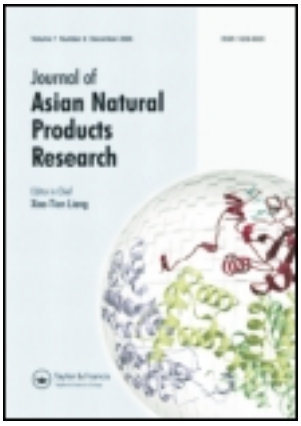

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Phytochemicals and bioactivities of *Paris* species

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Phytochemicals and bioactivities of *Paris* species

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The plants of genus *Paris*, as important Chinese traditional herbs, have been studied from phytochemicals and pharmacological viewpoints for decades, which resulted in the discovery of scores of secondary metabolites with various kinds of bioactivities. This article summarizes the research progress of the genus *Paris* in the phytochemical and pharmacological respects.

Keywords: *Paris*; phytochemicals; bioactivities

1. Introduction

The genus *Paris* (family: Liliaceae) comprises about 24 species, which are distributed mainly in the tropics and temperate latitudes of Eurasia, such as Bhutan, China, India, Japan, Korea, Laos, Mongolia, Myanmar, Nepal, Russia, Sikkim, Thailand, Vietnam, and Europe. There are 22 species in China, of which 12 species are endemic. The rhizomes of many species are used medicinally in China [1]. *Paris polyphylla* Smith var. *yunnanensis* (Franch.) Hand.-Mazz. (PPY) and *P. polyphylla* Smith var. *chinensis* (Franch.) Hara (PPC) were documented in the 'Chinese Pharmacopoeia' (2010 edition). Their dried rhizomes are the main resource of *Paris* [2]. Rhizoma Paridis (RP) ('Chonglou' in Chinese) was first recorded in 'Shennong Bencao' named as Zao Xiu. It appeared with the same time in Li Shizhen's 'Bencao Gangmu.' The dried RP has been used to treat fractures, parotitis, hemostasis, snakebite, and abscess in folk medicine for a long time. It is the main raw material for several Chinese patent drugs such as 'Yunnan Baiyao', 'Jidesheng Sheyaopian', 'Gong Xue Ning', and so on. It also plays an important role in the medicinal development for anti-tumor, immunity adjustment, analgesia, and anti-inflammation [3]. The history of phytochemical and pharmacological investigations on this genus goes back to the 1960s [4,5]. For decades, much attention has been paid to the applications of the *Paris* species in traditional medicine and its significant pharmacological activities. In particular, due to the rich resources especially in the southwest of China, Chinese scientists have been playing an important role in the area of study on *Paris*. Many valuable conclusions were reported in China. It is reported that RP saponins are the main and the active components in RP. About 70 steroidal saponins have been isolated from 22 species of this genus, which is about 80% of total compounds isolated from *Paris*. There are also phytoecdysones, phytosterols, and flavones found in the plants of *Paris*.

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To make a comprehensive and systematic understanding of this genus, we decided to review the state of the art in the study on bioactive chemical composition from *Paris*.

2. Chemical constituents

From 1960 to 2010, more than 90 secondary metabolites have been isolated from the genus *Paris*, including steroidal saponins, phytoecdysones, phytosterols, flavones, and some other compounds. Their structures are shown in Figures 1–4. As mentioned above, steroidal saponins are the predominant constituents within the genus *Paris*.

2.1 Steroidal saponins

Since 1962, scientists have isolated about 70 steroidal saponins from 22 species of *Paris* [6]. Their aglycons are mainly diosgenin and pennogenin. Moreover, there are also 13 types of aglycons, such as 24-hydroxy pennogenin, 27-hydroxy pennogenin, 23,27-dihydroxy pennogenin, 25*S*-isonuatigenin, nuatigenin, and C-21 steroidal saponins. The linkage sites of the sugar moieties in most of these compounds are at C-3 of their aglycones. The sugar residues include glucose, rhamnose, and arabinose. It is also found that the glucose is at C-26 and the galactose is at C-24. Recently, a steroidal saponin with the sugar moiety linked at C-1 has been reported in *Paris* sp. [7].

2.1.1 Diosgenin and pennogenin saponins

Diosgenin and pennogenin saponins are the major members of paris saponin. In view of the structural feature, they are composed of the aglycons, diosgenin and pennogenin, as well as the sugar residues at C-3. The units of the sugar residues contain D-glucose, L-rhamnose, and L-arabinose. As far as we know, 22 diosgenin saponins and 12 pennogenin saponins formed by these three sugars have been found from *Paris* (Tables 1 and 2).

(25*R*)-Spirost-5-en-3β,12α-diol-3-*O*-α-L-rhamnopyranosyl-(1 → 4)-α-L-rhamnopyranosyl-(1 → 4)-[α-L-rhamnopyranosyl-(1 → 2)]-β-D-glucopyranoside (**20**), (25*R*)-spirost-5-en-3β,7β-diol-3-*O*-α-L-arabinofuranosyl-(1 → 4)-[α-L-rhamnopyranosyl-(1 → 2)]-β-D-glucopyranoside (**16**), and its stereomer (25*R*)-spirost-5-en-3β,7α-diol-3-*O*-α-L-arabinofuranosyl-(1 → 4)-[α-L-rhamnopyranosyl-(1 → 2)]-β-D-glucopyranoside (**17**) were three diosgenin saponins found from PPY by Zhao [8] and named parisyunnanoside C, parisyunnanoside D, and parisyunnanoside E, respectively. Reclinatoside (**21**), loureiroside (**22**), and compound **24** were also isolated from PPY by Zhao [8]. Compound **28** was found in the aerial part of PPY by Chen *et al.* in 1990 and Wang in 2007 found it in the rhizome of this plant [9,10]. Compound **30** was a pennogenin saponin isolated from *P. axialis* by Chen and Zhou [11].

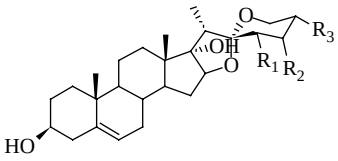
2.1.2 Prototype saponins

Sixteen prototype saponins were found in *Paris*. The differences between them are the substituent groups at C_{17} and C_{20} (Table 3). Parisyunnanoside A (**38**) and Th (**39**) were isolated from PPY by Zhao [8].

2.1.3 Other type saponins

Besides the above-mentioned saponins, there are also other types of saponins in plants of *Paris*, mainly containing various hydroxylated pennogenin, nuatigenin, isonuatigenin, pregnenolone, etc. as aglycones (Figure 1 and Table 4).

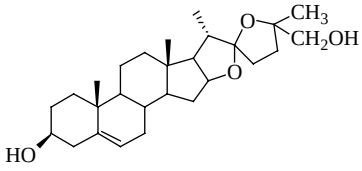
Compounds **54** and **52**, 24-hydroxy pennogenin saponins were discovered from *P. axialis* in 1984 and 1987. Compound **55**, a 27-hydroxy pennogenin saponin, and compound **57**, a 23,27-dihydroxy pennogenin saponin, were isolated from PPY in 1992. Compounds **61** and **63** were



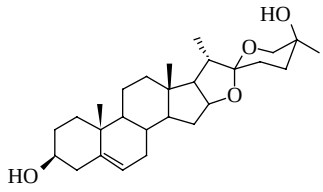
I R_1 = H, R_2 = OH, R_3 = CH_3, 24-hydroxy pennogenin

II R_1 = H, R_2 = H, R_3 = CH_2OH, 27-hydroxy pennogenin

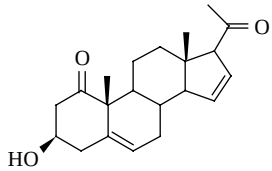
III R_1 = OH, R_2 = H, R_3 = CH_2OH, 23, 27-dihydroxy pennogenin



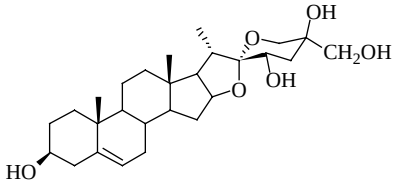
IV Nuatigenin



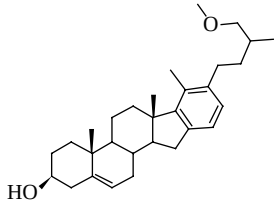
V Isonuatigenin



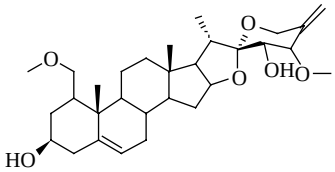
VI Pregna-5,16-dinen-3β-ol-20-one



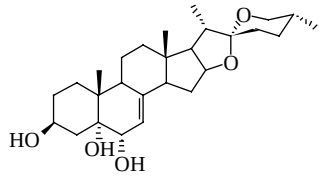
VII (23*S*,25*S*)-3β,23,27-Trihydroxy spirost-5-en



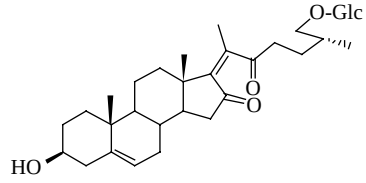
VIII Chacotriosyl



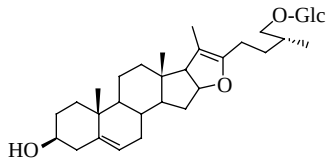
IX (23*S*,24*S*)-Spirostane-5,25-dien-1β,3β,23,24-tetrol



X 3β, 5α, 6α-Trihydroxy-7(8)-en-isospirostanol



XI (25*R*)-16,22-Dione-5,17-dien-furostan-3β,26-diol



XII Pseudoprotodioscin

Figure 1. Structures of other type saponins in *Paris*.

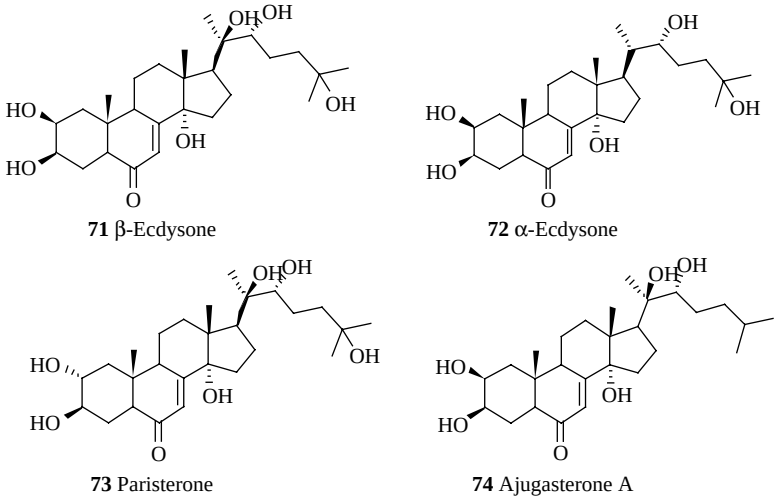


Figure 2. Structures of phytoecdysones in *Paris*.

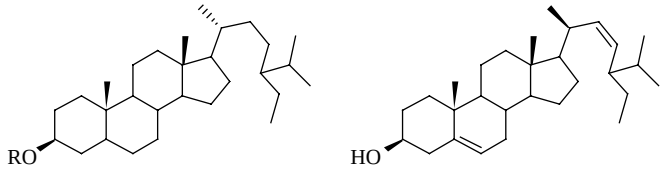
discovered from the aerial part of PPY by Chen [10]. (23*S*,25*S*)-3β,23,27-Trihydroxyspirost-5-en-3-*O*-β-D-glucopyranosyl-(1 → 6)-β-D-glucopyranoside (**64**) was a (23*S*,25*S*)-3β, 23,27-trihydroxy spirost-5-en type saponin found from PPY in 2006 by Liu *et al.* [12]. Parispolyside E (**65**) was confirmed as a steroidal glycoside, possessing a homo-cholestane skeleton with an aromatized ring E by Huang *et al.* [13] from PPC. Parispolyside A (**66**) was isolated from PPY as a steroidal saponin by Xu *et al.* [14]. Parisvietnaside A (**67**) was a spirostanol saponin isolated from *P. vietnamensis* by Huang *et al.* [15]. Parisyunnanoside B (**68**), pseudoproto-Pb (**69**), and parisyunnanoside F (**70**) were three steroidal saponins separated from PPY by Zhao [8].

2.2 Phytoecdysones

Up to now, β-ecdysone has been isolated or determined from PPY, *P. quadrifolia*, and other 15 species. α-Ecdysone and ajugasterone A were found from *P. verticillata*, and paristerone was isolated from PPC [8,9,16–21] (Figure 2).

2.3 Phytosterols

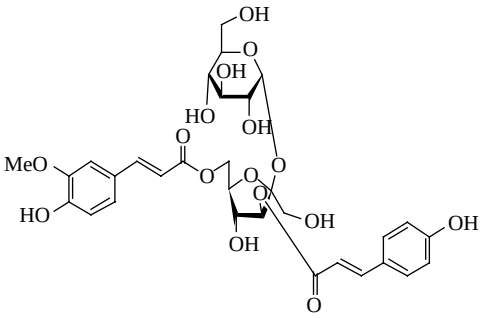
Phytosterols mainly contain stigmasterol, β-sitosterol, and their derivatives in *Paris* [9,19,22] (Figure 3). Daucosterol (**76**) was isolated from *P. delavayi* by Liu *et al.* [23].



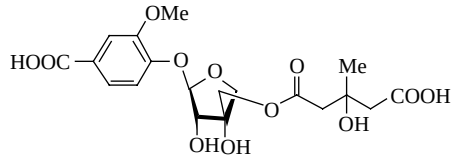
75 R = H β-sitosterol
76 R = glc Daucosterol

77 Stigmasterol

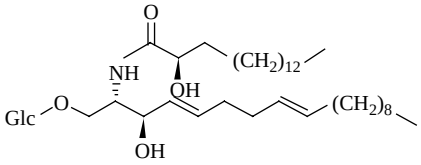
Figure 3. Structures of phytosterols in *Paris*.



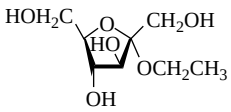
88 Parispolyside F



89 Parispolyside G



90 1-*O*-(β-D-glucopyranosyl)-(2*S*, 3*S*, 4*E*, 8*E*)-2-[(2′*R*)-2′-hydroxy-hexadecanoylamino]-4(*E*), 8(*E*)-octadecadiene-1, 3-diol



91 Ethyl-α-D-fructofuranoside

Figure 4. Structures of compounds **88**–**91**.

2.4 Flavones

Six flavonoid glycosides with kaempferol as aglycon, three with isorhamnetin as aglycon, and one with quercetin were isolated from PPY and other species, and they are kaempferol-3-*O*-α-L-glucopyranosyl-(1 → 2)-β-D-glucopyranoside (**78**), kaempferol-3-*O*-β-D-glucopyranosyl-(1 → 4)-*β*-D-glucopyranoside (**79**), 7-*O*-β-D-glucopyranosyl-kaempferol-3-*O*-α-L-glucopyranosyl-(1 → 2)-β-D-glucopyranoside (**80**), kaempferol-3-*O*-β-D-glucopyranosyl-(1 → 6)-β-D-glucopyranoside (**81**), 7-*O*-*α*-L-rhamnopyranosyl-kaempferol-3-*O*-β-D-glucopyranosyl-(1 → 6)-β-D-glucopyranosi-de (**82**), isorhamnetin-3-*O*-β-gentiobioside (**83**), isorhamnetin-3-*O*-β-D-rutinoside (**84**), isorhamnetin-3-*O*-β-D-glucopyranoside (**85**), quercetin (**86**), and kaempferol (**87**) [9,16,18,22] (Table 5). Most of them are discovered in the form of *O*-glycosides. Compounds **83**, **84**, and **85** are flavonoid glycosides of isorhamnetin discovered from the genus *Paris* by Wang [9]. Compound **86** was separated from *P. mairei* by Huang *et al.* [16].

2.5 Others

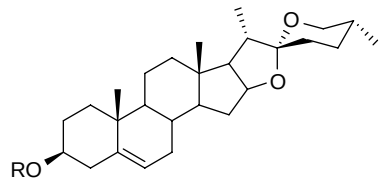
A phenylpropanoid glycoside parispolyside F (**88**) and a ramification of phenolic glycoside parispolyside G (**89**) together with a sphingolipid (**90**) and a glucoside **91** were isolated from PPY by Wang [9] (Figure 4).

3. Bioactivities

3.1 Stypticity

It was reported that compound **28** had stypticity effect in 1990 [10]. *In vivo*, the methanol extract of PPY, PPC, and other four species at a dose of 6 g/kg showed

Table 1. Diosgenin saponins in plants of *Paris*.



No.	Name	R	References
1	Trillin	3-*O*-Glc	[7,8,12,45,46]
2		3-*O*-Ara (1 → 4)-Glc	[7–9,12,15,16,47–49]
3	*Paris* V	3-*O*-Rha (1 → 2)-Glc	[3,7–9,12,15,23,45,50,51]
4	Polyphyllin C	3-*O*-Rha (1 → 3)-Glc	[3,52]
5	Prosapogenin B	3-*O*-Rha (1 → 4)-Glc	[3,8,46]
6	Polyphyllin D	3-*O*-Ara (1 → 4)[Rha (1 → 2)]-Glc	[3,9,15–18,45,50,51]
7		3-*O*-Rha (1 → 3)[Ara (1 → 4)]-Glc	[3,52]
8		3-*O*-Rha (1 → 4)[Ara (1 → 3)]-Glc	[3,53]
9	Parisaponin III	3-*O*-Rha (1 → 4)[Rha (1 → 2)]-Glc	[3,9,17,19,23,48]
10	Gracillin	3-*O*-Rha (1 → 2)[Glc (1 → 3)]-Glc	[3,8,11,18,23,45]
11	Parisaponin II	3-*O*-Rha (1 → 4)-Rha (1 → 4) [Rha (1 → 2)]-Glc	[3,8,9,17,18,23,45,48,54,55]
12	Polyphyllin E	3-*O*-Rha (1 → 2)-Rha (1 → 4) [Rha (1 → 3)]-Glc	[3,15,52]
13	Polyphyllin F	3-*O*-Rha (1 → 4) [Rha (1 → 3)] [Glc (1 → 2)]-Rha	[3,52]
14		3-*O*-Glc (1 → 3)-Rha (1 → 4) [Rha (1 → 3)]-Glc	[3,56]
15	3β,23,27-Triol	3-*O*-Glc (1 → 6)-Glc	[3]
16	Parisyunnanoside D 3β,7β-diol	3-*O*-Ara (1 → 4)[Rha (1 → 2)]-Glc	[3,8,57]
17	Parisyunnanoside E 3β,7α-diol	3-*O*-Ara (1 → 4)[Rha (1 → 2)]-Glc	[3,8]
18		3-*O*-Rha (1 → 2)[Ara (1 → 3)]-Glc	[58]
19		3-*O*-Glc (1 → 3)[Rha (1 → 2)]-Glc	[8,15,57]
20	Parisyunnanoside C 12α-OH	3-*O*-Rha (1 → 4)-Rha (1 → 4) [Rha (1 → 2)]-Glc	[8]
21	Reclinatoside	3-*O*-Rha (1 → 5)-Ara (1 → 4) [Rha (1 → 2)]-Glc	[8]
22	Loureiroside	3-*O*-Glc (1 → 5)-Ara (1 → 4) [Rha (1 → 2)]-Glc	[8]

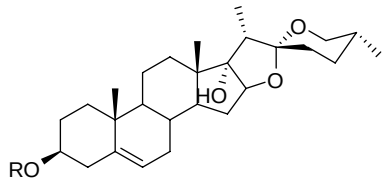
strong stypticity in mice [19]. Some saponin monomers can shorten coagulation time in mice and plasma recalcification time in rat, and also can induce rabbit aortic strip striction and reduce the capillary vessel permeability of mice abdominal cavity. Pennogenin saponin whose sugar chain is trisaccharide at low concentration *in vivo* presents strong stypticity. Hemostasis is a complex process that involves neurohumor, vasoconstriction, platelet aggregation, and clotting taking part in. However, it still needs further study on the exact action of RP crude drugs [24].

3.2 Cytotoxicity

3.2.1 Extracts

Both water and methanol extracts of RP can inhibit Ehrlich ascites tumor (EAC) *in vivo* [25]. *In vitro*, the methanol extract

Table 2. Pennogenin saponins in plants of *Paris*.



No.	Name	*R*	References
23		3-*O*-Glc	[3,45,50]
24		3-*O*-Ara (1 → 4)-Glc	[9,15,16,45,47–49]
25	Tb	3-*O*-Rha (1 → 2)-Glc	[3,9,15,22,45,51,59,60]
26		3-*O*-Rha (1 → 4)-Glc	[3,20]
27	Chonglouoside H	3-*O*-Rha (1 → 2) [Ara (1 → 4)]-Glc	[3,8,12,15–17,20, 23,45,50,51]
28		3-*O*-Rha (1 → 2) [Rha (1 → 4)]-Glc	[3,9,10]
29		3-*O*-Rha (1 → 4)-Rha (1 → 4)-Glc	[3,50]
30		3-*O*-Rha (1 → 2) [Glc (1 → 3)]-Glc	[3,8,11,15,50]
31		3-*O*-Rha (1 → 4)-Rha (1 → 3) [Rha (1 → 2)]-Glc	[3,42]
32	Tg	3-*O*-Rha (1 → 4)-Rha (1 → 4) [Rha (1 → 2)]-Glc	[3,9,12,15,16,18,20, 22,23,49,60,61]
33	Polyphylloside III 27-ol	3-*O*-Rha (1 → 4)-Rha (1 → 4) [Rha (1 → 2)]-Glc	[3]
34	Polyphylloside IV 23β,27-diol	3-*O*-Rha (1 → 4)-Rha (1 → 4) [Rha (1 → 2)]-Glc	[3]

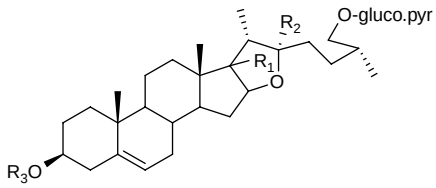
can inhibit Hela tumor. To fibroblastoma L-929 tumor, the methanol extract has stronger inhibiting ratio than the water extract, but the latter has lesser cytotoxic activity [24]. Ji *et al.* [26] proved that the water and methanol extracts of RP had inhibition effect on cells of human lung A-549, breast cancer MCF-7, colon carcinoma HT-29, renal adenocarcinoma A-496, pancreatic cancer PACA-2, and prostatic cancer PC-3. Li *et al.* [27] proved that paridis extract might inhibit the mitosis of tumor cells by inhibiting the synthesis of protein and DNA and then inhibit the proliferation of colon cancer SW480 cells, and the inhibitory effect might be stem cell factor independent. Hu *et al.* [28] proved that the alcohol extract of RP could suppress the tumor angiogenesis *in vitro*. The mechanism might be related to the inhibition of proliferation, migration, DNA synthesis of endothelial cell, and formation of canaliculization.

3.2.2 Saponins

Polyphylla saponins are the main active anti-tumor components in *Paris*. *In vitro*, polyphylla saponins have obvious inhibition effect mainly through inhibiting DNA synthesis on EAC, cervical carcinoma U_{14}, RS_{615}, mice sarcoma S_{180}, ascitic hepatoma (Hep), and mice liver cancer H_{22}. Additionally, parisaponins I and II possess strong cytotoxicity, the 50% effective dose (ED_{50}) to leukemia P_{388}, L_{1210}, and nasopharyngeal carcinoma KB cell lines are 0.94, 0.14, 0.16 and 0.22, 0.43, 0.029 μg/ml, respectively [29].

Rhizoma Paridis total saponin (RPTS) has effect on the growth of animal transplantable carcinomas and biosynthesis of nucleic acid. Detected by cell

Table 3. Prototype saponins in plants of *Paris*.



No.	Name	R_1	R_2	R_3	References
35		OH	OCH_3	3-*O*-Rha (1 → 2) [Ara (1 → 4)]-Glc	[3,11]
36		OH	OCH_3	3-*O*-Rha (1 → 2) [Glc (1 → 3)]-Glc	[3,54]
37	Methyl-Th	OH	OCH_3	3-*O*-Rha (1 → 4)-Rha (1 → 4) [Rha (1 → 2)]-Glc	[3,11]
38	Parisyunnanoside A	OH	OH	3-*O*-Rha (1 → 2) [Ara (1 → 4)]-Glc	[3,8]
39	Th	OH	OH	3-*O*-Rha (1 → 4)-Rha (1 → 4) [Rha (1 → 2)]-Glc	[3,8]
40		H	OCH_3	3-*O*-Rha (1 → 3) [Ara (1 → 4)]-Glc	[3,54]
41	Polyphyllin H	H	OCH_3	3-*O*-Rha (1 → 2) [Ara (1 → 4)]-Glc	[3]
42	Methylprotodioscin	H	OCH_3	3-*O*-Rha (1 → 2) [Rha (1 → 4)]-Glc	[3]
43	Methylprotogracillin	H	OCH_3	3-*O*-Rha (1 → 2) [Glc (1 → 3)]-Glc	[3,54]
44	Methyldichotomin	H	OCH_3	3-*O*-Rha (1 → 4)-Rha (1 → 4) [Rha (1 → 2)]-Glc	[3]
45	Trigofoenoside A protobioside	H	OH	3-*O*-Rha (1 → 2)-Glc	[3,62]
46		H	OH	3-*O*-Rha (1 → 2) [Ara (1 → 3)]-Glc	[3,62]
47	Parisaponins I	H	OH	3-*O*-Rha (1 → 2) [Ara (1 → 4)]-Glc	[3,8]
48		H	OH	3-*O*-Rha (1 → 3) [Ara (1 → 4)]-Glc	[3,63]
49	Protogracillin	H	OH	3-*O*-Rha (1 → 2) [Glc (1 → 3)]-Glc	[3,8,62]
50	Dichotomin	H	OH	3-*O*-Rha (1 → 4)-Rha (1 → 4) [Rha (1 → 2)]-Glc	[3,8]

respiration method, it was found that RP had the inhibition ratio between 85–87% to separate spleen sarcoma, and 75–96% to undifferentiated sarcoma of ileocecus [24].

RPTS could inhibit the proliferation of Hep G2 cells. It not only induces the apoptosis of Hep G2 cells but also affects the cell cycle distribution. Its cytotoxicity might be related to the induction of apoptosis and arrest of S phase in the cell cycle. It might exert its inhibition effects on Hep G2 cells through regulating multiple proteins expression directly or indirectly, such as deoxyuridine triphosphate pyrophosphatase, heterogeneous nuclear ribonucleoprotein K, guanine monophosphate synthase, deoxyribonuclease gamma, and nucleoside diphosphate kinase A. These findings would offer valuable insights into the mechanism of anti-tumor effect affected by RPTS treatment in Hep G2 cells [30].

3.3 Sterilization and anti-inflammatory effect

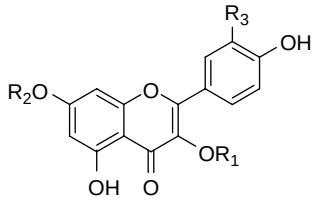
Experiments proved that chick embryos inoculated with the water and ethanol extracts of RP had strong inhibiting effect on type A and Asia type A flu virus. RP decoction has different degrees of inhibitory action on *Staphylococcus aureus*, *Hemolytic streptococci*, *Neisseria meningitides*, *Bacillus dysteriae*, *Salmonella typhi*, *Bacillus paratyphosus*, *Escherichia coli*, and *Pseudomonas aeruginosa*. Its ethanol extract at 7.8 mg/ml can kill

Table 4. Other type saponins in plants of *Paris*.

No.	Aglycon	Polypeptide part	References
51	I	3-*O*-Rha (1 → 3) [Rha (1 → 2)]-Glc	[11]
52	I	3-*O*-Rha (1 → 2) [Ara (1 → 4)]-Glc	[54]
53	I	3-*O*-Rha (1 → 4)-Rha (1 → 4) [Rha (1 → 2)]-Glc	[54]
54	I	3-*O*-Rha (1 → 2) [Glc (1 → 3)]-Glc	[45,54]
55	II		[64]
56	II	3-*O*-Rha (1 → 4)-Rha (1 → 4) [Rha (1 → 2)]-Glc	[65]
57	III		[64]
58	III	3-*O*-Rha (1 → 4)-Rha (1 → 4) [Rha (1 → 2)]-Glc	[65]
59	IV	26-*O*-Glc-3-*O*-Rha (1 → 4) [Rha (1 → 2)]-Glc	[66]
60	V	3-*O*-Rha (1 → 4) [Rha (1 → 2)]-Glc	[66]
61	VI	3-*O*-Rha (1 → 2) [Rha (1 → 4)]-Glc	[10]
62	VI	3-*O*-Rha (1 → 2) [Ara (1 → 4)]-Glc	[46]
63	VI	3-*O*-Rha (1 → 4)-Rha (1 → 4) [Rha (1 → 2)]-Glc	[10]
64	VII	3-*O*-Glc (1 → 6)-Glc	[12]
65	VIII	3-*O*-Ara (1 → 4) [Rha (1 → 2)]-Glc-26-*O*-Glc	[13]
66	IX	1-*O*-Xyl (1 → 6)-Glc (1 → 3)[Rha (1 → 2)]-Glc-24-*O*-Gal	[14]
67	X	3-*O*-Glc (1 → 3)- [Rha (1 → 2)]-Glc	[8,15]
68	XI	3-*O*-Ara (1 → 4)-[Rha (1 → 2)]-Glc	[8]
69	XII	3-*O*-Rha (1 → 4)-Rha (1 → 4) [Rha (1 → 2)]-Glc	[8]
70	XII	3-*O*-Ara (1 → 4)-[Rha (1 → 2)]-Glc	[8]

Leptospira. However, its water extract at the same concentration did not show the effect. RP decoction has antagonism effect on the aseptic inflammation induced by dextran. Additionally, it has been proved that RP has strong anti-*Candida albicans* effect with minimum inhibitory concentration 1.5 mg/ml and anti-microbial potency 6.25 mg/ml [31]. Li *et al.* have proved that PPY could inhibit the growth of common oral pathogens *in vitro.* It showed that PPY could be used in the treatment or prevention of oral bacterial diseases [32]. RPTS can protect acute lung injury rats subjected to two-hit induced by multiple fractures and lipopolysaccharide (LPS) via decreasing concentrations of tumor necrosis factor (TNF)-α, interleukin (IL)-1β, and IL-6 in blood serum and inhibiting the lung inflammatory reactions [33]. RPTS also can reduce the levels of TNF-α, IL-1β, and IL-6 in the blood serum of rats subjected to multiple trauma [34]. The activity of TNF-α and IL-1β secretion in rat peritoneal macrophages induced by LPS and heat-inactivated *E. coli* strain could be inhibited by RPTS [35,36]. Parisaponin II could increase the level of transforming growth factor (TGF)-β and IL-10 in lupus nephritis patients. The range of increase was influenced by the quantities of the added cells [37].

Table 5. Flavones in plants of *Paris*.



No.	R_1	R_2	R_3
78	Glc-(1 → 2)-Rha	H	H
79	Glc-(1 → 4)-Glc	H	H
80	Glc-(1 → 2)-Rha	Glc	H
81	Glc-(1 → 6)-Glc	H	H
82	Glc-(1 → 6)-Glc	Rha	H
83	Glc-(1 → 6)-Glc	H	OCH_3
84	Glc-(1 → 2)-Rha	H	OCH_3
85	Glc	H	OCH_3
86	H	H	OH
87	H	H	H

3.4 Respiratory system

Both RP decoction and ethanol extracts at 15 g/kg intragastric (ig) have protective effect on the guinea pig with tracheospasm caused by histamine spray. Ethanol extract has stronger effect, and its saponin section only at 0.35 g/kg ig shows evident protective effect. RP decoction at 15 g/kg ig also can relieve cough in mice induced by sulfur dioxide [24].

3.5 Calm and analgesic effects

The methanol extract of PPY shows obvious calm and analgesic effects, and its potency is equivalent to diazepam, which supplies the material base and scientific proof for Chinese medicine RP treating epilepsy [38].

3.6 Cardiovascular action

Diosgenin saponins in the standard and low calcium substrates can promote the increase in cardiomyocyte throb number and cardiomyocyte ingesting calcium ion more evidently than pennogenyl saponins. It is proved that the water extract of RP can partly antagonize the death of mice induced by endothelin (ET), and also has endothelium-dependent vasodilatation function of rat aortic rings contraction *in vitro*. It is worth screening ET antagonist from the constituent of RP and opening up new approaches for prevention and cure of angiocardiopathy [24].

3.7 Immunoregulation effect

Paris saponins can lead mouse lymphopoiesis induced by concanavalin A in the mouse fibroblasts L-929 substrate and promote the proliferation of mouse granulocyte-macrophage colony-forming cells (GM-CFC) [24]. Parisaponin II is a strong immunomodulator. *In vivo*, it can increase natural killer activity of C_3H–HeN mice and induce information of interferon [39].

Polysaccharides of paris could promote the formation of antibody and serum immunoglobin G (IgG) and the proliferation of T and B lymphocytes. They could also increase serum complement C_3. It can be seen that polysaccharides of *Paris* possess notable immunological potentiation [40].

3.8 Inhibiting sperm activity

Seventy percent ethanol extract of RP could kill the sperm of rat at the effective concentration 3 and 1.5–3 mg/ml of mice [41]. *In vitro*, the extract of RP can kill sperm in rat at the lowest effective concentration 0.6% and human sperm at 1.2%. Rabbit vagina administer inhibition fertilizing experiment shows that 60% of amphigamy is inhibited by RP extract at the dose of 100 mg each rabbit. Therefore, it possesses evident sperm killing effect [24].

3.9 Gastrointestinal effect

Steroid saponins from PPY have protective effects on ethanol or indomethacin-induced gastric mucosa lesions in rats. The protective effect is the result of inducing organism to produce a series of endogenous molecules, which take part in protecting gastric mucosa, such as prostaglandins, nitric oxide, and sulfhydryl compounds [42].

3.10 Others

The activation of nuclear factor-kappa B p65 (NF-κB p65) may play an important role in the pathological lesion in the glomerulus of membranous nephropathy. The protective effects of RP on the kidneys of rats with membranous nephropathy are related to NF-κB inhibition [43].

4. Conclusions

Our interest has always been on searching for bioactive compounds from nature. Along with more and more important pharmacological activities reported about RP, the market demand of PPC and PPY

becomes larger and larger. However, the growth speed of the roots of RP is very slow, and the consumption level of RP is more than the amount of growth of the wild RP, which result in the wild resource that is drying up. Meanwhile, the leaves of RP grow very fast, and their mass growth is about seven to eight times as the roots every year. At present, the application of the aerial part of *Paris* is still rare. According to the statistics department, at least 3500 tons leaves of PPY were abandoned in Yunnan Province every year, which resulted in huge waste of resources [44]. As a result, it is important and meaningful to study the overground part of PPY and PPC.

Paris saponins are the primary active constituents in *Paris*, most of which have been proved to possess particular pharmacological activity. According to the previous study, it is found that different aglycons and glycosides have obviously different pharmacological activities. Further studying the pharmacological activity of single paris saponin and clarifying structure–activity relationship can supply reasonable foundation for clinical medication.

Acknowledgements

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