. After hydrolyzing the polysaccharides, there were seven major monosaccharides, namely rhamnose 1.88%, ribose 5.22%, arabinose 2.21%, xylose 3.59%, mannose 4.08%, glucose 78.13%, and galactose 4.21%, with glucose having the highest relative content [29]. Yang *et al*. ultrasonically extracted polysaccharides from PMR with an extraction rate of 13.87±0.16%, and graded alcohol precipitation of total polysaccharides yielded four polysaccharide samples PM1~PM4, of which the PM4 sample was of high purity [30]. Zhang isolated five polysaccharide fractions, PJPS1~PJPS5, with the highest content of PJPS1 [31]. The volatile oils in PMR are mainly sesquiterpenes. Shi *et al*. identified 27 compounds from PMR with 37% sesquiterpene content [32]. Liu *et al*. identified 36 compounds from PMR, 15.39% of which were sesquiterpenes, with spathalenol being the most abundant. Interestingly, among the same genus, only the root of *Panax ginseng* contained a small amount of spathalenol, which can be taken as a characteristic component of PMR [33]. Guo *et al*. determined the volatile oils of the above-ground parts of PMR in three regions and identified more than 20 compounds with geographic variability in the volatile oils contained [34]. Zhang *et al*. found that PMR rhizomes are rich in panaxynol (5.48%) and palustrol (4.92%), which in a sense explains the anticancer effect of PMR; and in its leaves, there is a large amount of antioxidant phytol (22.21%) and Vitamin E (8.39%) [29]. Song *et al*. found PMR to be rich in Mg, Ca, with the highest Mg content. The leaves contained high amounts of Fe [35].

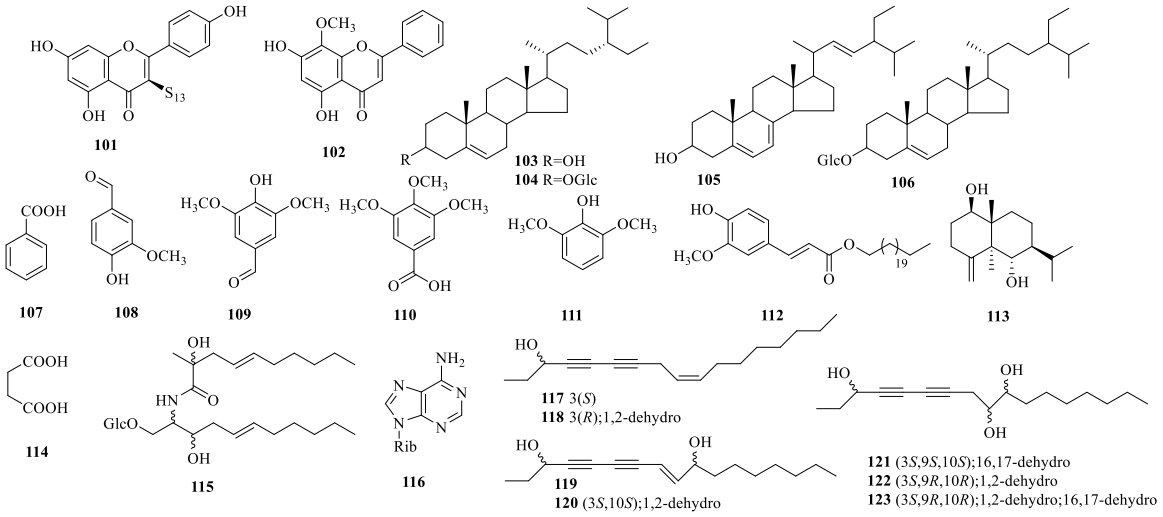


Figure 5. The structures of other compounds (**101-123**) isolated from PMR

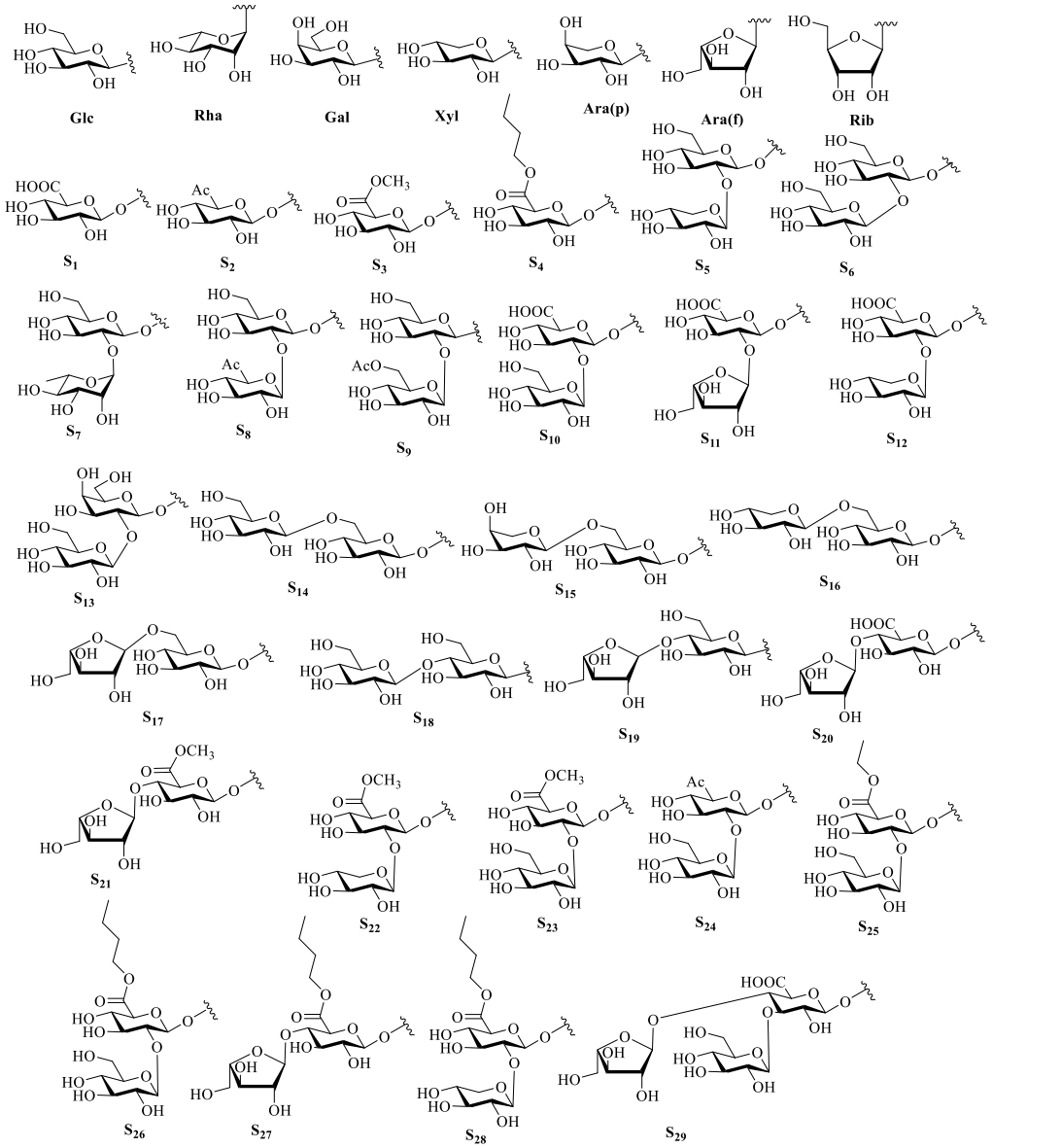


Figure 6. The structures of Sugar substituents appear in the paper

4. Pharmacological Activities

4.1. Hepatoprotective Effects

Hepatic fibrosis is a pivotal factor in the progression of liver diseases. If left uncontrolled, it can advance to cirrhosis and hepatocellular carcinoma, ultimately leading to mortality [36]. Early-stage effective treatment is crucial for intervening in this process. Research indicates that numerous traditional Chinese medicines demonstrate excellent hepatoprotective effects against liver fibrosis. Notably, total saponins from PMR(SPMR) have been extensively used in treating liver injury diseases, yielding favorable clinical outcomes. In a Vitro study, Zhang *et al*. discovered that SPMR provides a safeguard against LPS-induced inflammatory damage in L02 cells. The effect may involve hepatitis B, Th17 cell differentiation, TNF signaling pathway, and IL17 signaling pathway [37]. Zhang *et al*. reported that SPMR reverses the upregulation of TIMP1 mRNA expression while further enhancing the expression of MMP1 mRNA. This leads to a significant reduction in serum GSH-Px, SOD, and CAT activities in CCl_4-induced liver fibrosis mice, lowering XOD and MDA levels. Consequently, serum T-AOC levels are elevated, inhibiting oxidative stress responses and improving liver function. The research indicates that SPMR mitigates the effects of CCl4-induced liver fibrosis by boosting the liver's antioxidant capacity, curtailing lipid peroxidation in hepatic cell membranes, and lessening fibrosis and hepatocyte death in the liver. [38]. Wang *et al*. postulated that the protective role of SPMR against liver injury in rats is associated with the inhibition of lipid peroxidation reactions, reduction in free radical generation, enhancement of tissue antioxidant capacity, and promotion of protein synthesis [39]. Xu *et al*. reported that SPMR, Panax japlcus var Polysaccharide (PJPS), chikusetsusaponin IVa, and ginsenoside Ro, at specific doses, all demonstrate the capacity to reduce serum ALT and AST levels in mice. Chikusetsusaponin IVa was identified as the principal component responsible for its hepatoprotective effect [40].

Fatty liver disease is another prevalent hepatic condition marked by the excessive accumulation of fat within hepatocytes and hepatocellular lipid degeneration. If left untreated, this clinical-pathological syndrome has the potential to evolve into liver cirrhosis or hepatocellular carcinoma [41]. Guo *et al*. investigated the therapeutic effects of the aerial parts of PMR against fatty liver disease. Their findings indicate that the extracts significantly reduced TG and TC levels in obese mice. Moreover, they observed a decrease in the expression of the PTGS2 receptor in mouse liver tissue, coupled with an enhancement in the expression of MAPK3 and PPARG receptor proteins. [42].

Furthermore, as liver diseases advance to end-stage liver disease (ESLD), the regenerative capacity of liver tissue declines, ultimately leading to liver functional failure [43]. In situ liver transplantation offers an effective treatment for end-stage liver disease (ESLD), while the hepatic differentiation of BMSCs addresses issues related to organ availability and costliness. In an in vitro study, Zhang *et al*. observed that SPMR significantly enhances hepatocyte-specific characteristics. It elevates the gene expression of HGF, c-MET, AFP, Albumin, and CK18, as well as the protein expression of AFP, Albumin, and CK18. Consequently, this facilitates the differentiation of BMSCs into hepatocytes [44]. When co-administered with BMSCs, SPMR promotes the enrichment of BMSCs at the site of liver injury, facilitating hepatocyte proliferation. This leads to improved liver function in CCl4-induced liver fibrosis rats [45].

Furthermore, the monomeric components within PMR have been demonstrated to possess hepatoprotective properties. Li *et al*. intervened in nonalcoholic steatohepatitis (NASH) mouse model with varying doses of Chikusetsusaponin IVa and found that it could reduce liver index and collagen fiber deposition in the model mice through the miR-17-5p/MFN2 pathway. This compound demonstrated a protective role against NASH by reducing the expression levels of genes associated with lipid metabolism and inflammatory factors. [46]. Figure 7 illustrates the signal pathways related to the hepatoprotective effects of PMR.

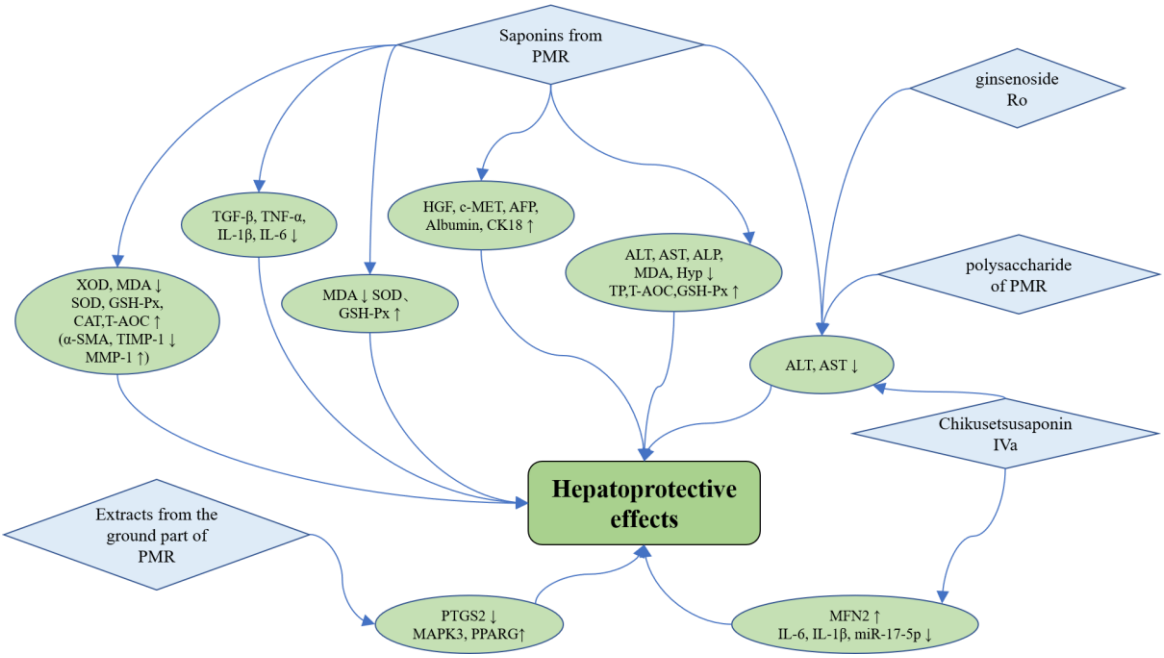


Figure 7. The signal pathways related to the Hepatoprotective effects of PMR

4.2. Anticancer Potential

Cancer is a significant health concern, marked by the uncontrolled proliferation and division of abnormal cells within the human body. Natural products play a crucial role as sources for innovative therapeutic agents, owing to their distinctive molecular properties, superior efficacy, and safety profiles. They are currently extensively researched as potential anticancer agents, displaying promising trends in preclinical studies [47]. Saponins, a major component in plants, are well-known for their anticancer properties, and ginsenosides are particularly acknowledged as highly effective constituents [48]. PMR, being rich in ginsenosides, has been found to exhibit potent anticancer properties. In vitro, Chang *et al*. used the MTT assay to show that SPMR has the ability to curb CRC cells proliferation, specifically HCT116 and SW620 cells. This effect is achieved by modulating mitochondrial-related signaling pathways and MAPK signaling pathways. At the molecular level, it elucidates the mechanism of cancer cell apoptosis and holds certain value for drug development in the treatment of colon cancer using SPMR [49]. In an in vitro study using the MTT assay, Zhang *et al*. observed that SPMR exerts a potent inhibitory effect on gastric cancer HGC-27 cells, with an IC_{50} value of 29.77 μg/mL, displaying concentration-dependent behavior. This effect is possibly mediated through the upregulation of miR-10a expression, which inhibits the activation of the PI3K/AKT/NAG-1 signaling pathway. Subsequently, SPMR is believed to participate in the regulation of BCL-2 and caspase family pathways, thereby impeding the invasion

migration, and proliferation of HGC-27 cells and ultimately inducing apoptosis [50]. Chen *et al*. found that SRPM exhibits a certain inhibitory effect on proliferation and induces differentiation in human acute promyelocytic leukemia HL-60 cells. The underlying mechanism for this effect could potentially be linked to the cell arrest in the G0/G1 phase [51]. Furthermore, Li *et al*. discovered, through in vitro experiments, that SRPM can promote the proliferation and differentiation of bone marrow-suppressed murine hematopoietic stem cells via the SDF-1/CXCR4 pathway, offering a theoretical basis for its potential application in the treatment of hematological disorders [52].

Furthermore, PJPS exhibits notable anticancer activity. Chen *et al*., using 5-fluorouracil as a positive control drug, conducted in vivo experiments on H22 liver cancer transplanted mice. They found that oral administration of PJPS at 50 mg/kg extended the survival time of mice, and promoted tumor cell necrosis and apoptosis. They postulated that the mechanism of its anti-liver cancer effect involves enhancing the host's cellular immune function, disrupting the tumor cell cycle, and reducing the expression of VEGF [53]. In vitro, Wang *et al*. utilized the CCK-8 assay and found that PJPS has the capability to inhibit the proliferation of MKN45 gastric cancer cells and induce apoptosis. This effect is realized through the modulation of the let-7a/CDK6 molecular axis. Specifically, PJPS elevates the expression of let-7a, which subsequently targets and suppresses the expression of CDK6. [54].

Research indicates that certain monomeric compounds within PMR exhibit notable inhibitory effects on the proliferation of cancer cells. Song *et al*. discovered through in vitro MTT assays that calenduloside E (**8**), taibaienoside IV (**10**), and taibaienoside I (**5**) exhibit significant inhibitory effects on HepG2, Hela, and A549 tumor cells. At a concentration of 0.1 μmol/mL, these compounds achieved more than 50% inhibition of cell proliferation in all three cell lines [9]. Oleanolic acid-3-*O*-*β*-*D*-glucopyranoside-(1→2)-*β*-*D*-glucorunopyranosy-6′-O-butyl ester (**28**) exhibits moderate anti-tumor activity against OVCAR-3 and A2780 cells, with IC_{50} values of 22.1 and 35.2 μg/mL, respectively [55]. Compounds Deglucose chikusetsusaponin IVa (**8**) and oleanolic acid-3-*O*-*β*-*D*-(6'-methyl ester)-glucuronopyranoside (**17**) exhibit significant activity against four different cancer cell lines, including Hela, BGC-823, HCT-116, and HepG2 cells. This activity displays a dose-dependent relationship. Notably, the former compound displays IC_{50} values of 9.94 μmol/L and 14.17 μmol/L against gastric cancer BGC-823 and colon cancer HCT-116 cells, respectively, while the latter exerts its strongest inhibitory effect on HepG2 liver cancer cells with an IC_{50} of 12.70 μmol/L. The varying levels of activity may be associated with the C-28 substituent [6].

Furthermore, the majority of traditional Chinese herbal medicines are primarily administered in the form of aqueous decoctions, and their anticancer properties are also readily evident. Yang *et al*. conducted in vitro experiments utilizing the MTT assay to evaluate the effects of the Water Decoction of PMR on glioblastoma U87 cells. They observed that it can inhibit the proliferation and promote apoptosis of U87 cells by modulating the PI3K/AKT signaling pathway, thereby reducing the phosphorylation levels of PI3K and AKT [56]. Hu *et al*. reported that the Water Decoction of PMR inhibits the proliferation of liver cancer cells. The mechanism underlying this effect may involve the prevention of G2/M phase cell transition, disruption of S-phase DNA synthesis, and induction of cancer cell apoptosis. Additionally, it can reduce abnormally elevated levels of TNF-α in mice, thereby modulating the host's immune response [57]. The signaling pathways related to the anticancer effect of PMR are illustrated in Figure 8.

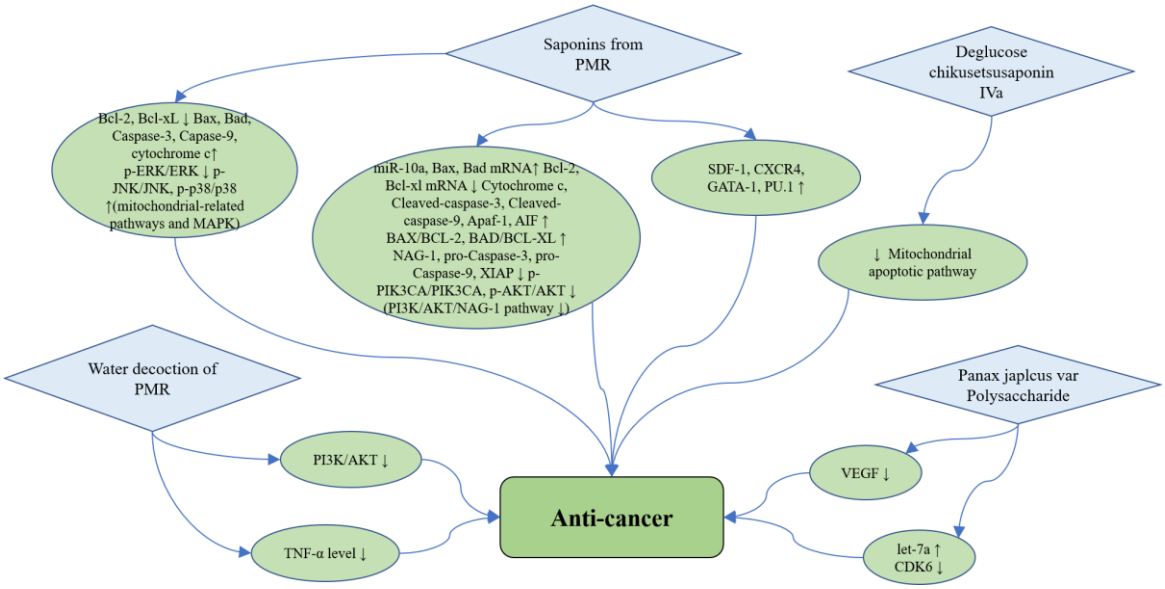


Figure 8. The signal pathways related to the Anti-cancer effect of PMR

4.3. Cardioprotective Effects

Heart disease is a common cardiovascular disorder, typically arising from inadequate coronary artery perfusion. Ischemic heart disease, especially acute myocardial ischemia, is regarded as a prevalent and major cause of mortality worldwide. Prolonged ischemia ultimately leads to myocardial infarction [58]. The treatment of this condition typically involves reperfusion therapy; however, this approach is a double-edged sword, as it simultaneously alleviates ischemia while exacerbating myocardial injury. In recent years, traditional Chinese herbal medicine has been increasingly recognized for its role in the treatment of ischemic heart disease and reperfusion injury, largely due to its minimal side effects. PMR has been found to possess certain cardioprotective effects. Li *et al*. reported that in vivo, SPMR and its degradation products exhibit protective effects against myocardial cell ischemia-reperfusion injury. The underlying mechanism may be closely associated with their enhanced antioxidative properties, alteration of blood viscosity, inhibition of platelet aggregation, and platelet adhesion. Overall, the degradation products of SPMR demonstrate a stronger ability to protect myocardial cells from ischemia-reperfusion injury [59]. Furthermore, clearing excess ROS can reduce the damage associated with ischemia-reperfusion. He *et al*. administered SRPM orally to mice for 14 days before modeling myocardial ischemia-reperfusion. The results showed that SRPM reduced ROS release, enhanced total antioxidant capacity, improved cardiac function, reduced infarct size, and activated Sirt1 and Nrf2-related antioxidant signaling pathways, thereby achieving cardioprotective effects [60]. Chen *et al*. confirmed in vitro experiments that SRPM exhibits an inhibitory effect on H_2O_2-induced apoptosis in myocardial cells. It significantly enhances myocardial cell viability, and its mechanism is associated with ROS clearance and the regulation of myocardial cells caspase-9, caspase-3, Bcl-2 and Bax [61]. Liu *et al*. discovered that the activation of the Nrf2 antioxidant pathway and the anti-lipid peroxidation effects may be one of the mechanisms underlying SRPM's protection against myocardial ischemia-reperfusion injury [62]. Yan *et al*. confirmed that Ginsenoside Rd (**44**) can induce antioxidant activity-mediated apoptosis in cardiac cells induced by AFB1 [63]. Furthermore, the inhibition of inflammatory responses is another significant mechanism for improving myocardial ischemia-

reperfusion injury. Zhang *et al*. demonstrated that SPMR can alleviate inflammation by inhibiting the expression of MCP-1, MIF, and TNF-α, thereby improving myocardial ischemia-reperfusion injury [64]. He *et al*. discovered that SPMR attenuates the inflammatory response, suppresses the expression of MCP-1, TGF-β1, TNF-α, and NF-κB p65, and ameliorates oxidative damage to myocardial cells [65].

Furthermore, end-stage cardiovascular diseases often involve myocardial fibrosis. Studies have shown that SRPM can effectively improve the degree of fibrosis in a rat model of acute myocardial ischemic injury. In particular, Chikusetsusaponin IVa (**9**) can activate autophagy through the AMPK/mTOR/ULK1 pathway, thereby alleviating myocardial fibrosis induced by isoproterenol [66]. In addition, SPMR also exhibits a certain protective effect against myocardial infarction. Bao *et al*. demonstrated through in vivo experiments in rats that SPMR achieves protection against myocardial infarction by enhancing SIRT1 expression, inhibiting IκB-α phosphorylation, NF-κB activation, and pro-inflammatory cytokine production [67]. Panax japonicus var Polysaccharide (PJPS) exhibits a certain improvement in hemodynamics in mice with heart failure. It can protect the heart by reducing MDA and NO to alleviate oxidative stress reactions [68]. The signaling pathways related to the cardioprotective effect of PMR are depicted in Figure 9.

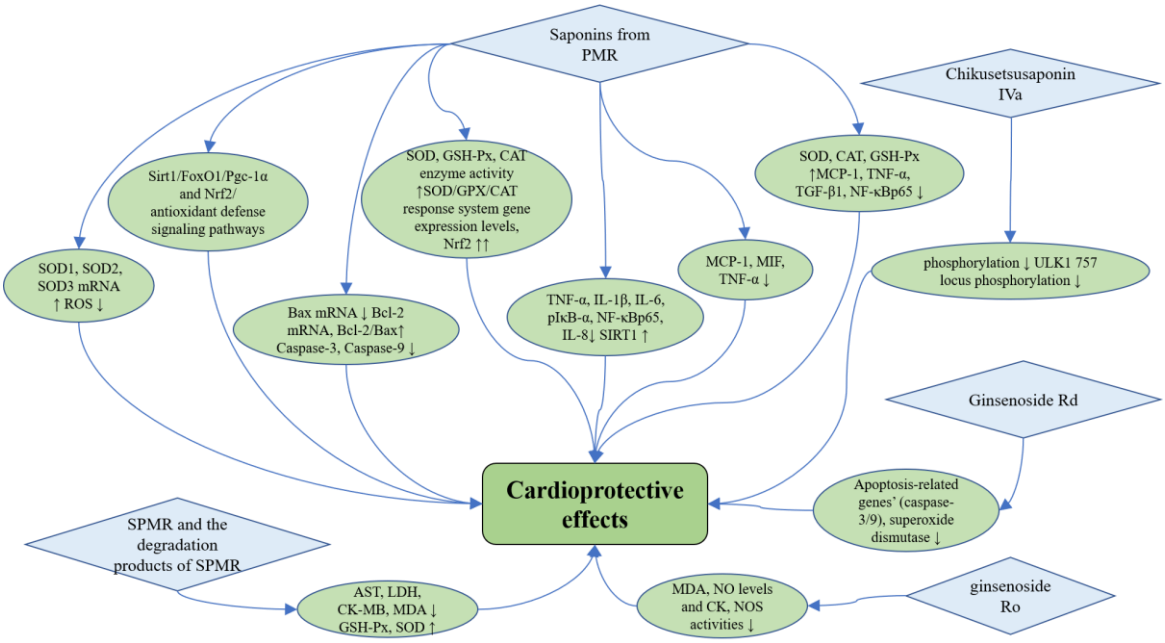


Figure 9. The signal pathways related to the Cardioprotective effect of PMR

4.4. Ischemic Brain Injury

Ischemic brain injury, commonly referred to as stroke, stands as the third leading cause of death and a significant contributor to global disability [69]. It is primarily caused by various factors leading to insufficient cerebral blood flow and extensive neuronal apoptosis. Research has revealed a close association between cerebral ischemia and mitochondrial autophagy, where damaged mitochondria generate and accumulate ROS, triggering cell death [70]. The autophagic process selectively eliminates damaged mitochondria to maintain cellular homeostasis, making the regulation of autophagy a reliable approach for the treatment of cerebral ischemic injury. "Duan *et*

al. intervened with SPMR in mice undergoing cerebral ischemia-reperfusion and found that it improved neurological deficits and brain tissue morphology in the model mice. It also reduced the degree of brain edema and infarct area. The suggested mechanism of action could potentially be tied to the stimulation of the PI3K/Akt pathway and the suppression of the mitochondria-mediated apoptotic pathway [71]. Tang *et al*. observed in vitro experiments that Ginsenoside Rg1 (**46**) promotes ATP production and mitigates mitochondrial dysfunction induced by OGD. Furthermore, the protective impact of Rg_1 on mitochondria in OGD-induced SK-N-SH cells was reduced by autophagy inhibitors, demonstrating its protective role against cerebral ischemic injury through the regulation of mitochondrial autophagy to improve mitochondrial dysfunction [72]. Ginsenoside Rg_1 has also been observed to decrease the number of errors in the water maze test in rats modeled with HIBD, decreases brain water content, inhibits neuronal apoptosis, and alleviates brain tissue damage [73]. In addition, it enhances learning and memory in neonatal rats with HIBD by reducing hippocampal neuronal apoptosis [74]. Tu *et al*. demonstrated that notoginsenoside R_1 (**35**) exerts neuroprotective effects by modulating the PI3K-Akt-mTOR/JNK signaling pathway to promote neuronal survival, inhibit apoptosis, and ameliorate the effects of hypoxic-ischemic brain injury [75].

Furthermore, Shi *et al*. conducted in vivo experiments and found that PMR ethanol extract significantly increased the survival rate of focal cerebral ischemia model mice, improved neurological symptoms following ischemia-reperfusion, reduced brain infarct size and brain water content, demonstrating a notable neuroprotective effect against cerebral ischemic injury [76]. In the same model, He *et al*. discovered that the ethanol extract of PMR exhibited a protective role against cerebral ischemic injury in mice. The mechanism of this protection may involve the upregulation of gene expression in the SOD/GPX/CAT antioxidant system, thereby reducing oxidative stress-induced damage to the brain caused by cerebral ischemia [77]. Su *et al*. discovered that the water extract of PMR could reduce the levels of TNF-α and IL-1β in the blood and brain tissue of mice with ischemic brain injury. It also decreased the expression of NF-κB in brain tissue and inhibited the generation of inflammatory cytokines. Consequently, it improved neurological symptoms after ischemia-reperfusion and exhibited a favorable protective effect against brain damage [78].

4.5. Antioxidant Capacity

Chinese herbal medicines are rich in various natural antioxidants that can neutralize free radicals in the body, reduce oxidative stress, help delay cellular aging, and alleviate inflammatory responses. In vitro, Yang *et al*. conducted experiments on free radical scavenging using Panax japonicus var Polysaccharide (PJPS), revealing its notable scavenging effects on superoxide anion radicals, hydroxyl radicals, and ABTS radicals. Specifically, PJPS demonstrated a 93.47% scavenging effect on hydroxyl radicals at a concentration of 10 mg/mL, and exhibited a 90.24% scavenging effect on ABTS radicals at a concentration of 8 mg/mL [79]. Wang *et al*. observed that the aqueous extract and 70% ethanol extract of PMR exhibited significantly enhanced inhibitory effects on superoxide anion radicals and hydroxyl radicals at concentrations greater than 5 mg/mL and 2.5 mg/mL, respectively [80]. An *et al*. found that the aqueous extract, saponins, and polysaccharides of PMR all exhibited in vitro antioxidant capabilities. Among them, SPMR demonstrated higher iron-reducing ability, DPPH radical scavenging activity, and protection against H_2O_2-induced damage to RAW 264.7 cells compared to the aqueous extract and polysaccharides. The aqueous extract demonstrated the most robust protective effect against Cu^{2+}/H_2O_2-induced

protein oxidation damage [81].

4.6. Anti-inflammatory and Analgesic Effect

Inflammatory responses occur widely in the pathological processes of various diseases and are typically the body's defensive reactions to external injuries or infections. Traditional Chinese medicine frequently exerts dual anti-inflammatory and analgesic effects through multiple pathways to alleviate symptoms, with a comparatively lower incidence of adverse effects. Liu *et al*. assessed the anti-inflammatory and analgesic activities of PMR ethanol extract using the acetic acid-induced writhing test, xylene-induced ear edema in mice, and egg white-induced arthritis. The results showed that a high dose (6 g/kg) significantly exhibited analgesic effects against acetic acid-induced pain and demonstrated anti-inflammatory and anti-edematous effects against both xylene-induced chemical inflammation and egg white-induced biological inflammation, with the latter showing more pronounced anti-inflammatory effects [82]. Guo *et al*. observed significant improvements in the symptoms of CIA mice with Chikusetsusaponin IVa (**9**) treatment. It achieved this by reducing inflammatory factors such as IFN-γ, IL-1β, IL-6, and TNF-α, and modulating the JAK/STAT signaling pathway, which led to the suppression of inflammation and bone destruction in mice. This suggests its potential as a targeted therapeutic agent for rheumatoid arthritis (RA) [83]. Gao *et al*. discovered in vitro experiments that SPMR could upregulate the expression of miR-216a, thereby reducing the apoptosis rate of HCMV-infected MRC-5 cells and the levels of TNF-α and IL-6. This inhibition of the inflammatory response resulted in diminished cellular damage [84]. Zhou *et al*. found that SPMR could upregulate the expression of miR-325-3p to suppress cell apoptosis and the inflammatory response [85]. Jiang *et al*. found in vitro experiments that the 70% methanol extract of PMR significantly inhibited NF-κB protein expression and reduced cellular levels of NO and TNF-α. In in vivo experiments, it reduced ear swelling in mice induced by xylene, and this effect showed a dose-dependent relationship. It exhibited anti-inflammatory properties both in vitro and in vivo [86].

4.7. Anticoagulant Effect

Anticoagulation dysfunction can result in diseases such as thrombosis, stroke, and myocardial infarction. Saponins, found in nature, serve as significant sources of anticoagulant agents, showcasing notable anticoagulant properties. Shu *et al*. confirmed that PMR displayed significant anticoagulant activity in vitro by significantly prolonging prothrombin time (PT) and activated partial thromboplastin time (APTT) while reducing the level of fibrinogen (FIB). This anticoagulant activity correlated with the content of Ginsenoside Rb2 (**42**) [87]. Li *et al*. reported a comparison of the in vitro anticoagulant effects of PMR subjected to different processing methods. Except for drying in the shade and air-drying, PMR processed using other methods prolonged both PT and APTT. In particular, vacuum freeze-dried PMR significantly reduced fibrinogen (FIB) levels [88]. Li *et al*. isolated yesanchinoside R_2 (**68**), vinaginsenoside R_{13} (**81**), (20*S*)-6-*O*-[*β*-*D*-glucopyranosyl-(1→2)-*β*-*D*-glucopyranosyl]-dammar-20,25-epoxy-3β,6α,12β,24α-tetraol (**90**), and 6-O-[β-D-glucopyranosyl-(1→2)-*β*-*D*-glucopyranosyl]-dammar-25(26)-ene-3*β*,6*α*,12*β*,20*S*,24*R*-pentaol (**63**), which exhibited inhibitory activity against adenosine diphosphate (ADP)-induced platelet aggregation with IC_{50} values of 18.27, 11.34, 23.24, and 18.43 μmol/L, respectively. Additionally, 3-*O*-[*β*-*D*-glucopyranosyl-(1→2)-*β*-*D*-(6′-*O*-ethyl)-glucuronopyranosyl]-oleanolic acid 28-*O*-*β*-*D*-glucopyranoside (**4**), vinaginsenoside R_8 (**78**), notoginsenoside E (**79**), and 6″-O-acetylginsenoside

Rb_1 (**55**) exhibited moderate activity with IC_{50} values of 40.54, 25.18, 29.45, and 36.9 μmol/L, respectively. Among them, notoginsenoside E (**79**), 6-*O*-[*β*-*D*-glucopyranosyl-(1→2)-β-D-glucopyranosyl]-dammar-25(26)-ene-3β,6*α*,12*β*,20*S*,24*R*-pentaol (**63**), displayed moderate inhibitory activity against arachidonic acid (AA)-induced platelet aggregation with IC_{50} values of 17.43 and 30.11 μmol/L [11] [89].

4.8. Others

The regulation of osteoblast differentiation and mineralization is crucial for bone protection and is key in the prevention and treatment of osteoporosis. In vitro experiments conducted by Pan *et al*. investigated primary osteoblast cells from rats. They found that PMR extracts could enhance osteoblast cell viability and increased their proliferation, differentiation, and mineralization capabilities. The suggested mechanism behind this effect may involve the regulation of OPG/RANKL expression [90].

Furthermore, PMR also exhibits anti-fatigue and anti-stress activities. Fan *et al*. reported that PMR significantly improves the ability of mice to tolerate hypoxia and low temperatures, as well as prolonging the time mice can engage in weighted swimming exercises [91]. Kao *et al*. noted that total saponins from PMR leaves prolonged the survival time of mice under hypoxic conditions, indicating the presence of anti-fatigue active substances in the above-ground parts [92].

Besides, PMR has some immune-regulating functions. It has been reported that PMR has a therapeutic effect on leukopenia. Its water extract can significantly counteract the damage caused by cyclophosphamide, increase the white blood cell levels in leukopenic mice, and protect against liver and kidney damage [93]. Zhang and colleagues reported that crude extracts of PMR, total saponins, and crude polysaccharides all promote the recovery of hematopoietic function in blood-deficient mice. They suggested that this mechanism may be related to the stimulation of the secretion of serum cytokines such as IL-6 and IL-3, as well as the inhibition of apoptosis in splenic cells [31]. SPMR enhances T-cell proliferation induced by PHA and ConA [94], indicating its potential immunomodulatory ability.

Furthermore, Chan reported that polyacetylenes isolated from PMR have a significant inhibitory effect on α-glucosidase, reducing carbohydrate digestion and absorption, which can help alleviate the progression of diabetes. Compounds such as Panaxjapyne A (**117**), Panaxjapyne C (**121**), (3*R*)-(–)-falcarinol (**118**), (3*S*,10*S*)-panaxydiol (**120**), vanillin (**108**), *β*-sitosteryl *β*-*D*-glucoside (**104**), and others isolated from PMR exhibited potent α-glucosidase inhibitory activity, with IC_{50} values ranging from 22.21 to 217.68 μM when compared to positive controls [28].

All the pharmacological effects of PMR are summarized in Table 3.

Table 3. Pharmacological Activities of PMR

Pharmacological effects	Effective compounds or fraction	Vitro or vivo	Models	Dosage	Pathway or possible target site	Ref.
Hepatoprotective effects	Saponins from PMR (SPMR)	In vivo	CCl_4-induced hepatic fibrosis Male SD rats	100~200 mg/kg gavage	SOD, GSH-Px, CAT, T-AOC ↑ XOD, MDA ↓ (α-SMA, TIMP-1 ↓ MMP-1 ↑)	[38]
	Total saponins of PMR	In vitro	LPS-induced L02 cells	50 or 100 μg /mL	TGF-β, TNF-α, IL-1β, IL-6 ↓	[37]
	Extracts from the ground part of PMR (0.2 g/mL)	In vivo	Obese mice fed a high-fat diet	0.1~0.2 ml gavage	PTGS2 ↓ MAPK3, PPARG ↑	[42]
	Total saponins and polysaccharides of PMR , chikusetsusaponin IVa, and Ginsenoside Ro	In vivo	CCl_4-induced acute liver injury rats	100~200, 50, 50~200 and 50~100 mg/kg respectively	ALT, AST ↓	[40]
	Saponins from PMR	In vitro	bone marrow stem cells (BMSCs)	200 μg /ml	HGF, c-MET, AFP, Albumin, CK18 ↑	[44]
	Saponins from PMR	In vivo	CCl_4-induced hepatic fibrosis SD rats	200 mg/kg gavage	SOD, CAT, GPX1, Nrf2 ↑	[95]
	Combination of Saponins from PMR and bone marrow stem cells	In vivo	CCl_4-induced hepatic fibrosis SD rats	200 mg/kg gavage	ALP, ALT, AST, Hyp ↓ TP, ALB, A/G ↑	[45]
	Total saponins of PMR	In vivo	CCl_4-induced hepatic fibrosis SD rats	50 or 100 mg/kg gavage	MDA ↓ SOD、GSH-Px ↑	[96]

	Total saponins of PMR	In vivo	CCl_4-induced chronic hepatic injury SD rats	60, 120, 240 mg/kg gavage	ALT, AST, ALP, MDA, Hyp ↓ TP, T-AOC, GSH-Px ↑	[39]
	Chikusetsusaponin IVa	In vivo	High-fat diet combined with CCl_4-induced NASH Balb/c male mice	7 or 35 mg/kg (Mixed in the feed)	IL-6, IL-1β, miR-17-5p ↓ MFN2 ↑	[46]
Anti-cancer	Calenduloside E (**8**), Taibaienoside IV (**10**) and Taibaienoside I (**5**)	In vitro	HepG2, Hela, A549 cells	0.1~0.2 μmol/mL	-	[9]
	Total saponins from PMR	In vitro	HCT116 and SW620 cells	IC_{50}=424.4 and 386.2 μg /ml (12h) 315.8 and 355.1 μg /ml (24h)	Bcl-2, Bcl-xL ↓ Bax, Bad, Caspase-3, Capase-9, cytochrome *c*↑ p-ERK/ERK ↓ p-JNK/JNK, p-p38/p38 ↑(mitochondrial-related pathways and MAPK)	[49]
	Deglucose chikusetsusaponin IVa (**8**)	In vitro	HepG2 cells	0.06~0.1μmol/mL	Bax ↑Bcl-2 ↓(mitochondrial apoptotic pathway)	[97]
	Oleanolic acid-3-*O*-*β*-*D*-glucopyranoside(1→2)-*β*-*D*-glucorunopyranosy-6′-*O*-butyl ester (**28**)	In vitro	A2780 and OVCAR-3 cells	IC_{50}=22.1 and 35.2 μg /ml	-	[55]
	Water extracts and ethyl acetate extracts of PMR	In vitro	MG380-3 cells	2.5~40 mg/mL	-	[80]
	Deglucose chikusetsusaponin IVa (**8**) and oleanolic acid-3-*O*-*β*-*D*-(6'-methyl ester)-glucuronopyranoside (**17**)	In vitro	BGC-823, HCT-116, Hela, HepG2 cells	IC_{50}=9.94, 14.17, 18.23, 17.76 and 17.12, 19.25, 18.96, 12.70 μmol/L	-	[6]

Panax japlcus var Polysaccharide (PJPS)	In vivo	H_{22} tumor transplanted BALB/c mice	50 mg/kg gavage	VEGF ↓	[53]
Panax japlcus var Polysaccharide	In vitro	MKN45 cells	IC_{50}=94.84 μg/mL	let-7a ↑ CDK6 ↓	[54]
Water decoction of PMR	In vitro	U87 cells	50~200 μg/mL	PI3K/AKT ↓	[56]
Water, ethanol precipitation, HPD-100 macroporous resin and 0.2 μm microfiltration membrane extract	In vitro	MCF-7 cells	0.01~0.2 mg/mL	-	[98]
Water decoction of PMR	In vivo	H_{22} tumor transplanted mice	Crude medicine 5~10 g/kg gavage	TNF-α level ↓	[57]
Saponins from PMR	In vitro	HGC-27 cells	IC_{50}=29.77 μg/mL	miR-10a, Bax, Bad mRNA↑ Bcl-2, Bcl-xl mRNA ↓ Cytochrome *c*, Cleaved-caspase-3, Cleaved-caspase-9, Apaf-1, AIF ↑ BAX/BCL-2, BAD/BCL-XL ↑ NAG-1, pro-Caspase-3, pro-Caspase-9, XIAP ↓ p-PIK3CA/PIK3CA, p-AKT/AKT ↓ (PI3K/AKT/NAG-1 pathway ↓) (12.5, 25, 50μg/mL)	[50]

	Saponins from PMR	In vitro	HL-60 cells	100, 200, 400 or 800 μg/mL	-	[51]
	Saponins from PMR	In vitro	Mice bone marrow hematopoietic cells	50, 100 or 200 μg/mL	SDF-1, CXCR4, GATA-1, PU.1 ↑	[52]
Cardioprotective effects	SPMR and the degradation products of SPMR	In vivo	myocardial ischemia-reperfusion injury male wistar rats	50, 100 or 200 mg/kg gavage	AST, LDH, CK-MB, MDA ↓ GSH-Px, SOD ↑	[59]
	Saponins from PMR	In vivo	ischemia/reperfusion (I/R) male SD rats	100 or 200 mg/kg/day	SOD1, SOD2, SOD3 mRNA ↑ ROS ↓	[99]
	Chikusetsusaponin IVa (**9**)	In vivo	Isoproterenol induced myocardial fibrosis in mice	5 or 15 mg/kg	p-AMPK ↑ m-TOR phosphorylation ↓ ULK1 757 locus phosphorylation ↓	[66]
	Saponins from PMR	In vivo	ischemia-reperfusion injury male wistar rats	200 mg/kg gavage	Sirt1/FoxO1/Pgc-1α and Nrf2/ antioxidant defense signaling pathways	[60]
	Ginsenoside Rd (**44**)	In vitro	aflatoxin B1 induced H9C2 cells and 3D heart spheroids	0~100 μM	apoptosis-related genes' (caspase-3/9), superoxide dismutase ↓	[63]
	Saponins from PMR	In vitro	H_2O_2 induced myocardial apoptosis neonatal rats	100 and 200 μg/mL	Bax mRNA ↓ Bcl-2 mRNA, Bcl-2/Bax↑ Caspase-3, Caspase-9 ↓	[61]
	Saponins from PMR	In vivo	Myocardium ischemia/Reperfusion injury rats	100 and 200 mg/kg gavage	SOD, GSH-Px, CAT enzyme activity ↑SOD/GPX/CAT response system gene expression levels, Nrf2 ↑	[62]

	Saponins from PMR	In vivo	Myocardial infarction in rats	100 and 200 mg/kg gavage	TNF-α, IL-1β, IL-6, IL-8, pIκB-α, NF-κBp65 ↓SIRT1 ↑	[67]
	Saponins from PMR	In vivo	Myocardium ischemia/Reperfusion injury rats	50, 100 and 200 mg/kg gavage	MCP-1, MIF, TNF-α ↓	[64]
	Total saponins from PMR	In vitro	H_2O_2 induced cardiomyocyte injury rats	100 and 200 μg/mL	SOD, CAT, GSH-Px ↑MCP-1, TNF-α, TGF-β1, NF-κBp65 ↓	[65]
	Polysaccharides Extracted from PMR	In vivo	Adriamycin induced chronic congestive heart failure rats	97 mg/kg	MDA, NO levels and CK, NOS activities ↓	[68]
Ischemic brain injury	Alcohol extractive of PMR	In vivo	Middle cerebral artery occlusion(MCAO) mice	2.5, 5.0 or 10.0 g/kg gavage	GSH-PX, SOD, Na^+-K^+-ATP, Ca^{2+}-Mg^{2+}-ATP ↑ LD, MDA ↓	[76]
	Ginsenoside Rg_1 (**46**)	In vitro	OGD induced SK-N-SH cells	6.25, 12.5, 25 μM	PGC1-α, NRF-1, TFAM-1 autophagy-related proteins ↑	[72]
	Notoginsenoside R_1 (**35**)	In vitro and vivo	OGD/R induced primary cortical neurons and CCL induced 7-day-old postnatal SD rats	10 μmol/L and 15 mg/kg	PI3K-Akt-mTOR/JNK signaling pathways	[75]
	Ginsenoside Rg_1 (**46**)	In vivo	HIBD 15-day SD rats prepared by Rice-Vannucci method	10 or 20 μg/g i.p.	-	[74]

	Ginsenoside Rg_1 (**46**)	In vivo	HIBD Wistar male rats prepared by Rice-Vannucci method	10, 20 and 40 mg/kg i.p.	Bax/Bcl-2, cleaved cas9/cas9, cleaved cas3/cas3 protein expression levels ↓ IL-6, iNOS ↓ IL-4 ↑	[73]
	Alcohol extractive of PMR	In vivo	Middle cerebral artery occlusion (MCAO) mice	2.5 and 5.0 g/kg gavage	gene expression of SOD/GPX/CAT response system ↑	[77]
	Aqueous extract of PMR	In vivo	Middle cerebral artery occlusion (MCAO) mice	2.5, 5 and 10 g/kg gavage	TNF-α, IL-1β, NF-κB ↓	[78]
	Aqueous extract of PMR	In vivo	Middle cerebral artery occlusion (MCAO) reperfusion model mice	2.5, 5 and 10 g/kg gavage	SOD, GSH-PX, CAT enzyme activity ↑ XOD enzyme activity ↓ MDA ↓	[100]
	Saponins from PMR	In vivo	Cerebral ischemia-reperfusion model mice	100 or 200 mg/kg	PI3K/Akt signaling pathways and Inhibition of the mitochondria-mediated apoptosis pathway	[71]
	Saponins from PMR	In vivo	ischemia/reperfusion (CI/R) injury mice	50, 100 and 200 mg/kg	improving the Nrf2-mediated antioxidant response (Nrf2 and Bcl-2 ↑)	[101]
Antioxidant	Polysaccharides from PMR	In vitro	Superoxide anion, hydroxyl radical and ABTS radical scavenging assay	1~10 mg/mL	-	[79]
	Water extracts and ethyl acetate extracts of PMR	In vitro	Superoxide anion and hydroxyl radical scavenging assay	5 mg/mL and 2.5 mg/mL	-	[80]

	Aqueous extracts, saponins and polysaccharides from PMR	In vitro	Reduce iron, scavenge DPPH free radical, O^{2-} free radical assay, Cu^{2+}/H_2O_2 induced BSA injury and H_2O_2 induced RAW 264.7 cells	0.5~5 mg/mL, 0.5~5 mg/mL, 2 mg/mL, 1~10 mg/mL and 6.25~100 μg/mL	-	[81]
	Polysaccharides from PMR	In vitro	Scavenge DPPH free radical assay	0.5~10 mg/mL	-	[102]
Anti-inflammatory and analgesic effect	Chikusetsusaponin IVa (**9**)	In vivo	Collagen-induced arthritis mice	50 and 100 mg/kg	IL-6, TNF-α, IL-1β, IFN-γ ↓(JAK/STAT signaling pathway ↓)	[83]
	Ethanol extracts from PMR	In vivo	torsion body method, daubing xylene on ears of mice and letting arthrosis swelling with egg proteins	1.5, 3 and 6 g/kg gavage	-	[82]
	70% methanol extracts of PMR	In vitro	LPS induced RAW264.7 cells	0.02 and 0.2 mg/mL	NO, TNF-α, p-NF-κB、IκBα ↓(NF-κB ↓)	[86]
	70% methanol extracts of PMR	In vivo	xylene induced ear swelling in mice	200 and 400 mg/kg	-	[86]

	Aqueous extracts of PMR	In vivo	Xylene induced auricle tumefaction, carrageenan induced hind paws swelling, cotton induced granuloma mice and acetic acid writhing test and hot plate test	2.5, 5 and 10 g/kg gavage	-	[103]
	Saponins from PMR	In vitro	MRC-5 cells infected by HCMV	100, 200 and 400 μg/mL	TNF-α, IL-6 ↓ miR-216a ↑	[84]
	Saponins from PMR	In vitro	LPS induced rat astrocytes	50, 100 and 200 μg/mL	cleaved-caspase3, cleaved-caspase9, TNF-α, IL-6 ↓miR-325-3p ↑	[85]
Anticoagulant effect	70% methanol extracts of PMR	In vitro	anticoagulant activity assay in mice	0.5~50 mg/mL	-	[87]
	Yesanchinoside R_2 (**68**), Vinaginsenoside R_{13} (**81**), 3-*O*-[*β*-*D*-glucopyranosyl-(1→2)-*β*-*D*-(6′-*O*-ethyl)-glucuronopyranosyl]-oleanolic acid 28-*O*-*β*-*D*-glucopyranoside (**4**), Vinaginsenoside R_8 (**78**), Notoginsenoside E (**79**) and 6″-*O*-Acetylginsenoside Rb_1 (**55**)	In vitro	ADP induced platelet aggregation	IC_{50}=18.27, 11.34, 40.54, 25.18, 29.45 and 36.9 μmol/L	-	[11]
	Notoginsenoside E (**79**)	In vitro	AA induced platelet aggregation	IC_{50}=17.43 μmol/L	-	[11]

	(20*S*)-6-*O*-[*β*-*D*-glucopyranosyl-(1→2)-*β*-*D*-glucopyranosyl]-dammar-20,25-epoxy-3*β*,6*α*,12*β*,24*α*-tetraol (**90**) and 6-*O*-[*β*-*D*-glucopyranosyl-(1→2)-*β*-*D*-glucopyranosyl]-dammar-25(26)-ene-3*β*,6*α*,12*β*,20*S*,24*R*-pentaol (**63**)	In vitro	ADP induced platelet aggregation	IC_{50}=23.24 and 18.43 μmol/L	-	[89]
	6-*O*-[*β*-*D*-glucopyranosyl-(1→2)-*β*-*D*-glucopyranosyl]-dammar-25(26)-ene-3*β*,6*α*,12*β*,20*S*,24*R*-pentaol (**63**)	In vitro	AA induced platelet aggregation	IC_{50}=30.11 μmol/L	-	[89]
	60% Ethanol Extract of PMR	In vitro	anticoagulant activity assay in mice	0.5~50 mg/mL	-	[88]
Others	Extract of PMR	In vitro	Rat primary osteoblasts	300~500 μg/mL	OPG mRNA ↑RANKL mRNA ↓	[90]
	Aqueous extracts of PMR	In vivo	Anti-fatigue, low-temperature and hypoxia resistance tests in mice	8 g/kg	-	[91]
	Total saponins from the leaves of PMR	In vivo	Swimming, heat and hypoxia tolerance in mice	0.125~0.5 g/mL	-	[92]

	Aqueous extracts of PMR	In vivo	Cyclophosphamide-induced leukopenia in mice	0.625~2.5 g/kg gavage	-	[93]
	Crude extract of PMR	In vivo	CPX induced leukopenia mice	0.625, 1.25 and 2.5 g/kg	WBC, LY, PLT ↑	[31]
	Crude extract, total saponins and polysaccharides from PMR	In vivo	CPX and APH induced blood deficiency mice	0.8 or 1.6 g/kg, 75 or 150 mg/kg and 75 or 150 mg/kg	IL-3, IL-6, EPO, GM-CSF, M-CSF ↑	[31]
	Panaxjapyne A (**117**), Panaxjapyne C (**121**), (3*R*)-(–)-falcarinol (**118**), (3*S*,10*S*)-panaxydiol (**120**), vanillin (**108**), *β*-sitosteryl *β-D*-glucoside (**104**)	In vitro	α-Glucosidase inhibitory assay	IC_{50}=71.82, 175.42, 67.78, 22.21, 217.68 and 75.00 μM	-	[28]

"-"means not mentioned.

5. Clinical application

As a traditional Chinese herbal medicine, *Panacis majoris* Rhizoma (PMR), also known as *Zhu zi shen*, is known for its effects in promoting blood circulation, relieving blood stasis, reducing swelling, and alleviating pain. It has a long history of clinical use, and in recent years, certain formulations have been developed. For example, the Tong Shu Capsules produced by Yunnan Institute of Pharmaceutical Research consist of PMR, Sanqi (roots of *Panax notoginseng*), and Qiyelian (roots or stem leaves of *Schefflera arboricola* Hayata) among other traditional Chinese herbs. These capsules are known for their effectiveness in reducing swelling, relieving pain, and promoting blood circulation. They are used to treat various types of pain and arthritis.

In a study by *Ding et al.*, 43 patients with shoulder periarthritis underwent a month-long treatment combining massage therapy and Tong Shu Capsules. The treatment group exhibited an effectiveness rate of 90.7%. Notably, when compared to the use of massage therapy alone, the combination with Tong Shu Capsules resulted in an almost 20% increase in the effectiveness rate [104]. Yang *et al*. treated 120 patients with rheumatoid arthritis using Tong Shu Capsules in combination with a topical analgesic ointment. Out of these patients, 16 were cured, and 90 showed improvement, resulting in an overall effectiveness rate of 87% [105]. Liang *et al*. treated 56 patients with knee osteoarthritis using TongShu Capsules in combination with intra-articular injections. The treatment was conducted in cycles of 5 weeks each, and after 2 years, the overall effectiveness rate was 96.43% [106]. Gan *et al*. treated 30 patients with lumbar disc herniation using Tong Shu Capsules in combination with acupuncture. The overall effectiveness rate in the treatment group was 96.67% [107], Sun *et al*. treated 54 cases of soft tissue injuries with Tong Shu Capsules, and after 21 days, the effectiveness rate reached 96.43% [108]. Xiao *et al*. treated 100 cases of lower back and leg pain with Tong Shu Capsules in combination with Shu Jing Huo Luo Tang, achieving an overall effective rate of 96% [109]. Tong Shu Capsules have also been used to treat cervical headaches with significant effectiveness. Yang *et al*. used Tong Shu Capsules in combination with ethyl aminobenzoate hydrochloride to treat 56 cases of cervical headache, achieving an effective rate of 98.21% [110].

Additionally, PMR has shown clinical efficacy in treating leukopenia. The Yang Zheng Sheng Bai Capsule, which contains PMR along with other Chinese herbal ingredients like *Huang qi* and *Gou qi zi*, is known for its effects in replenishing qi and nourishing blood, strengthening the body's vitality, and improving white blood cell counts by nourishing the spleen. Zhen *et al*. treated 98 cancer patients with leukopenia following chemotherapy using Yang Zheng Sheng Bai Capsule, achieving an overall effective rate of 81.6% [111]. This treatment also improved symptoms such as dizziness, fatigue, and poor appetite. Yang Zheng Sheng Bai Decoction was also found to be effective, with a 94% effective rate in treating 50 chemotherapy patients [112]. In a study by Xiong, Zhuzi Shen tablets were utilized to treat 30 patients with leukopenia, resulting in an 80% effective rate. Notably, supplementary administration of vitamin B6 was found to alleviate gastrointestinal symptoms in these patients [113].

Additionally, the leaves of PMR, referred to as *Han Zhong Shen Ye*, are commonly employed to make tea, with the belief that consuming this tea contributes to the protection of vocal cords and provides nourishment and strength to the body.

This article has collected folk remedies and commercially available medications containing PMR, offering a summarized overview of their clinical applications. Refer to Table 4 for details.

Table 4. Chinese patent medicines or preparations containing PMR

Prescription Name	Prescription composition	Functions and Treatments
Tongshu Capsules	Qi ye lian, Deng zhan xi xin, Yu pu tao gen, San qi, Zhu zi shen, Zhi zi, Chong lou, Gan cao	Traumatic injury Rheumatic joint pain Scapulohumeral periarthritis Gouty joint pain Lobular hyperplasia of the mammary glands
Panlongqi Tablets	Pan long qi, Zhuang jin dan, Wu jia pi, Du zhong, Dang gui, Zhu zi shen, Qing wa qi, Guo shan long, Qin jiao, Mu xiang, Zu si ma, Luo shi teng, Chuan wu, Bai mao qi, Tie bang chui, Cao wu, Lao shu qi, Zhi zhu liao, Hong hua, Mo yao, Zhu gen qi, Xie cao, Shen jin cao, Niu xi, Dan shen, Yang jiao qi, Ba li ma, Chong lou, Ru xiang	Rheumatoid arthritis Lumbar muscle strain Fracture Soft tissue injury
Yangzhengshengbai Decoction	Zhu zi shen, Huang jing, Tai zi shen, Huang qi, Nv zhen zi, Dang gui, Hei bu gu zhi	Leukopenia
Zhuzishen Pipaye Decoction	Zhu zi shen, Pi pa ye, Bai mao gen, Xian he cao, Bei mu	Hemoptysis
Zhuzishen Powder	Zhu zi shen	Hemorrhage Infantile convulsion
Zhuzishen Baisanqi Decoction	Zhu zi shen, Bai san qi, Di yu	Dysfunctional uterine bleeding
Zhuzishen Huangqi Decoction	Zhu zi shen, Huang qi, Dang gui	Deficiency of vital energy

6. Discussion

This review summarizes the research progress of PMR in botany, phytochemistry, pharmacological effects, and clinical applications. A total of 123 compounds have been isolated and identified from PMR. Modern pharmacological studies indicate that it primarily exhibits pharmacological effects such as hepatoprotection, anticancer activity, cardioprotection, protection against ischemic brain injury, antioxidation, anti-inflammation, analgesia, and anticoagulation. To date, all PMR review articles lack detailed information on its chemical structure, and pathway targets associated with its pharmacological effects, and fail to provide a comprehensive summary of its clinical applications; this paper refines this information and makes sensible suggestions. Additionally, no review articles on PMR have been published in English databases. Based on the content of its research, the following aspects need to be addressed in its further development and application.

The first, according to the compilation, a total of 123 compounds have been isolated from PMR. Among them, 23 compounds have been identified from *Panax japonicus* var. *bipinnatifidus*, and up to 117 compounds have been identified from *Panax japonicus* var. *major*. Additionally, only 37 compounds have been identified from PMR leaves. Based on Figure 10, it is observed that research on PMR primarily focuses on its roots and rhizomes, while the above-ground parts of PMR and *Panax japonicus* var. *bipinnatifidus* have not received comprehensive study.

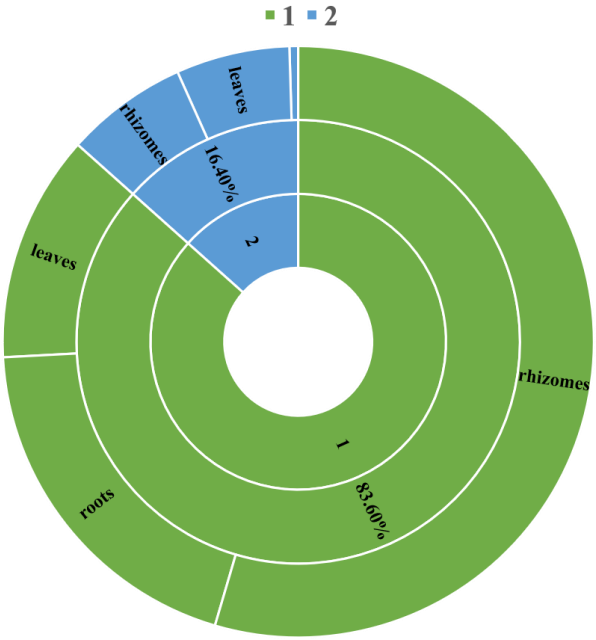
Second, triterpenoid saponins, with a total of 100 compounds belonging to this structural class, are the main active components in PMR. Notably, pentacyclic triterpenoids were not isolated from the above-ground parts of PMR, and the reasons for this structural difference between above-ground and underground parts seem worth exploring, possibly within the context of plant metabolic pathways. Additionally, all saponins mainly consist of 1-2 sugar units, with only one trisaccharide glycoside, stipuleanoside R_2 (**23**), isolated. Interestingly, the number of sugar units, hydroxyl groups, and sugar content is positively correlated with the saponin antiplatelet aggregation activity [7]. Exploring triterpenoid saponins with more sugar substituents may be another avenue to discover active monomers. Furthermore, besides triterpenoid saponins considered as the major active components, polyacetylene compounds in PMR also exhibit promising activity, indicating their potential as precursors for new drug development.

Third, PMR belongs to the *Panax* genus, and most of its saponins are Ginsenosides, which are also found in ginseng and are used as a substitute for ginseng in clinical practice. However, Majorosides in PMR are unique components not found in other Panax species. Further research into Majorosides could lead to better differentiation and identification of counterfeit products. Additionally, during our literature compilation, we noticed that some scholars often confuse PMR with PJR (*Panacis Japonici* Rhizoma), which is detrimental to botanical taxonomy and subsequent phytochemical studies. Therefore, in-depth research into characteristic components is expected to better address this issue.

Fourth, the traditional medicinal parts of PMR are the roots and rhizomes, and the development of its above-ground parts is still not mature enough. According to its chemical composition analysis and isolation results, the above-ground parts of PMR also contain active ingredients. Moreover, there is a folk habit of brewing PMR leaves as tea, which has the effect of protecting the vocal cords. To utilize resources rationally and avoid waste, research on PMR leaves deserves attention.

Fifth, PMR is widely used in folk medicine, but its formulation development efforts are still insufficient. According to current information, there are relatively few types of PMR-based drugs available on the market, mainly focused on treating conditions such as pain and arthritis. It has not been well utilized for developing formulations with broader therapeutic effects. Additionally, the development of PMR as a dietary supplement may greatly leverage its resources.

Finally, PMR is a valuable plant resource worthy of further development. The content summarized in this article serves as a tool for professionals in the field to gain an understanding of its current status and to explore subsequent development methods and research directions.



1. *Panax japonicus* C. A. Mey. var. *major* (Burk.) C. Y. Wu et K. M. Feng
2. *Panax japonicus* C. A. Mey. var. *bipinnatifidus* (Seem.) C. Y. Wu et K. M. Feng

Figure 10. Distribution of compounds in PMR

7. Conclusion

PMR is a widely used traditional Chinese medicine with a history of extensive applications in both traditional and folk medicine for the treatment of various ailments. This article provides a comprehensive review of its primary chemical constituents, including triterpene saponins, as well as trace amounts of flavonoids, aromatic hydrocarbons, steroids, and alkynes. Triterpene saponins are considered the most important active compounds in PMR and have been extensively studied. Modern pharmacological research has shown that compounds isolated from PMR and its extracts exhibit pharmacological effects such as hepatoprotection, anticancer activity, cardioprotection, neuroprotection against ischemic brain injury, antioxidation, anti-inflammation, analgesia, and anticoagulation. In summary, PMR is a traditional Chinese medicine with a long history of use, and it is essential to provide a comprehensive review to facilitate its broader development.

Author contributions

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Competing Interests

The authors declare that there is no conflict of interest.

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