Journal of Pharmacy and Pharmacology, 2022, **74**, 646–659
https://doi.org/10.1093/jpp/rgab110
Review

JPP Journal of Pharmacy and Pharmacology

OXFORD

Review

Platycarya strobilacea Sieb. et Zucc.: a review of its traditional uses, botany, phytochemistry, pharmacology and toxicology

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Abstract

Objectives *Platycarya strobilacea* Sieb. et Zucc. is the dry infructescence of *P. strobilacea*, a Juglandaceae plant and is a traditional Chinese medicine with great development potential and utilization value. This study summarizes the research progress on the traditional uses, botany, phytochemistry, extraction methods, pharmacology and toxicology of *Platycarya strobilacea* Sieb. et Zucc., and provides potential therapeutic uses and drug development prospects for this plant.

Key findings Phytochemical studies showed that this plant mainly contains volatile constituents, phenols, terpenoids and a carbohydrate. The pharmacological activity of *Platycarya strobilacea* Sieb. et Zucc. includes antibacterial and anti-inflammatory effects, anti-tumour effects and antioxidant effects. This plant is especially effective in the treatment of allergic rhinitis and chronic sinusitis.

Summary In this review, the phytochemistry and pharmacological effects of *Platycarya strobilacea* Sieb. et Zucc. are described in detail, which will have guiding significance for the future development of this drug.

Keywords: *Platycarya strobilacea* Sieb. et Zucc.; traditional uses; botany; phytochemistry; pharmacology

Introduction

Platycarya strobilacea Sieb. et Zucc. (PSZ) is the dry infructescence of *P. strobilacea*, a Juglandaceae plant, which is distributed in East China, Central China, South China, Southwest China, Gansu and Shaanxi.[1] It has a pungent warm taste, and has the effects of relieving qi, dispelling wind, relieving swelling, pain, dryness, dampness and kill insects. It is mainly used to treat symptoms such as nasal abyss, chest distension, abdominal pain, carbuncle swelling, wet sores, muscle and bone pain.[1] PSZ is used as the main medicine in Xiangju tablets to treat allergic rhinitis and chronic sinusitis,[2, 3] and its decoction is generally used to treat rhinitis, sinusitis and acute upper respiratory tract infections.[4, 5] The known components of PSZ mainly include volatile constituents, phenols, terpenoids and a carbohydrate,[6–9] and has antibacterial, anti-inflammatory, anti-tumour, antioxidant, anti-virus and other pharmacological effects.[9, 10]

At present, research on PSZ is still in its infancy. There are few studies on its toxicology and pharmacokinetics, and the research direction of this plant in the future is unclear. Therefore, in this study, research progress on the traditional uses, botany, phytochemistry, extraction methods, pharmacology and toxicology of PSZ are reviewed and its development prospects are discussed. It is hoped that these findings will reflect the importance of PSZ, and provide some guidance for the future development of this plant (Figure 1).

Methods

To understand the present research progress on PSZ, articles related to the phytochemistry, extraction methods, pharmacology and toxicology of PSZ were collected from CNKI, Google Scholar, PubMed, Web of Science, SpringerLink, Wiley, Wanfang Database and Baidu Scholar. The information on botany and traditional uses was obtained from books such as *The Great Dictionary of Traditional Chinese Medicine*[1] and *A textual Research on the name and reality of plants*.[9] We used keywords to search for information related to PSZ on these websites, including botany, phytochemistry, extraction methods, pharmacology and toxicology. The search identified a total of 76 articles, most of which were related to phytochemistry and pharmacology.

Received: April 5, 2021. Editorial Acceptance: July 8, 2021

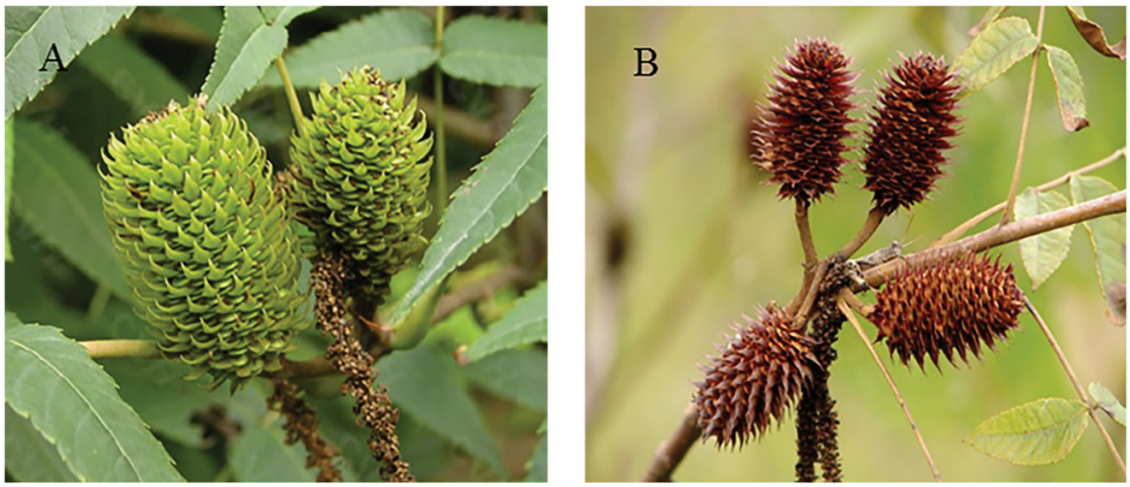


Figure 1 (A) the infructescence of immature *Platycarya strobilacea* Sieb. et Zucc.; (B) the infructescence of mature *Platycarya strobilacea* Sieb. et Zucc.

Results

Traditional Uses

PSZ has a wide range of biological and pharmacological activity and has a long history in China. Fossil records indicate that the genus was widely distributed in all continents of the Northern Hemisphere at the beginning of the Tertiary period, but after the Quaternary Ice Age, it became extinct in most places and survived only in East Asia, a plant that is endemic to East Asia.[11] The original PSZ plant was first included in the *A textual Research on the name and reality of plants*,[9] and was mainly used for relieving qi and dispersing phlegm. In *The Great Dictionary of Traditional Chinese Medicine*,[1] PSZ was used to treat internal injuries, chest distension, abdominal pain, muscle pain and eczema. In *Zhejiang Medicinal Flora*, it was mainly used to treat sore muscles and bones, toothache, chronic pain, headache and eczema.[12] In *Qinling Bashan Natural Flora*, PSZ was mainly used to treat sores, furuncles and swelling.[13] At present, PSZ is known to have antibacterial, anti-inflammatory, anti-tumour, antioxidant and antiviral effects.[9] In addition, PSZ has other pharmacological effects, such as anti-atherosclerosis,[14] anti-ageing[15] and antihypertensive sedation effects.[16]

China has a long history of treating rhinitis with PSZ and has achieved good results. In recent years, PSZ has been used as the main medicine in clinical Chinese medicine preparations, including Xiangju tablets, Xiangju granules, Xiangju capsules and PSZ syrup, among others. PSZ has the effects of clearing heat and detoxification, promoting blood circulation and removing blood stasis, reducing swelling and purging, clearing orifices and relieving pain. It has good therapeutic effects on acute and chronic rhinitis, sinusitis, cold and fever, nasal congestion and runny nose.[17] Of these preparations, Xiangju tablet is mainly effective in dispelling wind, clearing heat and dredging orifices and is used for the treatment of various types of nasal cavity disorders.[18] Pharmacological studies have proved that Xiangju tablets have anti-inflammatory, anti-allergic and analgesic effects, can inhibit the secretion of the nasal mucosa and restore the function of nasal mucosa to achieve a complete cure.[19] Xiangju tablet is suitable for all types of sinusitis based on syndrome differentiation in traditional Chinese medicine. In these syndromes, PSZ in the lung meridian wind-heat type, the lung-spleen-qi deficiency type and the gallbladder stagnation-heat type has outstanding curative effects, and the total effective rate is more than 80%[20] (Table 1).

Botany

Platycarya strobilacea is a deciduous shrub or small tree with a height of 5 to 20 m. Young branches are often covered with brown tomentose. They have alternate singular pinnate compound leaves, 15–30 cm long; 7–23 leaflets, ovate-lanceolate or oblong-lanceolate, 4–12 cm long, 2–4 cm wide and are broad-wedge-shaped or microcentric at the base. The shape is slightly slanted, the tip is tapered, the edges are heavily serrated and the underside has dense hairs when young.[13] The flowers are unisexual, monoecious, with spikes and corymbs; the top of the centre is often bisexual. The female infructescence is at the lower end and the male inflorescence is at the upper end. PSZ infructescence fall off after flowering, leaving only the female infructescence. The buds of the male flower are lanceolate, light yellow-green, without bracteoles and a perianth, with eight stamens; The female flower has one ovate-lanceolate bract, no bracteoles, with two tepals, one pistil, no style and a 2-lobed stigma.[1, 12, 13]

The pharmacognostic and microscopic characteristics of the infructescence of *P. strobilacea* were identified by a paraffin section method, powder slicing method and physicochemical identification method.[4] The results showed that PSZ was cone-shaped, oval-elliptic or oblong, about 2.5–5 cm long, 2–3 cm in diameter and yellowish-brown to brown in color. The bracts were persistent, woody, brown, lanceolate and hard, with fish-like scales arranged on the infructescence axis. The nutlets are flattened, narrowly winged on both sides, located under lanceolate bracts, the seeds are ovate, are the seed coat is membranous. According to microscopic observations of PSZ, the results showed that the bracts were hard, the inner and outer epidermis cells were thickened with a large number of parenchyma cells, no palisade tissue and numerous vascular bundles and fibres. The pith of the infructescence axis is obvious, the parenchyma cells contain calcium oxalate crystal clusters, the pith rays reach directly to the bracts and the vascular bundles are arranged in a circle. Most of the non-glandular hairs, parenchyma cells, calcium oxalate crystal clusters, stone cells with various properties, fibre bundles and ducts can be found in the powder of PSZ.[4]

Table 1 The traditional and clinical uses of *Platycarya strobilacea* Sieb. et Zucc. in China

Preparation name	Main compositions	Traditional and clinical uses	References
Xiangju tablets	Platycarya strobilacea Sieb. et Zucc. (HuaXiangShuGuoXu), Chrysanthemum indicum L. (YeJuHua), Astragali Radix (HuangQi), Magnolia denudata Desr. (XinYi), Saposhnikovia divaricata (Trucz.) Schischk. (FangFeng), Prunella vulgaris L (XiaKuCao), Glycyrrhizae Radix Et Rhizoma (GanCao), Angelicae Dahuricae Radix (Baizhi) and Ligusticum chuanxiong hort (Chuanxiong)	Treating allergic rhinitis and chronic sinusitis	[21, 22]
Xiangju granules	Platycarya strobilacea Sieb. et Zucc. (HuaXiangShuGuoXu), Chrysanthemum indicum L. (YeJuHua), Astragali Radix (HuangQi), Magnolia denudata Desr. (XinYi), Saposhnikovia divaricata (Trucz.) Schischk. (FangFeng), Prunella vulgaris L (XiaKuCao), Glycyrrhizae Radix Et Rhizoma (GanCao), Angelicae Dahuricae Radix (Baizhi) and Ligusticum chuanxiong hort (Chuanxiong)	Treating chronic rhinitis and sinusitis	[23–26]
Xiangju capsules	Platycarya strobilacea Sieb. et Zucc. (HuaXiangShuGuoXu), Chrysanthemum indicum L. (YeJuHua), Astragali Radix (HuangQi), Magnolia denudata Desr. (XinYi), Saposhnikovia divaricata (Trucz.) Schischk. (FangFeng), Prunella vulgaris L (XiaKuCao), Glycyrrhizae Radix Et Rhizoma (GanCao), Angelicae Dahuricae Radix (Baizhi) and Ligusticum chuanxiong hort (Chuanxiong)	Treating chronic sinusitis and allergic rhinitis	[27–33]
PSZ syrup	Platycarya strobilacea Sieb. et Zucc. (HuaXiangShuGuoXu), Prunella vulgaris L (XiaKuCao), Akebia quinata (Houtt.) Decne. (MuTong), Xanthium sibiricum Patrin ex Widder (CangErZi), Dendranthema morifolium (Ramat.) Tzvelev (JuHua) andMagnolia denudata Desr. (XinYi)	Treating chronic rhinitis, sinusitis and allergic rhinitis	[5]

Phytochemistry

In the past few decades, approximately 104 compounds have been isolated from PSZ, including volatile constituents (**1–52**), phenolic compounds (**53–87**), terpenoids (**88–97**), a carbohydrate (**98**) and other constituents (**99–104**). Volatile constituents and phenolic compounds have a variety of pharmacological activity and are considered to be the main active components of PSZ. Their structure is shown in (Table 2, Figures 2–6).

Volatile constituents

Volatile constituents are one of the most important active substances in PSZ. At present, 52 types of volatile constituents have been isolated from PSZ, including sesquiterpenes, long-chain hydrocarbons, fatty acids and fatty amides. The main components are sesquiterpenes. The aromatic small molecular compounds isolated from the volatile constituents of PSZ include acetic acid pentyl ester (**1**), 6-methyl-1-heptanol (**2**), 1-methanol,α,α,4-trimethyl-(S)-3-cyclo-hexene (**3**), methyl salicylate (**4**), l,2-methoxy-5-(1-propenyl)-(E)-phenol (**5**), 4α,8-dimethyl-2-(1-methylethylidene)-1,2,3,4,4α,5,6,8α-octahydronaphthalene (**6**), 1,6-dimethyl-4-(1-methylethyl)-naphthalene (**7**), anthracene (**8**), 4-isopropyl-1,6-dimethyl-tetralin (**9**) and 4-isopropyl-1,6-dimethylnaphthalene (**10**).[7, 34] Terpenoids in volatile constituents include aromadendrene (**11**), guaiol (**12**), β-epi-eudesmol (**13**), γ-epi-eudesmol (**14**), dehydro-aromadendrene (**15**), cadinene (**16**), α-calacorene (**17**), α-elemol (**18**), nerolidol (**19**), (-)-spathulenol (**20**), globulol (**21**), α-guaiene (**22**), aromadendrene oxide (**23**), isoaromadendrene epoxide (**24**), α-eudesmol (**25**), β-eudesmol (**26**), eudesm-7(11)-en-4-ol (**27**), cubenol (**28**) and T-muurolol (**29**).[7, 34] Aliphatic small molecule compounds include nonanoic acid (**30**), n-decanoic acid (**31**), tetradecanoic acid (**32**), 6,10,14-trimethyl-2-pentadecanone (**33**), 1,2-benzenedicarboxylic acid butyl octyl ester (**34**), n-nexadecanoic acid (**35**), dibutyl phthalate (**36**), hexadecanoic acid ethyl ester (**37**), tetrapentacontane (**38**), hexadecanamide (**39**), octadecanamide (**40**), dotriacontane (**41**), fitone (**42**), diisobutyl phthalate (**43**), pentadecanoic acid (**44**), 14-methylpentadecanoate (**45**), 9-hexadecenoic acid (**46**), palmitic acid (**47**), 8,11-octadecatrienoate (**48**), (Z,Z,Z)-9,12,15-octadecatrienoate (**49**), oleic acid (**50**), (Z,Z,Z)-9,12,15-octadecatrienoic acid (**51**) and hexacosene (**52**) (Table 2, Figure 2).[6, 7, 34]

Phenolic compounds

It has been reported in the literature that tannins and gallic acid are the main chemical components in PSZ, and tannins are phenolic compounds with complex structures that exist in plants.[39, 46–51] Phenolic compounds in PSZ include phenolic acids, flavonoids and ellagitannins.

Phenolic acids

A total of nine phenolic acids were isolated from PSZ, including 3-cadalenol (**53**), (-)-(7S,10R)-3-hydroxycalamenene (**54**), platycarynol (**55**), platycaryanind A-D (**56–59**), platycariin (**60**) and strobilanin (**61**) (Table 2, Figure 3).[15, 35]

Flavonoids

To date, 15 flavonoids have been isolated and identified from the infructescence, bark and leaves of PSZ, including 4′-hydroxyl-7-O-β-D-galactoside (**62**), rutin (**63**), quercetin (**64**), myricetin (**65**), myricitrin (**66**), quercitrin (**67**), morin hydrate (**68**), aftoside (**69**), 3′,4′,5′,5,6,7-hexahydroflavonel (**70**), eriodictyol (**71**), quercetin-3-O-(2″-O-galloyl)-β-D-glucopyranoside (**72**), quercetin-3-O-(2″-O-galloyl)-β-D-galactoside (**73**), quercetin-3-O-α-L-rhamnopyranoside (**74**), catechin (**75**) and epicatechin (**76**) (Table 2, Figure 4).[6, 20, 36, 37]

Ellagitannins

At present, 13 ellagitannins have been isolated, including gallic acid (**77**), ellagic acid (**78**), 3,3′-dimethoxylellagic acid (**79**), 3,3′-dimethoxylellagic acid-4′-O-β-D-xyloside (**80**), ellagic acid 4-O-xylopyranoside (**81**), 3′-O-methylellagic acid 4-O-xylo-pyranoside (**82**), 3,3′-di-O-methy-lellagic acid 4-O-xylpyranoside (**83**), 3-O-methyl ellagic acid (**84**), 4-O-ellagic acid (**85**), pedunculagin (**86**) and casuarictin (**87**) (Table 2, Figure 5).[6, 15, 35, 38]

Table 2 Chemical compounds isolated from *Platycarya strobilacea* Sieb. et Zucc

Classification	No.	Chemical component	Part of plant	Reference
Volatile constituents	1	Acetic acid pentyl ester	Infructescence	[7]
	2	6-methyl-1-heptanol	Infructescence	[7]
	3	1-methanol, α, α, 4-trimethyl-(S)-3-cyclo-hexene	Infructescence	[7]
	4	Methyl salicylate	Infructescence	[7]
	5	l, 2-methoxy-5-(1-propenyl)-(E)-phenol	Infructescence	[7]
	6	4α, 8-dimethyl-2-(1-methylethylidene)-1, 2, 3, 4, 4α, 5, 6, 8α-octahydronaphthalene	Infructescence	[7]
	7	1, 6-dimethyl-4-(1-methylethyl)-naphthalene	Infructescence	[7]
	8	Anthracene	Infructescence	[7]
	9	4-isopropyl-1,6-dimethyl-tetralin	Infructescence	[34]
	10	4-isopropyl-1,6-dimethylnaphthalene	Infructescence	[34]
	11	Aromadendrene	Infructescence	[7]
	12	Guaiol	Infructescence	[7]
	13	β-epi-eudesmol	Infructescence	[7]
	14	γ-epi-eudesmol	Infructescence	[7]
	15	Dehydro-aromadendrene	Infructescence	[7]
	16	Cadinene	Infructescence	[34]
	17	α-calacorene	Infructescence	[34]
	18	α-elemol	Infructescence	[34]
	19	Nerolidol	Infructescence	[34]
	20	(-)-spathulenol	Infructescence	[34]
	21	Globulol	Infructescence	[34]
	22	α-guaiene	Infructescence	[34]
	23	Aromadendrene oxide	Infructescence	[34]
	24	Isoaromadendrene epoxide	Infructescence	[34]
	25	α-eudesmol	Infructescence	[34]
	26	β-eudesmol	Infructescence	[34]
	27	Eudesm-7(11)-en-4-ol	Infructescence	[34]
	28	Cubenol	Infructescence	[34]
	29	T-muurolol	Infructescence	[34]
	30	Nonanoic acid	Infructescence	[7]
	31	n-decanoic acid	Infructescence	[7]
	32	Tetradecanoic acid	Infructescence	[7]
	33	6,10,14-trimethyl-2-pentadecanone	Infructescence	[7]
	34	1,2-benzenedicarboxylic acid butyl octyl ester	Infructescence	[7]
	35	n-nexadecanoic acid	Infructescence	[7]
	36	Dibutyl phthalate	Infructescence	[7]
	37	Hexadecanoic acid ethyl ester	Infructescence	[7]
	38	Tetrapentacontane	Infructescence	[7]
	39	Hexadecanamide	Infructescence	[7]
	40	Octadecanamide	Infructescence	[7]
	41	Dotriacontane	Infructescence	[7]
	42	Fitone	Infructescence	[34]
	43	Diisobutyl phthalate	Infructescence	[34]
	44	Pentadecanoic acid	Infructescence	[34]
	45	14-methylpentadecanoate	Infructescence	[34]
	46	9-hexadecenoic acid	Infructescence	[34]
	47	Palmitic acid	Infructescence	[34]
	48	8,11-octadecatrienoate	Infructescence	[34]
	49	(Z, Z, Z)-9,12,15-octadecatrienoate	Infructescence	[34]
	50	Oleic acid	Infructescence	[34]
	51	(Z, Z, Z)-9,12,15-octadecatrienoic acid	Infructescence	[34]
	52	Hexacosene	Infructescence	[6]

Table 2 Continued

Classification	No.	Chemical component	Part of plant	Reference
Phenolic acids	53	3-cadalenol	Fresh woods	[35]
	54	(-)-(7S,10R)-3-hydroxycalamenene	Fresh woods	[35]
	55	Platycarynol	Fresh woods	[35]
	56	Platycaryanind A	Infructescence	[15]
	57	Platycaryanind B	Infructescence	[15]
	58	Platycaryanind C	Infructescence	[15]
	59	Platycaryanind D	Infructescence	[15]
	60	Platycariin	Infructescence	[15]
	61	Strobilanin	Infructescence	[15]
Flavonoids	62	4′-hydroxyl-7-O-β-D-galactoside	Infructescence	[6]
	63	Rutin	Infructescence	[20]
	64	Quercetin	Infructescence	[20]
	65	Myricetin	Barks	[36]
	66	Myricitrin	Barks	[36]
	67	Quercitrin	Barks	[36]
	68	Morin hydrate	Barks	[36]
	69	Aftoside	Barks	[36]
	70	3′, 4′, 5′, 5, 6, 7-hexahydroflavonel	Barks	[36]
	71	Eriodictyol	Leaves	[37]
	72	Quercetin-3-O-(2″-O-galloyl)-β-D-glucopyranoside	Leaves	[37]
	73	Quercetin-3-O-(2″-O-galloyl)-β-D-galactoside	Leaves	[37]
	74	Quercetin-3-O-α-L-rhamnopyranoside	Leaves	[37]
	75	Catechin	Infructescence	[20]
	76	Epicatechin	Infructescence	[20]
Ellagitannins	77	Gallic acid	Infructescence	[6, 38]
	78	Ellagic acid	Infructescence	[6, 15, 38]
	79	3,3′-dimethoxylellagic acid	Infructescence	[6]
	80	3,3′-dimethoxylellagic acid-4′-O-β-D-xyloside	Infructescence	[6]
	81	Ellagic acid 4-O-xylopyranoside	Fresh woods	[35]
	82	3′-O-methylellagic acid 4-O-xylo-pyranoside	Fresh woods	[35]
	83	3,3′-di-O-methy-lellagic acid 4-O-xylpyranoside	Fresh woods	[35]
	84	3-O-methyl ellagic acid	Fresh woods	[35]
	85	4-O-ellagic acid	Infructescence	[15]
	86	Pedunculagin	Infructescence	[38]
	87	Casuarictin	Infructescence	[38]
Terpenoids	88	Uosolic acid	Infructescence	[6, 39]
	89	β-sitosterol	Infructescence	[6]
	90	Daucosterol	Infructescence	[6]
	91	8,11-dihydroxy-2,4-cycloeudesmane	Woods	[40]
	92	11-hydroxy-2,4-cycloeudesman-8-one	Woods	[40]
	93	2,4-cyclo-7(11)-eudesmen-8-one	Woods	[40]
	94	7-hydroperoxy-11-hydroxy-2,4-cycloeudesman-8-one	Woods	[41]
	95	8-hydroxy-13-nor-2,4-cycloeudesman-7-en-11-one	Woods	[41]
	96	2,4-cycloeudesma-7(11), 8-dien-(12, 8)-olide	Woods	[41]
	97	8-hydroxy-8,12-peroxy-2,4-cycloeudesm-7(11)-ene	Woods	[41]
Carbohydrate	98	D-glucose	Infructescence	[42]
Others	99	2,5,8-Trihydroxy-3-methoxy-1,4-naphthoquinone	Infructescence	[6]
	100	Vitamin C	Infructescence	[43]
	101	5-hydroxy-1,4-naphthoquinone	Leaves	[44]
	102	5-hydroxy-2-methoxy-1,4-naphthoquinone	Leaves	[37, 44, 45]
	103	5-hydroxy-3-methoxy-1,4-naphthoquinone	Leaves	[44]
	104	4,8-dihydroxynaphthalene-1-O-β-D-glucoside	Leaves	[37]

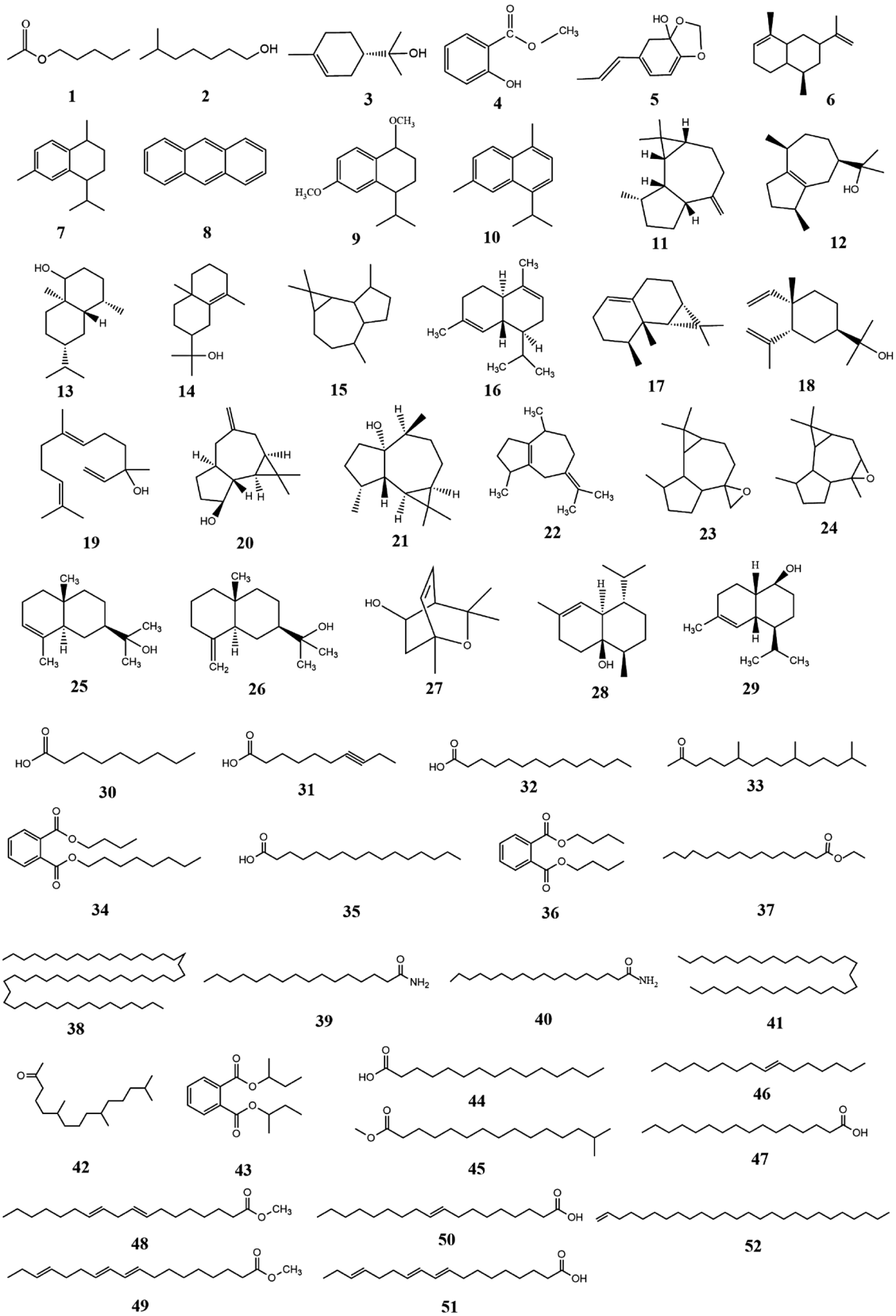


Figure 2 The chemical structures of volatile constituents.

Terpenoids

At present, 10 terpenoids have been isolated from the infructescence and wood of PSZ, including uosolic acid (**88**), β-sitosterol (**89**), daucosterol (**90**), 8,11-dihydroxy-2,4-cycloeudesmane (**91**), 11-hydroxy-2,4-cycloeudesman-8-one (**92**), 2,4-cyclo-7(11)-eudesmen-8-one (**93**),

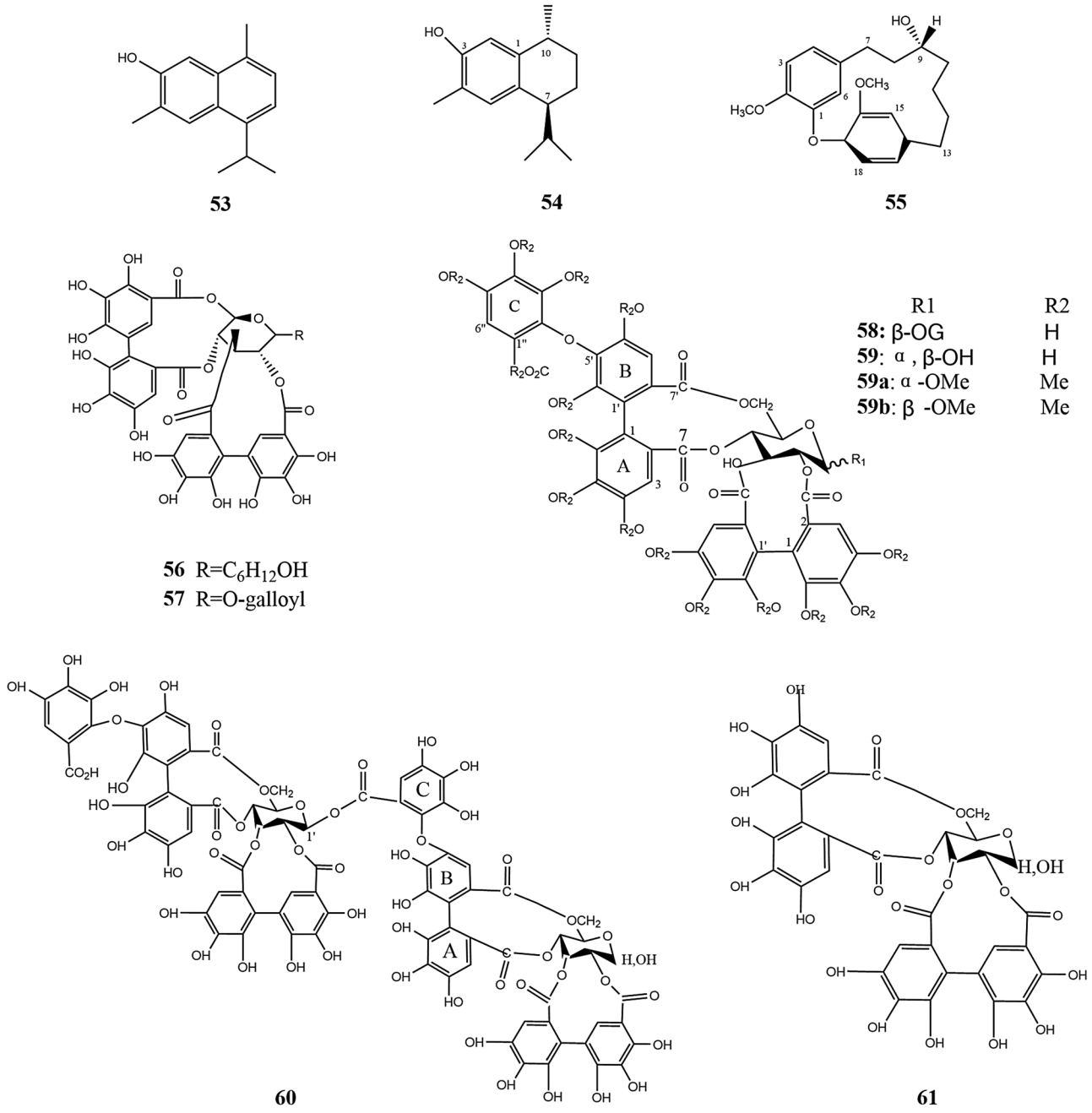


Figure 3 The chemical structures of phenolic acids.

7-hydroperoxy-11-hydroxy-2,4-cycloeudesman-8-one (**94**), 8-hydroxy-13-nor-2,4-cycloeudesman-7-en-11-one (**95**), 2,4-cycloeudesma-7(11),8-dien-(12, 8)-olide (**96**) and 8-hydroxy-8,12-peroxy-2,4-cycloeudesm-7(11)-ene (**97**) (Table 2, Figure 6).[6, 40, 41]

Carbohydrate

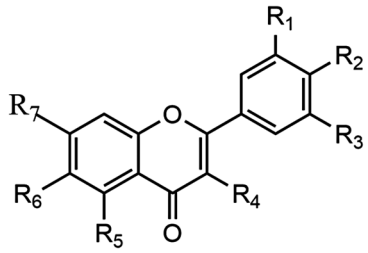
To date, d-glucose (**98**) has been isolated and identified from the ethanol extract of the infructescence of PSZ[42] (Table 2, Figure 6).

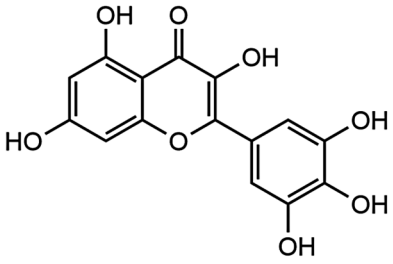
Other compounds

There are also other components in PSZ, including 2,5,8-Trihydroxy-3-methoxy-1,4-naphthoquinone (**99**), vitamin C (**100**), 5-hydroxy-1,4-naphthoquinone (**101**), 5-hydroxy-2-methoxy-1,4-naphthoquinone (**102**), 5-hydroxy-3-methoxy-1,4-naphthoquinone (**103**) and 4,8-dihydroxynaphthalene-1-O-β-D-glucoside (**104**) (Table 2, Figure 6).[6, 37, 44, 45]

Extraction Methods

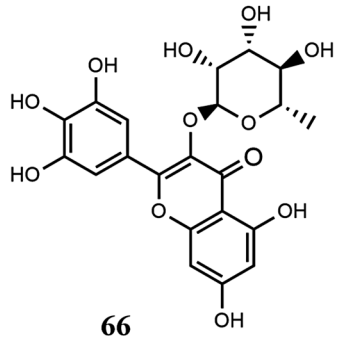
The extraction of PSZ mainly involves the extraction of flavonoids, phenols, polysaccharides, ellagic acid, tannins and other active ingredients. The response surface method is mostly used to optimize the extraction process, but the extraction time varies greatly. When extracting one of the effective parts, the extraction rate of the other effective parts is not fully considered. Single components are





62 R1=R2=R4=R5=R7= H;R3=OH;R6=O− β −D-gal
63 R1=R6=H;R2=R3=R5=R7=OH;R4=O- α −L−rha-(1→6)- β −D-glc
64 R1=R2=R4=R5=R7=OH;R3=R6=H

65



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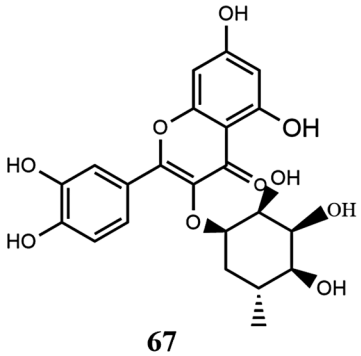

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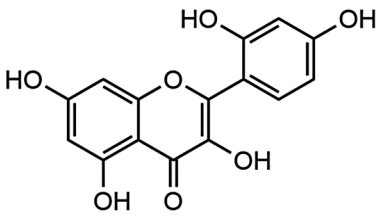

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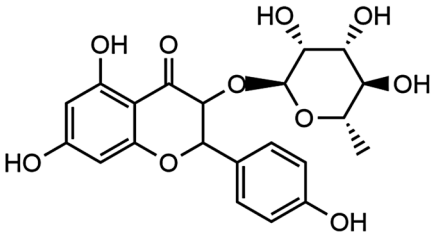

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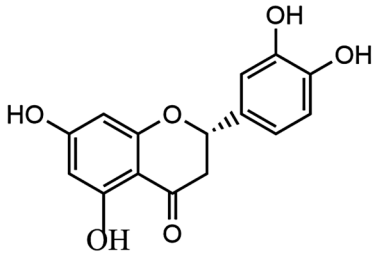

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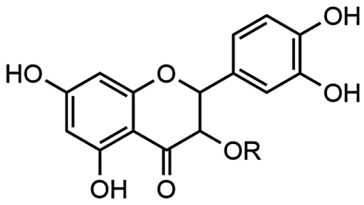
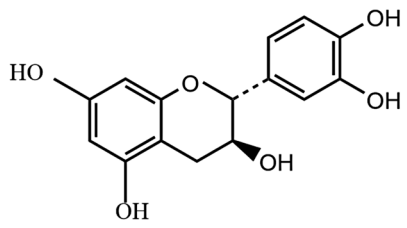


72: R=(2-O-galloyl)- β -D-glucose
73: R=(2-O-galloyl)- β -D-galactose
74: R= α -L-rhamnose



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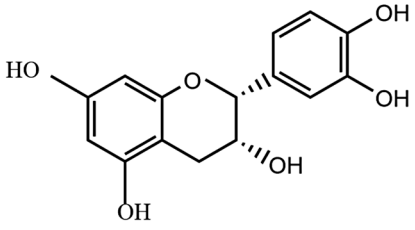

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Figure 4 The chemical structures of flavonoids.

extracted, and there are fewer optimization processes for volatile constituents, terpenoids and other components. In the future, more consideration should be given to the comprehensive extraction of multiple components, and optimization of the extraction process for volatile constituents and terpenoids, and in-depth research on the extraction methods should be conducted.[8] The PSZ extraction methods are summarized in Table 3.

Pharmacology

Antibacterial and anti-inflammatory effects

Modern pharmacological studies have shown that the phenolic compounds of PSZ have a strong inhibitory effect on the bacteria found in patients with rhinitis and sinusitis.[20, 55]

Lin[20] studied the antibacterial activity of the extract of PSZ, using the main infectious bacteria *Staphylococcus aureus* ATCC25923, *Escherichia coli* ATCC35218, *Streptococcus*

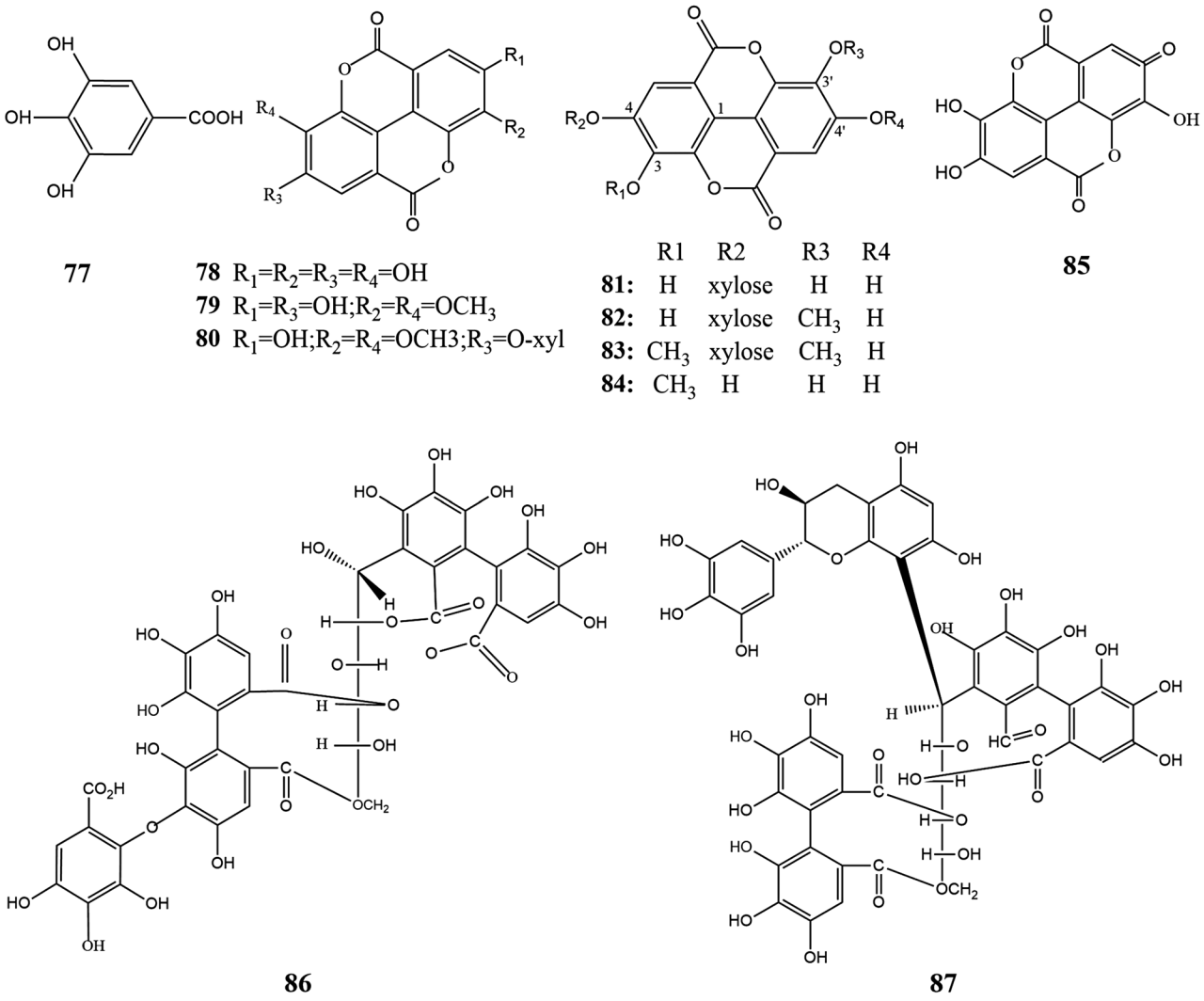

Figure 5 The chemical structures of ellagitannins.

pneumoniae ATCC49619 and *Pseudomonas aeruginosa* ATCC27853 as test bacteria. The in vitro antibacterial test showed that flavonoids had strong antibacterial effects on these four types of bacteria, and it was determined for the first time that flavonoids were one of the main antibacterial components for rhinitis and sinusitis. Liu[55] investigated the antibacterial activity of plant polyphenols against the above four bacteria by determining the inhibition zone, minimal inhibitory concentration (MIC) and minimal bactericidal concentration. The results showed that PSZ polyphenols have a strong inhibitory effect on bacteria.

Zhang et al.[62] extracted and purified tannin polymer fractions with a different molecular weight distribution from *P. strobilacea* infructescence (PSI), and tested the antimicrobial activity of these tannin polymer fractions. The results showed that all PSI tannin polymer fractions (TPF-1, TPF-2, TPF-3, TPF-4 and TPF-5) showed significant antibacterial activity against *S. aureus* and *E. coli* with low MIC values.

Anti-tumour effect

Liu et al.[63] found that an extract of the infructescence of *P. strobilacea* Sieb. et Zucc. (EPS) had a significant anti-nasopharyngeal carcinoma (NPC) effect in vitro. These results indicate that EPS may induce the death of NPC cells and inhibit NPC by regulating the Ras proto-oncogene (RAS)/mitogen-activated protein kinase (MAPK) signaling pathway and the transcription factor c-Fos proto-oncogene (c-FOS) and death of its downstream genes, to play a role in fighting NPC.

Zhang et al.[64] evaluated the anti-tumour activity of this plant in A549, HepG2, SH-SY-5Y, HCT116 and U2OS-NKFB cell lines. Among the different extracts from PSI, methanol extract had the strongest cytotoxic effect on SH-SY-5Y cells, and ethyl acetate extract had a strong anti-cancer effect on A549, HepG2, HCT116 and U2OS-NKFB cell activity. Moreover, Li YP et al.[65] determined the cytotoxic effect of PSI on human CNE2 NPC cells using the MTT method. These results showed that PSI had a strong inhibitory effect on the growth of human CNE2 NPC cells.

Antioxidant effect

Babu et al.[66] found that the antioxidant components of EPS can prevent the activation of NF-κB induced by TNF-α, the induction of chemokines and the adhesion of monocytes in intestinal inflammation. EPS inhibited the increase of reactive

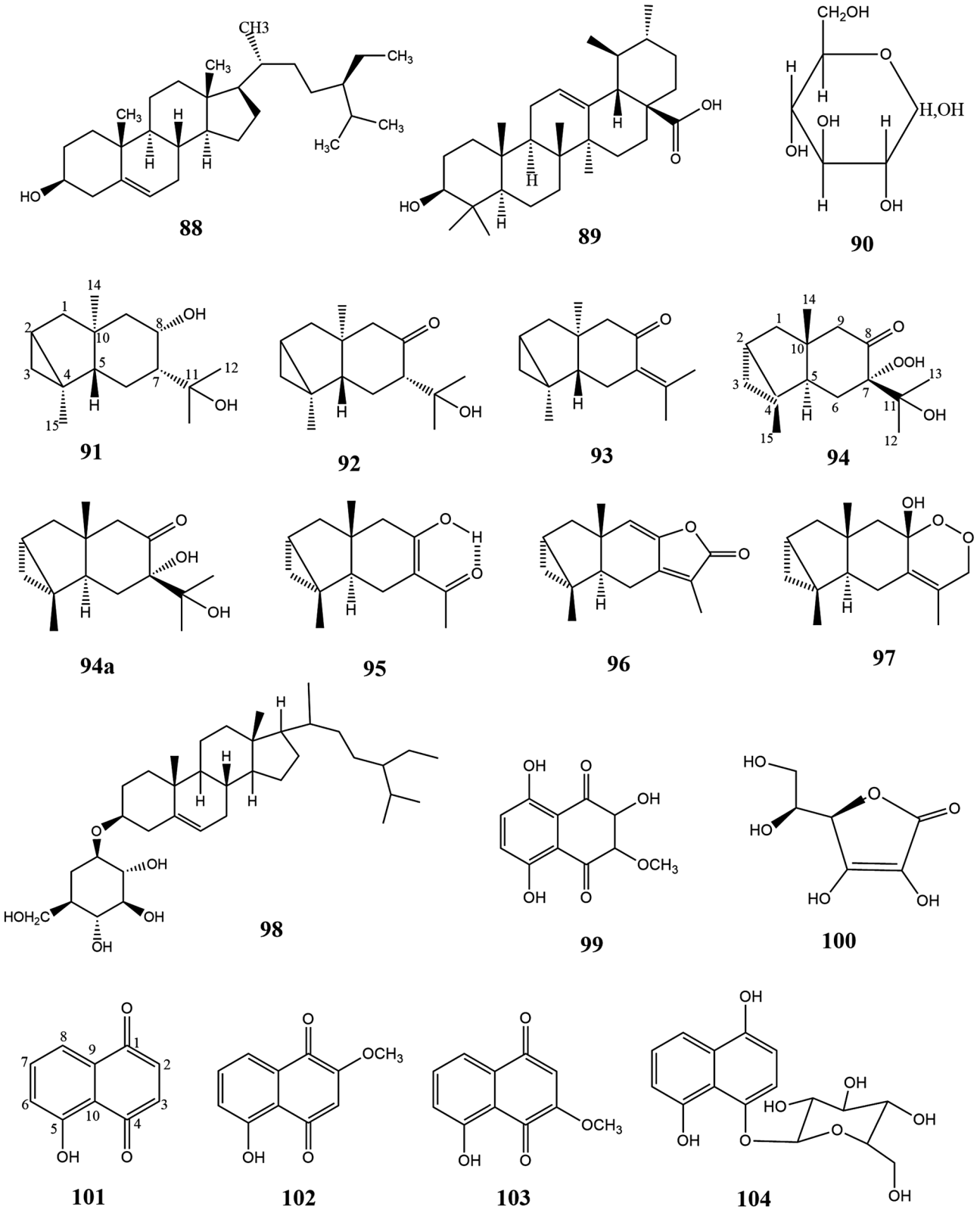

Figure 6 The chemical structures of terpenoids, carbohydrate and other compounds.

oxygen species induced by TNF-α, and showed scavenging activity of DPPH free radicals.

Xu et al.[67] measured the DPPH free radical scavenging ability and the total antioxidant capacity of the plant (FRAP method). The results showed that both the crude extract of PSZ and the purified product of PSZ extract had strong antioxidant activity, and the antioxidant activity of the purified polyphenols was further enhanced.

Table 3 Method for extracting *Platycarya strobilacea* Sieb. et Zucc

Active ingredients	Extraction method	Extraction reagent	Extraction temperature (°C)	Extraction time (h)	Material to liquid ratio (mL/g)	Number of extractions	Extraction rate (%)	References
Flavonoids	Ultrasonic extraction	60% Ethanol	/	0.77	10.50	3	4.01	[17, 52]
Flavonoids	Ethanol reflux extraction method	70% Ethanol	60°C	4.5	10	3	4.25	[17, 53]
Flavonoids	Ethanol reflux extraction method	65% Ethanol	60°C	2	9	3	4.29	[20, 54]
Phenols	Ethanol reflux extraction method	55% Ethanol	77°C	1.5	14	3	3.646	[54, 55]
Phenols	Ethanol reflux extraction method	55% Ethanol	77°C	1.5	14	3	3.746	[56]
Ellagic acid	Ultrasonic extraction	Methanol	70°C	0.67	22.5	2	1.961	[57]
Ellagic acid	Alkaline extraction and acid precipitation	/	85°C	1.3	13	3	1.47	[58]
Tannins	/	Water	90°C	1.3	17.5	2	50	[59]
Volatile constituents	Steam distillation	Ethyl acetate	/	4	/	/	0.12	[34]
Polysaccharides	/	Ethanol	85°C	2.8	22	2	3.57	[60]
Polysaccharides	Ultrasonic extraction	95% Ethanol	52°C	0.67	25	3	3.959	[61]

Antiviral effect

Li YP et al.[65] first used an indirect immunoenzyme method to study the effect of PSZ on the expression of Epstein-Barr (EB) virus capsid antigen (VCA) in $B_{95\text{-}8}$ cells. The results showed that the plant had a significant inhibitory effect on the expression of EB VCA in $B_{95\text{-}8}$ cells stimulated by sodium butyrate at a non-toxic concentration.

Prevention and treatment of COVID-19

COVID-19 belongs to the category of 'damp toxin epidemic'. It is a disease caused by cold and dampness, which invades the human body. The disease is located in the lungs and spleen, which can spread to the heart, liver and kidneys, with cold-dampness injuring yang and has the syndrome of transforming heat, injuring yin, causing blood stasis and shutting off.[68] A network pharmacology study found that the main effective components on COVID-19 are quercetin, luteolin and β-sitosterol.[69, 70] These active ingredients are all contained in PSZ, and the plant has antibacterial, anti-inflammatory and anti-virus effects. The use of PSZ to prevent and cure COVID-19 can play a role in removing dampness, invigorating the stomach, relieving exterior factors and dispelling pathogens. Therefore, PSZ has a potential preventive and therapeutic effect on COVID-19, which is worthy of further study.

Other pharmacological effects

Some studies had shown that plant polyphenols have an effect on cardiovascular and cerebrovascular diseases, can increase blood flow rate, and reduce the probability of cerebral infarction and cerebral hemorrhage, and may play a role in preventing cardiovascular and cerebrovascular diseases.[55] In addition, polyphenols have an anti-atherosclerotic effect by regulating blood lipid metabolism, anticoagulation and promoting fibrinolysis and inhibiting platelet aggregation.[14] Lee et al.[71] found that *P. strobilacea* leaf extract (PLE) can inhibit the loss of alveolar bone caused by periodontitis, and may be beneficial ingredient in promoting oral health. Additionally, Kim et al.[15] found that *P. strobilacea* Sieb. et Zucc. extract can be added to cosmetic preparations as it has an anti-ageing effect. Some studies have shown that PSZ polysaccharides have a protective effect on cerebral ischemia reperfusion injury in rats.[72]

Toxicology

At present, there are few studies on the toxicology of PSZ. PSZ syrup is the main medicine used for the treatment of acute chronic rhinitis and allergic rhinitis. After two years of clinical observation, PSZ syrup was shown to have a rapid effect on the above symptoms, without adverse reactions.[5]

Studies have shown that ellagic acid (EA) is rapidly eliminated from mice after oral administration. The levels of EA in the blood, lung and liver of mice were very low or undetectable. The pharmacokinetic characteristics of EA indicate that both animals and humans can tolerate EA, it is rapidly eliminated and is malabsorbed, and there is no evidence of systemic toxicity even at high doses.[46, 73]

Discussion and Conclusion

This review systematically summarized the traditional uses, botany, phytochemistry, extraction methods, pharmacology and toxicology of PSZ, and provided comprehensive information on this plant. To date, a total of 104 compounds have been identified in PSZ, including volatile constituents, phenolic compounds, terpenoids and a carbohydrate. PSZ has a wide range of pharmacological effects, including antibacterial, anti-inflammatory, anti-tumour, antioxidant and antiviral effects, especially in the treatment of allergic rhinitis and chronic sinusitis, with significant curative effects and wide applications. Although continuous progress has been made in all aspects of PSZ, research is still needed on development of the plant and the research and development of new drugs.

First, there are very few studies on the pharmacokinetics and toxicology of PSZ, which is the reason why there is little research and development of the plant. Therefore, more research on the pharmacokinetics and toxicology of the drug

should be carried out. Second, most of the studies on the pharmacological activity of this plant are limited to the study of single components such as volatile constituents, flavonoids or polyphenols and the pharmacological activity of the plant such as anti-tumour and antioxidation has only been studied in animal experiments or *in vitro*, without the support of clinical trials. Therefore, systematic clinical trials of PSZ infructescence should be performed in the future. Third, with the exception of studies on the infructescence of the plant, there are few studies on the other parts of the plant such as the flowers, leaves, trunk and fruits. Therefore, it is necessary to carry out basic studies on the chemical constituents and pharmacological effects of other parts of the plant to fully determine the medicinal potential of the plant. Fourth, due to the complex chemical composition of PSZ, an international unified method of content determination and identification is needed to control the quality and to establish a standardized fingerprint of the plant. Finally, PSZ is effective in the treatment of rhinitis and sinusitis. At present, the traditional Chinese medicine preparations containing PSZ as the main drug include Xiangju tablets, Xiangju granules and Xiangju capsules, but the compatibility of these preparations is not versatile enough. Thus, more preparations should be developed to meet clinical needs.

This study systematically summarizes the traditional uses, botany, chemical constituents, extraction methods, pharmacology and toxicology of PSZ. We hope that this review will reflect the importance of the plant, and provide some guidance for the future development of this plant.

Acknowledgement

We thank International Science Editing (http://www.internationalscienceediting.com) for editing this manuscript.

Author Contributions

Peiyuan Zhao wrote the manuscript; Lizhu Han and Yunlan Wang completed the Figure 1 and Figure 2; Jinqing Qiu and Xinbo Zhang collected some literature; Xi Duan and Zhishu Tang systemically revised the manuscript for important content; Xiao Song proposed the conception and designed the structure of the manuscript.

Funding

This work was supported by the National Key Research and Development Program for Traditional Chinese Medicine Modernization [grant number 2019YFC1711200, 2019YFC1711204]; the Project of Shaanxi Provincial Education Department [grant number 17JS031]; the Project of Shaanxi Provincial Department of Science and Technology [grant number 2017SF-359]; Shaanxi Provincial Key Laboratory of TCM Foundation and New Drug Research [grant number 1008]; and the Special Grant for Shaanxi Key Discipline of Traditional Chinese Medicine Pharmacy [grant number 303061107].

Conflict of Interest

The authors declare no conflict of interest.

Ethics Statement

This study has no privacy issues regarding participants, therefore the review will not require ethical approval.

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