



Review article

A review of the research progress on *Pinellia ternata* (Thunb.) Breit.: Botany, traditional uses, phytochemistry, pharmacology, toxicity and quality control

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ABSTRACT

Ethnopharmacological relevance: *Pinellia ternata* (Thunb.) Breit. is a well-known perennial herb that is used in traditional medicine in China, Japan and Korea. It's drawing worldwide interests in medicinal applications owing such as anti-diarrhea, lipid-lowering, anti-tumor, anti-cough, expectorant, anti-gastric ulcer, etc.

Aim of the study: This review aims to provide useful information on the botany, traditional uses, phytochemistry, pharmacology, toxicity and quality control of *Pinellia ternata* to help increase its efficiency. In addition, this review will discuss the future research trends and development prospects of this plant.

Materials and methods: Data was obtained through a systematic search of published literature and online databases such as Google Scholar, Web of Science, PubMed, Science Direct, and Sci-Finder. The botanical names were confirmed using the World Flora Online and chemical structures were drawn using the ChemBio Draw Ultra Version 19.0 Software.

Results: *Pinellia ternata* is distributed in regions of China and other areas. *Pinellia ternata* and its compound preparations can be used for cough, vomiting, gastric ulcer and other diseases. Approximately 212 chemical constituents have been isolated from *Pinellia ternata*, including alkaloids, volatile oils, amino acids, organic acids, flavonoids, cerebrosides, phenylpropanoids and other compounds. Considerable pharmacological experiments *in vitro* and *in vivo* have demonstrated that *Pinellia ternata* possessed antitumor effect, antitussive effects, antiasthmatic effects, increasing resistance to gastric ulcer, and antidiarrheal effect. However, these extracts can also lead to various toxicities such as irritant toxicity, cardiotoxicity, hepatotoxicity and embryonic toxicity. Considerable experiments have demonstrated that different processing methods and suitable compatibility with other herbs can effectively reduce the toxicities and increase the efficiency of *Pinellia ternata*.

Conclusions: *Pinellia ternata* is an ancient herbal medicine with a broad spectrum of pharmacological activities that has been used for thousands of years in China. Future studies should perform an in-depth analyses of the pharmacokinetics and mechanisms of toxicity of *Pinellia*

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ternata. Quality standards should be developed to correspond to the various application methods to ensure the efficacy of drugs in actual treatment.

1. Introduction

Pinelliae Rhizoma (PR), also named Shoutian (守田), Shuiyu (水玉), Diwen (地文), and Xiezicao (蝎子草), is a tuber of *Pinellia ternata* (Thunb.) Breit. from the family Araceae, which comprises approximately 115 genera and more than 2000 species distributed worldwide, with more than 92 % of them produced in the tropics. PR was first recorded as a herbal medicine in the Shennong Herbal Classic. It is acrid in flavor, warm and toxic, and acts on the spleen, stomach, and lung channels, where it can promote the circulation of Qi and eliminate dampness. In the spleen and lung, it can eliminate dampness and activate the spleen to clear phlegm; thus, it is applicable to the treatment of cough and asthma due to damp phlegm, cold phlegm, retention of dampness, and stasis in middle-jiao (中焦). As PR can also regulate the stomach and lower the adverse Qi to stop vomiting and eliminate stasis, it is indicated for vomiting due to the adverse flow of Qi caused by failure of the descending of stomach-Qi, stasis, and distention due to cold and heat.

To date, phytochemical studies have shown that PR is rich in various ingredients, including alkaloids, volatile oils, amino acids, organic acids, flavonoids, cerebrosides, phenylpropanoids and other chemical components. With increasing interest in research on the pharmacological activities of PR, researchers have revealed the significant pharmacological effects of PR, including as a cough suppressant and expectorant, as well as its antiasthmatic, antiemetic, anti-gastric ulcer, antidiarrheal, hypolipidemic, and antitumor effects. PR is one of 28 clinically toxic herbs [1], it causes violent irritation of the mucous membranes of the mouth and laryngopharynx when taken incorrectly, and its toxicity can be effectively minimized by proper handling. The common processing products of PR include Pinelliae Rhizoma Praeparatum Cum Alumine (PRPCA, Qing-Banxia, 清半夏), Pinelliae Rhizoma Praeparatum Cum Zingibere et Alumine (PRPZA, Jiang-Banxia, 姜半夏), and Pinelliae Rhizoma Praeparatum (PRP, Fa-Banxia, 法半夏). For its pharmacological effects, toxicity mechanism of action, has become a hot spot for researchers. The aim of this paper is to provide up-to-date and comprehensive information on botanicals, traditional uses, processing, phytochemistry, quality control, pharmacology and toxicity in order to lay the foundation for further development and utilization of *Pinellia ternata*. (Fig. 1).

2. Materials and methods

To cultivate a comprehensive understanding of the current research status of PR, we performed a no language restrictions the use of database search, including China National Knowledge Infrastructure (CNKI), Google Scholar, PubMed, Web of Science, SpringerLink, Wiley, Wanfang Data and Baidu Academic to retrieve articles on the botany, phytochemistry, extraction methods, and pharmacology of PR, for information about PR. We also searched for articles on the botany and traditional uses of PR from PhD and MS dissertations and books such as Ben Cao Tu Jing, A Textual Research on the Name and Reality of Plants and Modern Practical Chinese Medicine. By

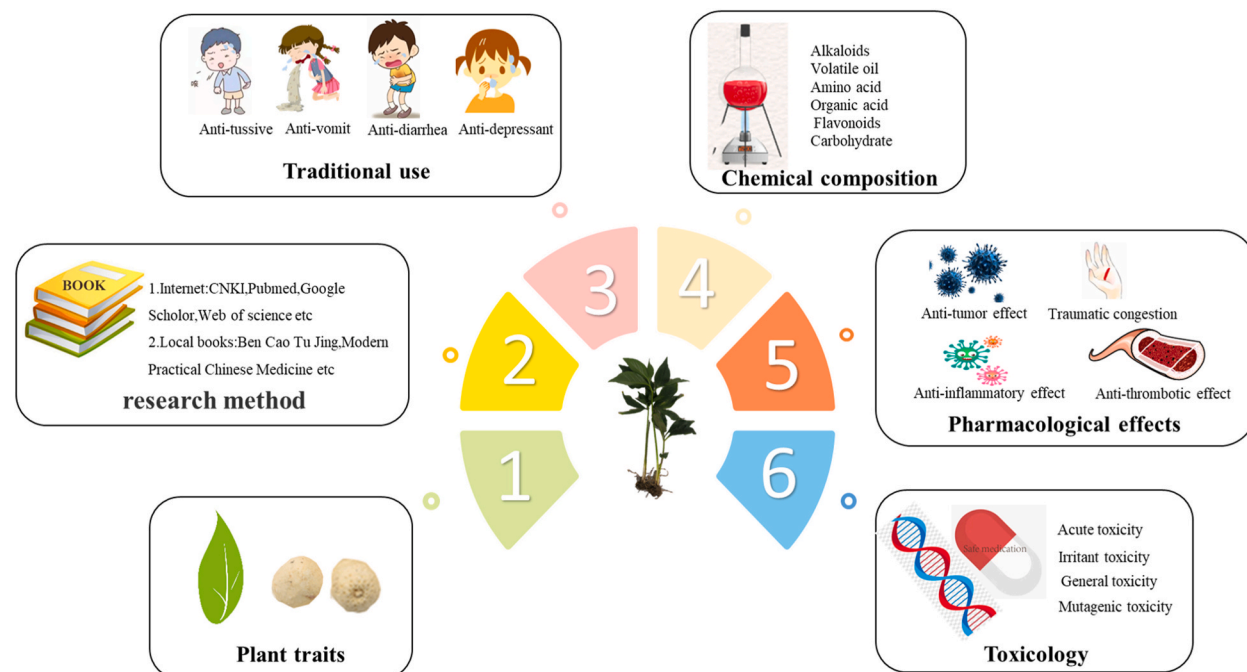


Fig. 1. Graphical abstract.

summarizing and organizing this review, this review covers extraction methods as well as botanical, phytochemical, pharmacological, and toxicological research on PR from 1975 to 2023. Publications on unrelated topics and non-SCI indexed journal issues were excluded. In total, we found more than 300 articles, as well as books. We here cite a total of 165 sources, mostly phytochemical and pharmacological studies.

3. Botany

PR is a perennial herb of Araceae (Fig. 2A), with a plant height of 10–35 cm. The metamorphic stems of PR are mostly spherical with a diameter of 0.5–4 cm, and many fibrous roots under the tuber; the pearl buds are 0.5–1 cm, and the lower fibrous roots are few and thin. The seedlings of pearl buds or small tubers are mainly single-leaved, ovoid; seedlings born from tubers of ≥ 2 years have 2–7 leaves, usually three compound leaves, with a larger one in the middle (Fig. 2B). The flowering period of PR is from May to July, and the fruit period is August [2].

PR is spherical in shape, some slightly inclined, with a diameter of 0.7–1.6 cm. The surface is white or light yellow, with sunken stem scars at the top and pitted root scars around; the lower layer is blunt and smooth. Oral administration of PR will cause numbness of the tongue and tingling of the throat (Fig. 2C).

Fa-Banxia are spherical or broken into irregular granules. The surface is yellowish white, yellow, or brownish yellow. The texture is more flimsy or hard and brittle, yellow or pale yellow in cross-section, and the granules are slightly hard and brittle. Fa-Banxia have a mild odor, a light and slightly sweet taste, and a slight numbing sensation on the tongue (Fig. 2D).

Jiang-Banxia are characterized as flaky, irregularly granular, or sphere-like, with a brown to tan surface. The texture is hard and brittle, yellowish brown at the cross-section, often with a horny luster. The smell is slightly fragrant, the taste is light, and it causes slight numbness of the tongue and slightly sticky teeth when chewing (Fig. 2E).

Qing-Banxia decoction pieces are characterized by oval, round or irregular pieces. The section is grayish to grayish white or yellowish white to yellowish brown, with grayish white dotted or short linear vascular bundle traces, and some residual embolisms showing light purplish-red markings below. Qing-Banxia decoction pieces are brittle and easily broken, and its sections are slightly powdery or horny. The smell is slight, while the taste is slightly astringent and leaves a slightly numb tongue feeling (Fig. 2F).

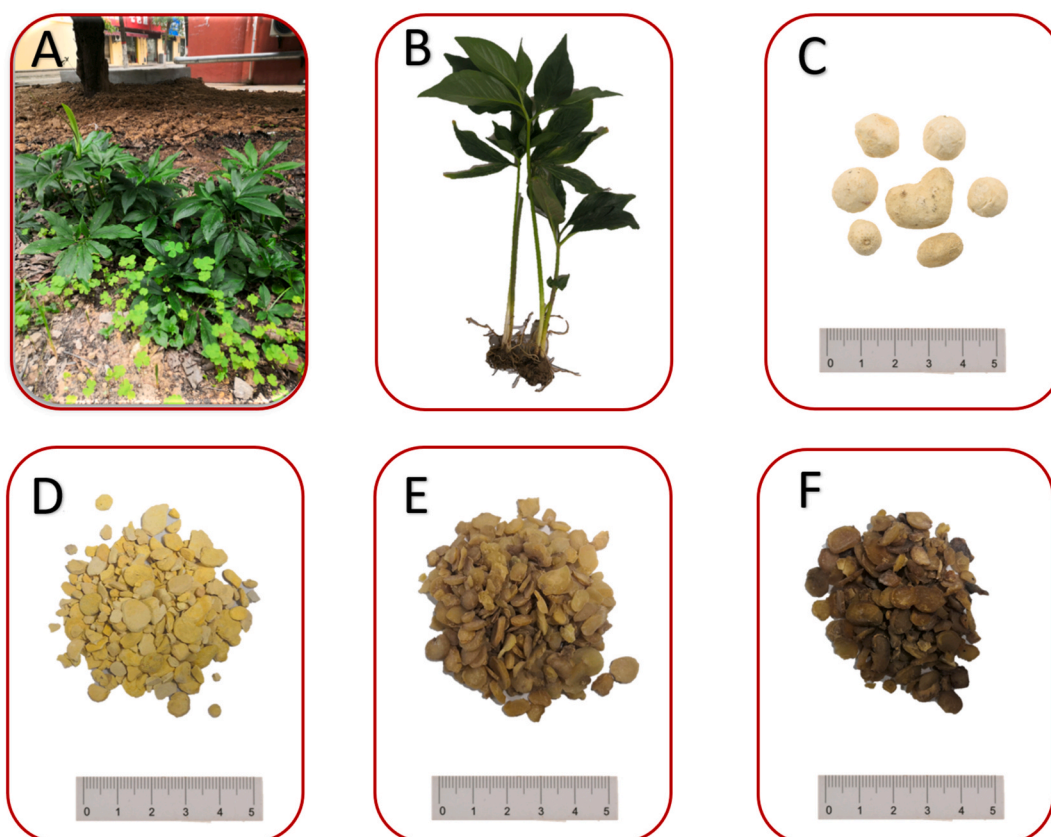


Fig. 2. Photograph of *Pinellia ternata* (Thunb.) Breit. **Note:** (A) The morphology of the *Pinellia ternata* (Thunb.) Breit; (B) the whole plant or overground part of *Pinellia ternata* (Thunb.) Breit; (C) *Pinellia ternata* decoction pieces; (D) *Pinelliae Rhizoma Praeparatum* (Fa-Banxia, 法半夏); (E) *Pinelliae Rhizoma Praeparatum Cum Zingibere et Alumine* (Jiang-Banxia, 姜半夏); (F) *Pinelliae Rhizoma Praeparatum Cum Alumine* (Qing-Banxia 清半夏).

Table 1
The traditional and clinical uses of *Pinellia ternata* (Thunb.) Breit. in China.

Preparation name	Main compositions	Formulation	Traditional and clinical uses	References
Xiaoqinglong soup	<i>Ephedra sinica</i> Stapf 9 g, <i>Paeonia lactiflora</i> Pall. 9 g, <i>Asarum sieboldii</i> Miq 6 g, <i>Zingiber officinale</i> Rosc. 6 g, <i>Glycyrrhiza uralensis</i> Fisch processing with honey 6 g, <i>Cinnamomum cassia</i> Presl 9 g, <i>Schisandra chinensis</i> (Turcz.) Bail. 6 g, <i>Pinellia ternata</i> (Thunb.) Breit. 9 g	Decoction	Dispersing cold from the exterior of the body, warming the lung to dissolve drinks.	Treatise On Febrile Disease《伤寒论》
Shegan Mahuang soup	<i>Belamcanda chinensis</i> (L.) DC. 9 g, <i>Ephedra sinica</i> 9 g, <i>Zingiber officinale</i> 6 g, <i>Asarum sieboldii</i> 6 g, <i>Aster tataricus</i> L. f. 6 g, <i>Ziziphus jujuba</i> Mil. 3 piece, <i>Pinellia ternata</i> 9 g, <i>Schisandra chinensis</i> (Turcz.) 3 g	Decoction	Expelling phlegm from the lung, relieving cough by lowering the Qi.	Jin Kui Yao Lue《金匱要略》
Jinfeicao powder	<i>Inula japonica</i> Thunb. 90 g, <i>Ephedra sinica</i> 90 g, <i>Peucedanum praeruptorum</i> Dunn 90 g, <i>Schizonepeta tenuifolia</i> Briq. 120 g, <i>Glycyrrhiza uralensis</i> process with honey 30 g, <i>Pinellia ternata</i> 30 g, <i>Paeonia lactiflora</i> Pall. 30 g	Powder	Dispersing wind and cold, lowering Qi and resolving phlegm	Bo Ji Fang《博济方》
Dachaihu soup	<i>Bupleurum chinense</i> DC. 15 g, <i>Scutellaria baicalensis</i> Georgi 9 g, <i>Paeonia lactiflora</i> . 9 g, <i>Pinellia ternata</i> 9 g, <i>Zingiber officinale</i> 15 g, <i>Citrus aurantium</i> 9 g, <i>Ziziphus jujuba</i> 4 piece, <i>Rheum palmatum</i> L. 6 g	Decoction	Harmonizing Shao Yang, Internal diarrhea of hot knots	Jin Kui Yao Lue《金匱要略》
Shensu decoction	<i>Panax ginseng</i> C. A. Mey. 6 g, <i>Perilla frutescens</i> (L.) Brit. 6 g, <i>Pueraria lobata</i> (Willd.) Ohwi 6 g, <i>Pinellia ternata</i> 6 g, <i>Peucedanum praeruptorum</i> 6 g, <i>Poria cocos</i> (Schw.) Wolf 6 g, <i>Citrus aurantium</i> L. 4 g, <i>Platycodon grandiflorum</i> (Jacq.) A. DC. 4 g, <i>Aucklandia lappa</i> Decne. 4 g, <i>Citrus reticulata</i> Blanco 4 g, <i>Glycyrrhiza uralensis</i> processing with honey 4 g	Decoction	Benefiting Qi and relieving symptoms, regulating Qi and resolving phlegm	Taiping Huimin Heji Ju Fang《太平惠民和剂局方》
Xiaochaihu soup	<i>Bupleurum chinense</i> 12 g, <i>Scutellaria baicalensis</i> 9 g, <i>Panax ginseng</i> 6 g, <i>Pinellia ternata</i> 9 g, <i>Glycyrrhiza uralensis</i> 5 g, <i>Zingiber officinale</i> 9 g, <i>Ziziphus jujuba</i> 4 piece	Decoction	Harmonizing Shaoyang, harmonizing the stomach and lowering rebelliousness	Treatise On Febrile Disease《伤寒论》
Zhuye Shigao soup	<i>Lophatherum gracile</i> Brongn 6 g, <i>Gypsum Fibrosum</i> 50 g, <i>Pinellia ternata</i> 9 g, <i>Ophiopogon japonicus</i> (L.f) Ker-Gawl. 20 g, <i>Panax ginseng</i> 6 g, <i>Oryzae semen</i> 10 g, <i>Glycyrrhiza uralensis</i> 6 g	Decoction	Clearing heat and promoting the production of body fluid, benefiting Qi and harmonizing the stomach	Treatise On Febrile Disease《伤寒论》
Xiangsha Liujunzi soup	<i>Panax ginseng</i> 3 g, <i>Atractylodes macrocephala</i> 6 g, <i>Glycyrrhiza uralensis</i> 2 g, <i>Citrus reticulata</i> 2.5 g, <i>Pinellia ternata</i> 3 g, <i>Amomum kravanh</i> Pierre ex Gagnep. 2.5 g, <i>Aucklandia lappa</i> 2 g	Decoction	Benefiting Qi and strengthening the spleen, moving Qi and resolving phlegm	Gu Jin Ming Yi Fang Lun《古今名方论》
Huiyang Jiuji soup	<i>Aconitum carmichaelii</i> Debx. processing with digestion 9 g, <i>Zingiber officinale</i> 6 g, <i>Panax ginseng</i> 6 g, <i>Glycyrrhiza uralensis</i> 6 g, <i>Atractylodes macrocephala</i> Koidz. processing with bran fried 9 g, <i>Cinnamomum cassia</i> 3 g, <i>Citrus reticulata</i> 6 g, <i>Schisandra chinensis</i> 3 g, <i>Poria cocos</i> 9 g, <i>Pinellia ternata</i> 9 g	Decoction	Returning Yang to consolidate detachment, benefiting Qi and generating pulse	Shang Han Liu Shu《伤寒六书》
Sixjunzi soup	<i>Panax ginseng</i> 9 g, <i>Atractylodes macrocephala</i> 9 g, <i>Poria cocos</i> 9 g, <i>Glycyrrhiza uralensis</i> 6 g, <i>Citrus reticulata</i> 3 g, <i>Pinellia ternata</i> 4.5 g	Decoction	Benefiting Qi and strengthening the spleen, drying dampness and resolving phlegm	Yi Xue Zheng Chuan《医学正传》
Binglang powder	<i>Areca catechu</i> 30 g, <i>Pinellia ternata</i> 30 g, <i>Prunus armeniaca</i> 30 g, <i>Platycodon grandiflorum</i> 30 g, <i>Citrus reticulata</i> 30 g, <i>Inula Japonica</i> 30 g, <i>Zingiber officinale</i> 30 g, <i>Atractylodes macrocephala</i> 30 g, <i>Panax ginseng</i> 15 g, <i>Glycyrrhiza uralensis</i> 15 g	Powder	Phlegm and phlegm in the chest and diaphragm, and a deficient sound in the abdomen	Chong Ding Yan Shi Ji Sheng Fang《重订严氏济生方》
Buqi Huatan soup	<i>Astragalus membranaceus</i> 45 g, <i>Platycodon grandiflorum</i> 9 g, <i>Adenophora stricta</i> Miq 24 g, <i>Prunus armeniaca</i> 9 g, <i>Aster tataricus</i> 9 g, <i>Poria cocos</i> 10 g, <i>Lilium brownii</i> var. <i>viridulum</i> Baker 12 g, <i>Pinellia ternata</i> 12 g, <i>Glycyrrhiza uralensis</i> 9 g	Decoction	Tonifying Qi and calming asthma, relieving cough and resolving phlegm	Li Shao Nan Fang《李绍南方》
Shengyang Yiwei soup	<i>Astragalus membranaceus</i> (Fisch.) Bge. 30 g, <i>Pinellia ternata</i> 5 g, <i>Panax ginseng</i> 15 g, <i>Glycyrrhiza uralensis</i> 15 g, <i>Angelica pubescens Maxim. f. biserrata</i> Shan et Yuan 9 g, <i>Saposhnikovia divaricata</i> (Turcz.) Schischk. 9 g, <i>Paeonia lactiflora</i> . 9 g, <i>Notopterygium incisum</i> Ting ex H. T. Chang 9 g, <i>Citrus reticulata</i> 6 g, <i>Poria cocos</i> 5 g, <i>Bupleurum chinense</i> 5 g, <i>Alisma orientate</i> (Sam.) Juzep. 5 g, <i>Atractylodes macrocephala</i> 5 g, <i>Coptis chinensis</i> Franch. 1.5 g	Decoction	Benefiting Qi and raising Yang, clearing heat and removing dampness	Nei Wai Shang Bian Huo Lun《内外伤辨惑论》
Anzhong Tiaoqi pill	<i>Citrus reticulata</i> 60 g, <i>Pinellia ternata</i> 30 g, <i>Poria cocos</i> (Schw.) Wolf. 30 g, <i>Atractylodes macrocephala</i> 60 g, <i>Citrus aurantium</i> 30 g, <i>Perilla frutescens</i> 18 g, <i>Ligusticum chuanxiong</i> 15 g, <i>Angelica sinensis</i> (Oliv.) Diels 15 g, <i>Paeonia lactiflora</i> 24 g, <i>Aucklandia lappa</i> 3 g, <i>Glycyrrhiza uralensis</i> 9 g, <i>Cyperus rotundus</i> L. 90 g, <i>Massa Medicata Fermentata</i> 30 g, <i>Coptis chinensis</i> 30 g, <i>Amomum kravanh</i> 15 g, <i>Raphanus sativus</i> L. 15 g	Pills	Turning the stomach and phlegm diaphragm	Gu Jin Yi Jian《古今医鉴》
Banfu soup	<i>Aconitum carmichaelii</i> 7.5 g, <i>Pinellia ternata</i> 7.5 g, <i>Zingiber officinale</i> 10 piece	Decoction	Warming the stomach and resolving phlegm	Yi Xue Ru Men《医学入门》

(continued on next page)

Table 1 (continued)

Babao Huichun soup	<i>Aconitum carmichaelii</i> 30 g, <i>Panax ginseng</i> 30 g, <i>Ephedra sinica</i> 30 g, <i>Scutellaria baicalensis</i> 30 g, <i>Stephania tetrandra</i> S. Moore 30 g, <i>Cyperus rotundus</i> 30 g, <i>Prunus armeniaca</i> L. var. <i>ansu</i> Maxim. 30 g, <i>Ligusticum chuanxiong</i> 30 g, <i>Angelica sinensis</i> 30 g, <i>Poria cocos</i> 45 g, <i>Citrus reticulata</i> 30 g, <i>Saposhnikovia divaricata</i> 30 g, <i>Paeonia lactiflora</i> 150 g, <i>Aquilaria sinensis</i> (Lour.) Gilg 15 g, <i>Pinellia ternata</i> 45 g, <i>Aconitum carmichaelii</i> 15 g, <i>Cinnamomum cassia</i> 30 g, <i>Atractylodes macrocephala</i> 60 g, <i>Lindera aggregate</i> (Sims) Kosterm. 15 g, <i>Zingiber officinale</i> 30 g, <i>Astragalus membranaceus</i> 90 g, <i>Glycyrrhiza uralensis</i> 30 g, <i>Rehmannia glutinosa</i> Libosch. processing with wine 30 g, <i>Rehmannia glutinosa</i> 30 g	Decoction	Expelling wind, harmonizing Qi, invigorating blood	Zhu Shi Ji Yan Fang《朱氏集验方》
Basheng yinzi	<i>Aconitum carmichaelii</i> 60 g, <i>Arisaema erubescens</i> (Wall.) Schott 30 g, <i>Typhonium giganteum</i> 30 g, <i>Gastrodia elata</i> 30 g, <i>Atractylodes macrocephala</i> 30 g, <i>Ligusticum chuanxiong</i> 15 g, <i>Aucklandia lappa</i> 15 g, <i>Buthus martensii</i> Karsch 15 g, <i>Pinellia ternata</i> 15 g	Decoction	Yang Qi does not converge, wind and evil invade outside	Zhu Shi Ji Yan Fang《朱氏集验方》
Bajunzi soup	<i>Panax ginseng</i> 3 g, <i>Poria cocos</i> 3 g, <i>Atractylodes macrocephala</i> 3 g, <i>Glycyrrhiza uralensis</i> 1.5 g, <i>Pinellia ternata</i> 3 g, <i>Citrus reticulata</i> 2.4 g, <i>Atractylodes lancea</i> (Thunb.) DC. 2.4 g, <i>Angelica sinensis</i> 7.5 g	Decoction	Dampness and phlegm in the spleen and stomach	Chen Nang An Fu Ke Bu Xie《陈囊庵妇科补解》
Bafeng nord	<i>Talcum</i> 30 g, <i>Gastrodia elata</i> Bl. 30 g, <i>Cinnamomum camphora</i> (L.) Presl 0.3 g, <i>Moschus berezovskii</i> Flerov 0.3 g, <i>Bombyx mori</i> Linnaeus 15 g, <i>Typhonium giganteum</i> Engl. 9 g, <i>Pinellia ternata</i> 60 g, <i>Calcium</i> 250 g	Pills	Phlegm-heat attack	Taiping Huimin Heji Ju Fang《太平惠民和剂局方》
Bawu soup	<i>Rehmannia glutinosa</i> processing with wine 6 g, <i>Ligusticum chuanxiong</i> 6 g, <i>Paeonia lactiflora</i> 6 g, <i>Angelica sinensis</i> 6 g, <i>Panax ginseng</i> 4.5 g, <i>Atractylodes macrocephala</i> 9 g, <i>Citrus reticulata</i> 3 g, <i>Pinellia ternata</i> 6 g	Decoction	Enrich the Qi and the blood	Nu Ke Qie Yao《女科切要》
Bailuo pill	<i>Atractylodes lancea</i> (Thunb.) DC. 60 g, <i>Gardenia jasminoides</i> Ellis 60 g, <i>Cyperus rotundus</i> 60 g, <i>Arisaema erubescens</i> 60 g, <i>Citrus aurantium</i> 15 g, <i>Citrus reticulata</i> 15 g, <i>Aucklandia lappa</i> 15 g, <i>Pinellia ternata</i> 15 g, <i>Amomum kravanh</i> 15 g	Pills	Accumulation of phlegm and beverages, pain in the stomach and epigastric region	Dan Xi Xin Fa《丹溪心法》
Banxia soup	<i>Pinellia ternata</i> 10 g, <i>Setaria italica</i> (L.) Beauv. 15 g	Decoction	Relieving phlegm and harmonizing the stomach	Ling Shu《灵枢》
Baiziren soup	<i>Platycladus orientalis</i> (L.) Franco 15 g, <i>Codonopsis pilosula</i> (Franch.) Nannf. 15 g, <i>Atractylodes macrocephala</i> 10 g, <i>Pinellia ternata</i> 6 g, <i>Schisandra chinensis</i> 10 g, <i>Ostrea gigas</i> Thunberg 20 g, <i>Ephedra sinica</i> 10 g, <i>Triticum aestivum</i> L 15 g, <i>Ziziphus jujuba</i> Mill. 5 piece	Decoction	Calming the mind and tranquilizing the soul, nourishing Yin and astringing sweat	Zhou Mi Dao Fang《周明道方》
Baiziren pill	<i>Platycladus orientalis</i> 60 g, <i>Rhizoma Pinelliae Fermentata</i> 60 g, <i>Ostrea gigas</i> 30 g, <i>Panax ginseng</i> 30 g, <i>Atractylodes macrocephala</i> 30 g, <i>Ephedra sinica</i> 30 g, <i>Schisandra chinensis</i> 30 g, <i>Triticum sativum</i> 15 g	Pills	Deficiency of heart yang, heart twitching and night sweating	Yi Zong Bi Du《医宗必读》
Banxia Baizhu Tianma soup	<i>Pinellia ternata</i> 4.5 g, <i>Atractylodes macrocephala</i> 6 g, <i>Gastrodia elata</i> 4.5 g	Decoction	Strengthening the spleen and resolving phlegm, calming the liver and calming the wind	Gu Jin Yi Jian《古今医鉴》
Baiqian soup	<i>Cynanchum glaucescens</i> (Decne.) Hand.-Mazz. 6 g, <i>Aster tataricus</i> 9 g, <i>Pinellia ternata</i> 9 g, <i>Cirsium japonicum</i> Fisch. ex DC. 3 g	Decoction	Treatment of cough and upper air, body swelling	Wai Tai Mi Yao《外台秘要》
Bangua pill	<i>Pinellia ternata</i> 150 g, <i>Trichosanthes kirilowii</i> Maxim. 150 g, <i>Platycodon grandiflorum</i> 60 g, <i>Citrus aurantium</i> 45 g, <i>Dioscorea opposita</i> Thunb. 30 g	Pills	Relieve phlegm and cough	Yi Xue Ru Men《医学入门》
Banjie soup	<i>Paeonia lactiflora</i> 30 g, <i>Bupleurum chinense</i> 6 g, <i>Angelica sinensis</i> 9 g, <i>Ligusticum chuanxiong</i> 15 g, <i>Glycyrrhiza uralensis</i> 3 g, <i>Vitex trifolia</i> L. 3 g, <i>Pinellia ternata</i> 3 g	Decoction	Clearing the liver and relieving depression, invigorating the blood and dispelling wind	Bian Zheng Lu《辨证录》
Banbei pill	<i>Pinellia ternata</i> 9 g, <i>Fritillaria cirrhosa</i> D. Don 9 g	Pills	Truncated malaria	Chong Ding Tong Shu Treatise on Febrile Disease《重订通俗伤寒论》
Banxia Buxin soup	<i>Pinellia ternata</i> 12 g, <i>Zingiber officinale</i> 10 g, <i>Poria cocos</i> 6 g, <i>Cinnamomum cassia</i> 6 g, <i>Citrus aurantium</i> 6 g, <i>Citrus reticulata</i> 6 g, <i>Atractylodes macrocephala</i> 8 g, <i>Saposhnikovia divaricata</i> 4 g, <i>Polygala tenuifolia</i> Willd. 4 g	Decoction	Warming the stomach and invigorating the spleen, regulating Qi and resolving drinks	Bei Ji Qian Jin Yao Fang《备急千金要方》
Banxia Lige pill	<i>Atractylodes macrocephala</i> 30 g, <i>Panax ginseng</i> 30 g, <i>Poria cocos</i> 30 g, <i>Alumen</i> 30 g, <i>Talcum</i> 30 g, <i>Fritillaria cirrhosa</i> 30 g, <i>Arisaema erubescens</i> 45 g, <i>Typhonium giganteum</i> 60 g, <i>Pinellia ternata</i> 90 g	Pills	Expelling wind and resolving phlegm, benefiting Qi and strengthening the spleen	Yu Yao Yuan Fang《御药院方》
Banxia Renshen wine	<i>Pinellia ternata</i> 30 g, <i>Scutellaria baicalensis</i> 30 g, <i>Zingiber officinale</i> 20 g, <i>Panax ginseng</i> 20 g, <i>Glycyrrhiza uralensis</i> processing with honey 20 g, <i>Coptis chinensis</i> 6 g, <i>Ziziphus jujuba</i> 10 g, Liquor 700 mL	Decoction	Harmonizing the stomach and subduing rebelliousness, opening up knots and dispersing lumps	Shang Han Lun《伤寒论》

(continued on next page)

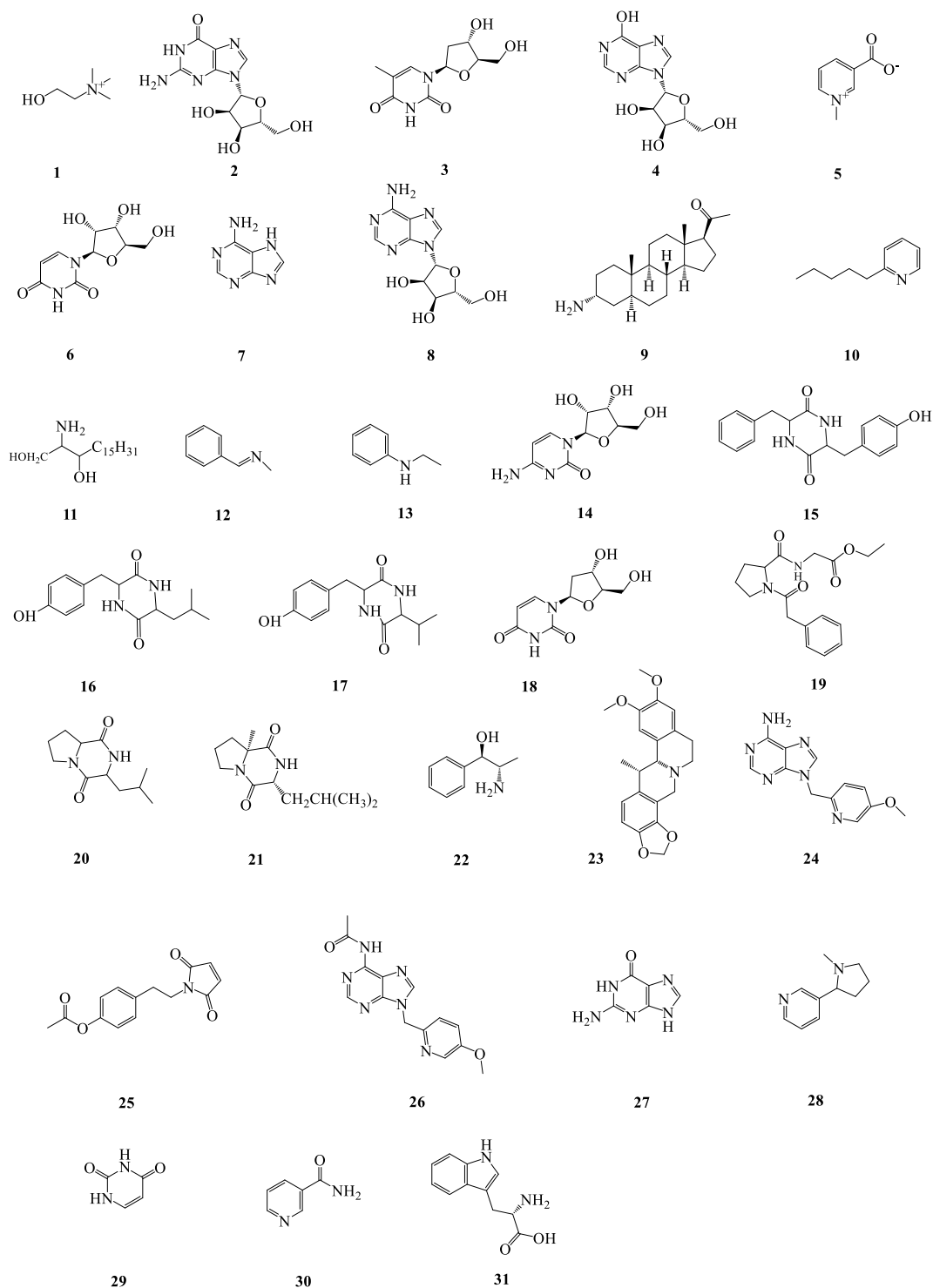
Table 1 (continued)

Banxia powder	<i>Pinellia ternata</i> 60 g, <i>Euodia rutaecarpa</i> (Juss.) Benth. 15 g, <i>Cinnamomum cassia</i> 30 g, <i>Panax ginseng</i> 30 g, <i>Atractylodes macrocephala</i> 30 g, <i>Angelica sinensis</i> 30 g, <i>Magnolia officinalis</i> 45 g, <i>Citrus aurantium</i> 15 g	Powder	warming in the middle and lowering the rebellion	Tai Ping Sheng Hui Fang《太平圣惠方》
Banxia Shengjiang soup	<i>Zingiber officinale</i> 15 g, <i>Pinellia ternata</i> 10 g	Decoction	Warming the stomach and lowering rebellion	Lei Zheng Huo Ren Shu《类证活人书》
Banxia xingren soup	<i>Pinellia ternata</i> 3 g, <i>Prunus armeniaca</i> 2.4 g, <i>Citrus aurantium</i> 1.5 g, <i>Platycodon grandiflorum</i> 1.5 g, <i>Scutellaria baicalensis</i> 1.5 g, <i>Perilla frutescens</i> 1.5 g, <i>Ephedra sinica</i> 1.8 g, <i>Glycyrrhiza uralensis</i> 12 g	Decoction	Mainly for wind and phlegm asthma	Xing Yuan Sheng Chun《杏苑生春》
Banxia yunfang	<i>Pinellia ternata</i> 90 g, <i>Zingiber officinale</i> 90 g, <i>Asarum sieboldii</i> 90 g, <i>Cinnamomum cassia</i> 20 g, <i>Aconitum carmichaelii</i> 10 piece	Decoction	Mainly for pediatric craniosynostosis	Bei Ji Qian Jin Yao Fang《备急千金要方》
Banxia yinzi	<i>Pinellia ternata</i> 12 g, <i>Magnolia officinalis</i> 9 g, <i>Panax ginseng</i> 9 g, <i>Atractylodes macrocephala</i> 9 g, <i>Zingiber officinale</i> 9 g, <i>Ziziphus jujuba</i> 9 g, <i>Semen Oryzae Sativae</i> 10 g, <i>Citrus reticulata</i> 6 g	Decoction	Benefiting Qi and tonifying the middle Jiao, lowering rebellion and stopping vomiting	Wai Tai Mi Yao《外台秘要》
Banxia pill	<i>Alumen</i> 450 g, <i>Pinellia ternata</i> 1500 g	Pills	Relieve phlegm and cough	Taiping Huimin Heji Ju Fang《太平惠民和剂局方》
Buqi Zhenjing soup	<i>Astragalus membranaceus</i> 24 g, <i>Platycladus orientalis</i> 12 g, <i>Ligusticum chuansiong</i> 6 g, <i>Polygala tenuifolia</i> 10 g, <i>Acorus tatarinowii</i> 10 g, <i>Poria cocos</i> 10 g, <i>Angelica sinensis</i> 10 g, <i>Paeonia lactiflora</i> 10 g, <i>Ziziphus jujuba</i> Mill 10 g, <i>Pinellia ternata</i> 10 g, <i>Arisaema Cum Bile</i> 6 g, <i>Asarum sieboldii</i> 3 g, <i>Glycyrrhiza uralensis</i> 4.5 g	Decoction	Tonifying Qi and expelling blood stasis, relieving spasm and resolving phlegm	Lu Ji Ping Fang《路际平方》
Bengtun soup	<i>Glycyrrhiza uralensis</i> 6 g, <i>Angelica sinensis</i> 6 g, <i>Pinellia ternata</i> 12 g, <i>Scutellaria baicalensis</i> 6 g, <i>Pueraria lobata</i> 15 g, <i>Paeonia Lactiflora</i> 6 g, <i>Zingiber officinale</i> 12 g, <i>Euonymus tenguuehensis</i> W. W. Smith 12 g	Decoction	Treatment of Penetrating Dolphin Qi up to the chest and abdominal pain	Jin Kui Yao Lue《金匱要略》
Bishengyin	<i>Pinellia ternata</i> 6 g, <i>Citrus aurantium</i> 6 g, <i>Gypsum Fibrosum</i> 9 g, <i>Prunus sibirica</i> L. 3 g, <i>Tea</i> 3 g, <i>Ephedra sinica</i> 3 g, <i>Trichosanthes kirilowii</i> 3 g, <i>Glycyrrhiza uralensis</i> 3 g, <i>Zingiber officinale</i> 5 piece	Decoction	Promoting the lowering of the lung and Qi, clearing heat and resolving phlegm	Dan Tai Yu An《丹台玉案》
Canglian soup	<i>Atractylodes lancea</i> 3 g, <i>Coptis chinensis</i> 3 g, <i>Citrus reticulata</i> 3 g, <i>Pinellia ternata</i> 3 g, <i>Poria cocos</i> 3 g, <i>Massa Medicata Fermentata</i> 3 g, <i>Euodia rutaecarpa</i> 1.5 g, <i>Amomum kravanh</i> 1.5 g, <i>Glycyrrhiza uralensis</i> 0.9 g	Decoction	Drying dampness and resolving phlegm, clearing the stomach and harmonizing the middle	Wan Bing Hui Chun《万病回春》
Biantong Shiwei Wendan decoction	<i>Citrus reticulata</i> 9 g, <i>Poria cocos</i> 12 g, <i>Pinellia ternata</i> 12 g, <i>Glycyrrhiza uralensis</i> 3 g, <i>Citrus aurantium</i> 6 g, <i>Rehmannia glutinosa</i> 15 g, <i>Ziziphus jujuba</i> 15 g, <i>Polygala tenuifolia</i> 6 g, <i>Acorus tatarinowii</i> Schott 6 g, <i>Succus Bambusae</i> 3 spoons	Decoction	Palpitations and insomnia, mental dementia	Zhong Yi Zhi Fa Yu Fang Ji《中医治法与方剂》
Canheyin	<i>Terminalia chebula</i> Retz 7.5 g, <i>Atractylodes macrocephala</i> 7.5 g, <i>Astragalus Membranaceus</i> 7.5 g, <i>Poria cocos</i> 7.5 g, <i>Panax ginseng</i> 7.5 g, <i>Rhizoma Pinelliae Fermentata</i> 7.5 g, <i>Citrus reticulata</i> 6 g, <i>Schisandra chinensis</i> 6 g, <i>Glycyrrhiza uralensis</i> 3 g, <i>Aster tataricus</i> 3 g	Decoction	Treatment of cold and phlegm cough	Wei Shi Jia Cang Fang《魏氏家藏方》
Biejiajian pill	<i>Trionyx sinensis</i> Wiegmann 90 g, <i>Scutellaria baicalensis</i> 22.5 g, <i>Bupleurum chinense</i> 45 g, <i>Zingiber officinale</i> 22.5 g, <i>Rheum palmatum</i> 22.5 g, <i>Paeonia Lactiflora</i> 37.5 g, <i>Cinnamomum cassia</i> 22.5 g, <i>Lepidium apetalum</i> Willd 7.5 g, <i>Pyrosia shearerii</i> (Bak.) Ching 22.5 g, <i>Magnolia officinalis</i> 22.5 g, <i>Paeonia Suffruticosa</i> Andr. 37.5 g, <i>Dianthus superbus</i> L. 15 g, <i>Pinellia ternata</i> 7.5 g, <i>Equus asinus</i> Linnaeus 37.5 g, <i>Copris reflexus</i> 45 g, <i>Prunus persica</i> (L.) Batsch 15 g	Pills	Promoting circulation of Qi, resolving blood stasis, softening hardness and dispersing knots	Jin Kui Yao Lue《金匱要略》
Banqin soup	<i>Pinellia ternata</i> 15 g, <i>Poria cocos</i> 15 g, <i>Coptis chinensis</i> 3 g, <i>Magnolia officinalis</i> Rehd. et Wils. 9 g, <i>Tetrapanax papyrifer</i> (Hook.) K. Koch 24 g	Decoction	Dry dampness and promote water	Wen Bing Tiao Bian《温病条辨》
Bixaosan	<i>Cortex Hibisci</i> 120 g, <i>Mylabris phalerata</i> Pallas 3 g, <i>Pinellia ternata</i> 15 g, <i>Momordica cochinchinensis</i> (Lour.) Spreng 15 g, <i>Areca catechu</i> L.15 g, <i>Realgar</i> 9 g, <i>Arsenic</i> 3 g	Powder	Treatment of rheumatic scabies and long-standing ringworm	Gu Jin Yi Jian《古今医鉴》

4. Traditional uses

4.1. Processing drugs

Raw PR is a toxic traditional Chinese medicine (TCM) that has been described as having strong irritant toxicity [3]. The toxicity of PR has been recorded in the Shennong Herbal Classic. In ancient times, water, ginger juice, licorice, tofu, alum, and rice vinegar were the common ingredients used in the processing of PR. In modern research, licorice, lime, ginger, and alum are more effective than the



Alkaloid (1-31)

Fig. 3. Structures of alkaloid isolated from *Pinellia ternata* (Thunb.) Breit.

previously used substances in reducing toxicity and improving efficiency. However, only three kinds of processed products were included in the Chinese pharmacopoeia, including Fa-Banxia, Jiang-Banxia, and Qing-Banxia [4].

Fa-Banxia is made by long-term soaking of PR, licorice extract, and lime, which has the effects of drying dampness and resolving phlegm. Licorice can enhance the role of removing the phlegm while reducing toxicity; in contrast, lime can ensure that PR will not rot by long-term soaking. Jiang-Banxia is made by boiling PR, ginger, and alum, which has the effects of resolving phlegm and stopping vomiting. Ginger and alum can enhance the effect of resolving phlegm and reduce toxicity. Additionally, ginger can also enhance the effect of stopping vomiting. Qing-Banxia is made by long-term soaking in PR and lime, which has the effects of drying dampness and resolving phlegm. Alum can enhance the role of resolving phlegm while reducing toxicity and ensuring that the PR will not rot by long-term soaking. Modern research has found that researchers using mice ammonia cough method, tracheal phenol red excretion method, electrical stimulation of the cat supraglottic nerve due to cough model, ammonia fumigation cough model mice, have confirmed that the PR has the efficacy of analgesic cough expectorant. The antiemetic effect of PR was confirmed using a model of mink locomotor

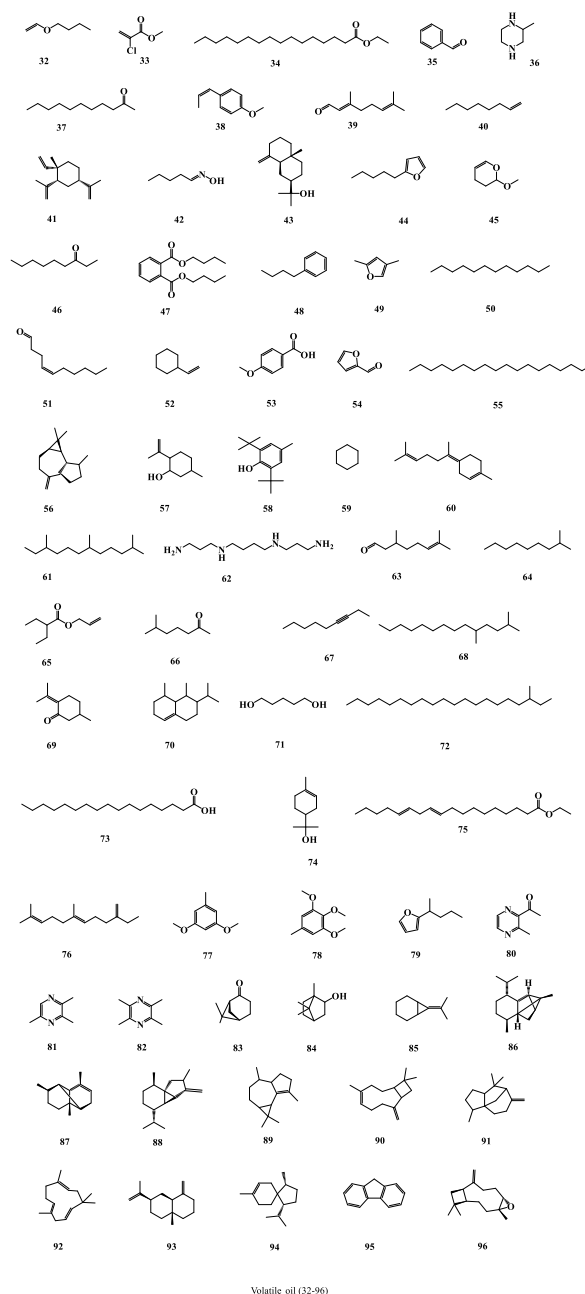


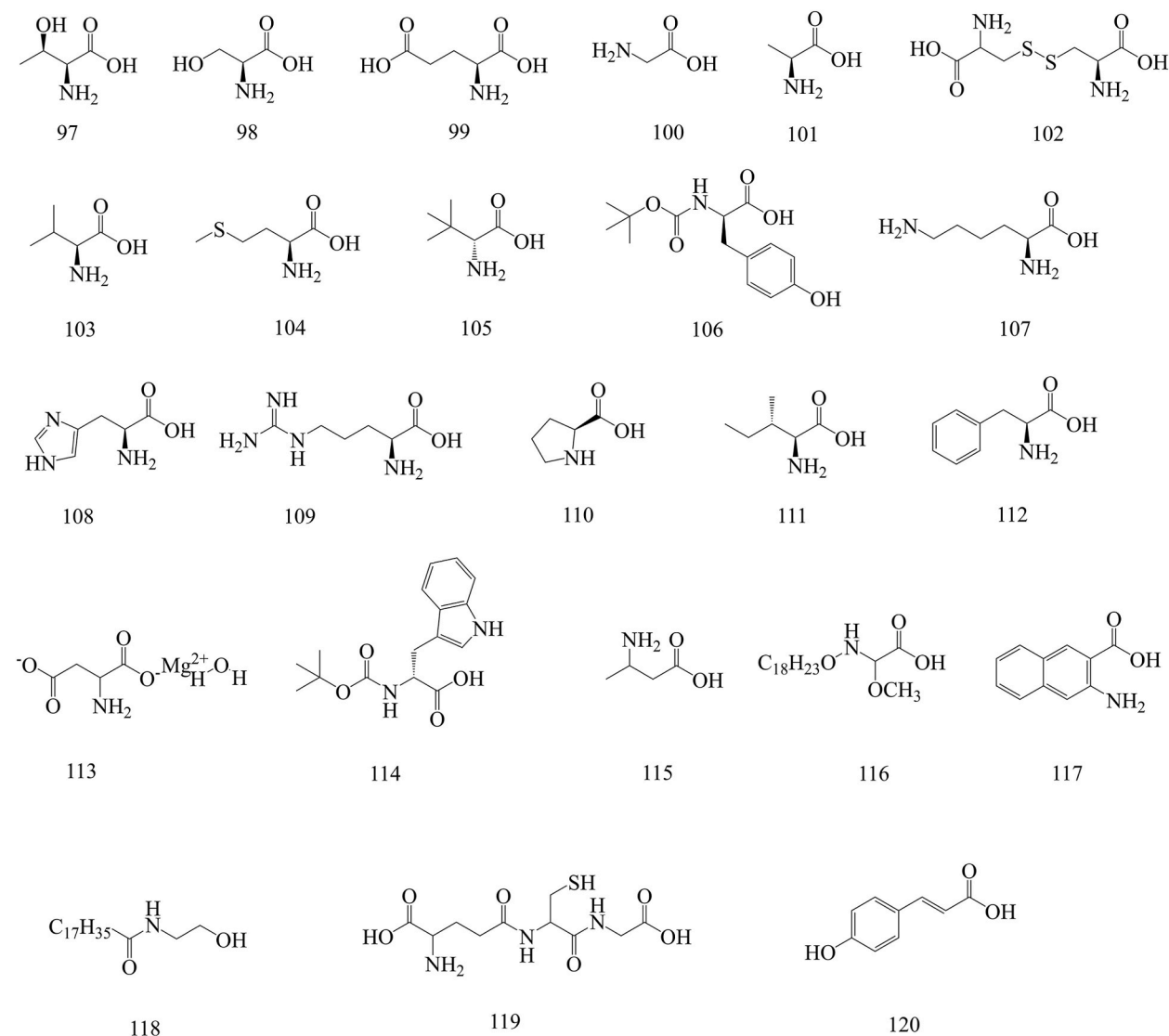
Fig. 4. Structures of volatile oil isolated from *Pinellia ternata* (Thunb.) Breit.

vomiting induced by various vomitogenic agents such as digitalis, apomorphine and copper sulfate. Using a mouse model of colon adenocarcinoma under the intervention of chemotherapeutic drugs, as well as Ehrlich ascites carcinoma cells, gastric cancer BGC823 cells, and chronic myelogenous leukemia cells (5K62), the anticancer effect of PR was confirmed. The anti-inflammatory and analgesic effects of PR were confirmed using the xylene-induced auricular swelling model in mice, and the pain model in mice caused by the hot plate method [1,5].

In summary, although modern studies have shown that processing PR reduces its toxicity and enhances its efficacy, there have been relatively few studies on the changes in its components before and after processing. In future research work, comparisons of different compositions will be key for clarifying the processing principles and will provide a more accurate scientific basis for clinical use.

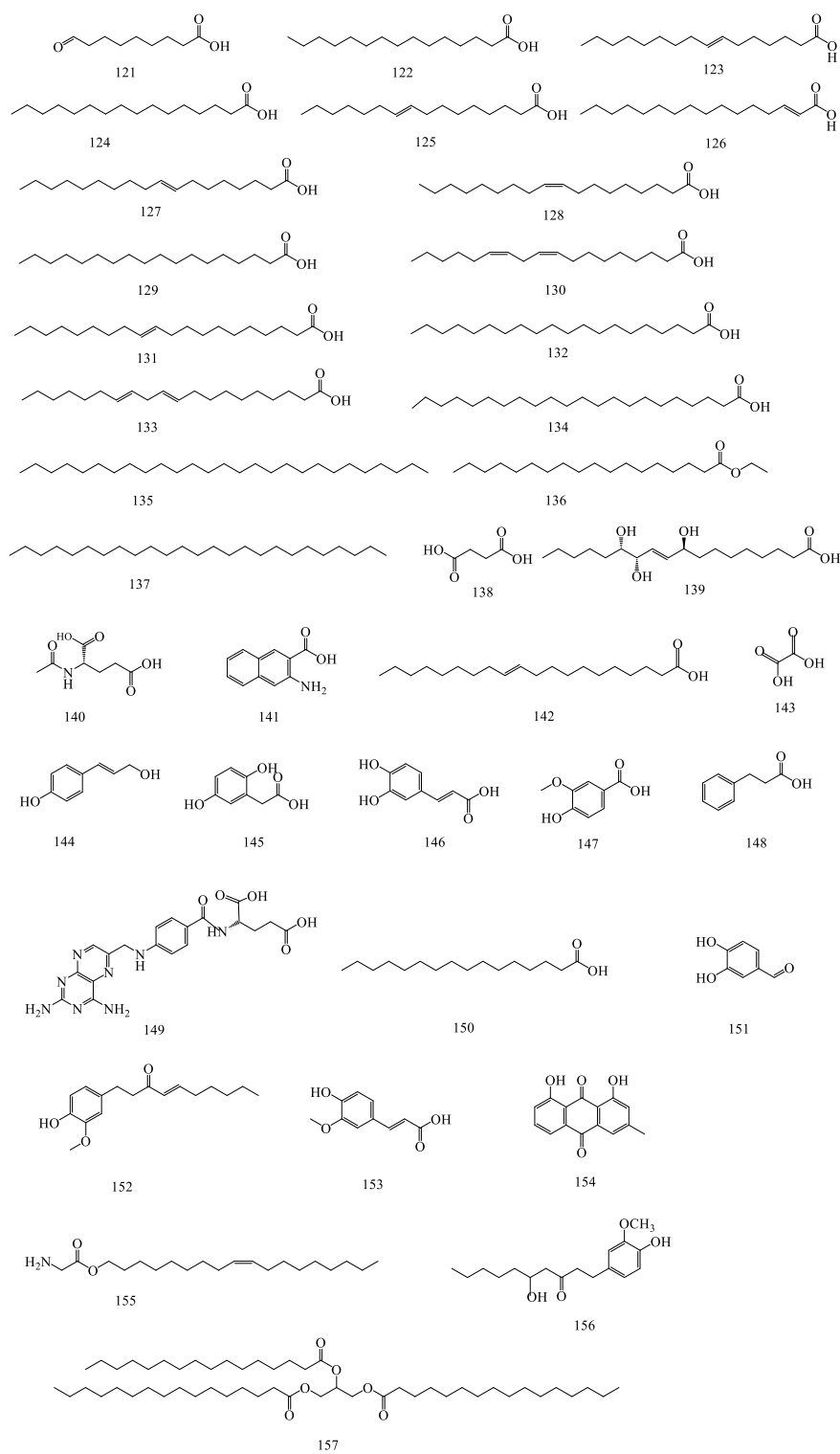
4.2. Prescription application

PR, as a TCM, has a history of more than 2000 years in China. It was first published in the Shennong Herbal Classic (Han Dynasty), which states that it was used to treat cough, excessive phlegm, nausea and vomiting, and soreness and swelling due to poison. The Liu juan zi gui yi fang (Jin Dynasty) states that it was used to treat carbuncles and gangrene; the Bei ji qian jin yao fang (Tang Dynasty) recorded that was used for treating kidney yang deficiency; the Wai tai mi yao (Tang Dynasty) states that it was used for the treatment



Amino acids (97-120)

Fig. 5. Structures of Amino acids isolated from *Pinellia ternata* (Thunb.) Breit.



Organic acids (121-157)

Fig. 6. Structures of Organic acid isolated from *Pinellia ternata* (Thunb.) Breit.

of cough and asthma; the Taiping Huimin Mixture (Song Dynasty) recorded that it was used to treat wind phlegm; and the Yao lei fa Xiang (Yuan Dynasty) recorded its efficacy in treating headache. Modern studies have shown that Huang et al. [6] found that *Pinellia ternata* alkaloids can improve the immune function of tumor model mice, improve the immune microenvironment, and have a certain inhibitory effect on tumor cells. Cheng et al. [7] used the total alkaloids of PR in mice by gavage for 13 d and found that the total alkaloids of PR prolonged the latency period of epilepsy and attenuated the extent of seizures in rats with chronic ignition of penicillin. Huang et al. [8] found that PR polysaccharide can inhibit mucus secretion in lung tissue and reduce sputum production in allergic asthma model rats, etc.

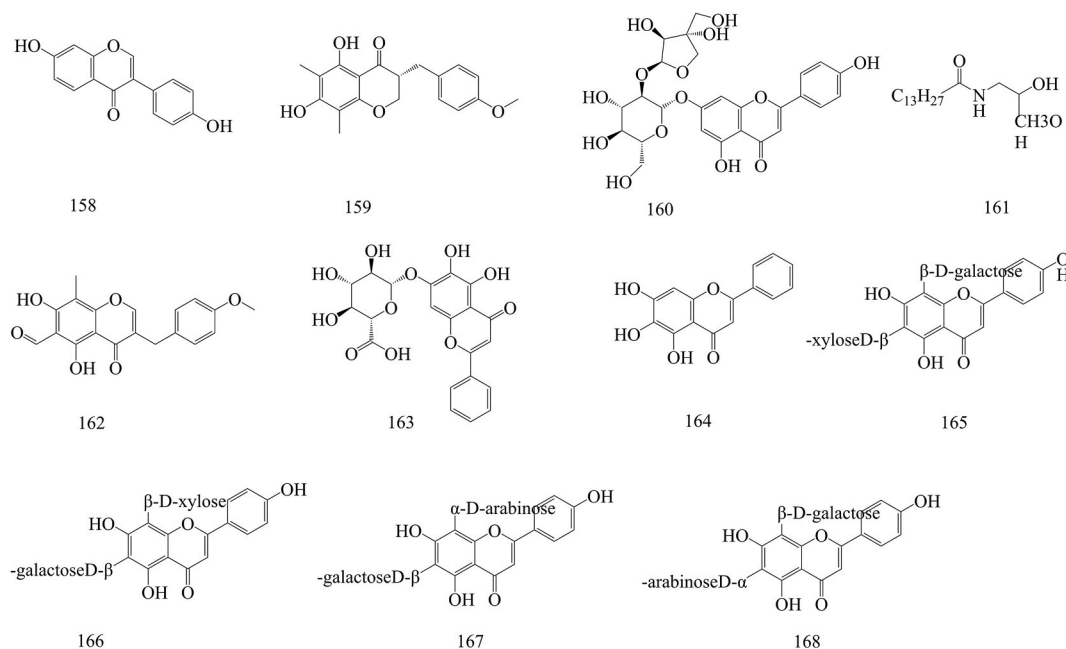
PR has become an important herbal medicine, which is commonly used in the clinical treatment of tumor, gastric ulcer, diarrhea, epilepsy, and other diseases. Simultaneously, various forms of formulations have been developed, including powders, pills, and tablets, to better meet the clinical needs (Table 1)

5. Phytochemistry

In the past few decades, 212 compounds have been separated and authenticated, predominantly comprising alkaloids (1–31) (Fig. 3), volatile oils (32–96) (Fig. 4), amino acids (97–120) (Fig. 5), organic acids (121–157) (Fig. 6), flavonoids (158–168) (Fig. 7), cerebrosides (169–177) (Fig. 8), phenylpropanoids (178–194) (Fig. 9) and others (195–212) (Fig. 10). Based on previous phytochemical investigations, the compounds have been isolated from different parts of PR (Table 2). Alkaloids, flavonoids, and organic acid are the most important and abundant bioactive constituents in PR extracts. It is considered as a promising ingredients for future evaluation. Nevertheless, quantitative detection of the active components requires further research [9–25].

Lectin is a type of protein or glycoprotein that can agglutinate red blood cells (RBCs). There have been many studies on it, too. Sun et al. [26] isolated and purified for the first time a protein with coagulant activity on rabbit erythrocytes from *Pinellia Pedatisecta* Agglutinin (PPA), which was confirmed by chemical analysis. PPA was first isolated and purified from PR, and its amino terminus was alanine, and the sugar chain part contained mannose, fucose and ethylphthalazinylglucosamine, as confirmed by chemical analysis. Liu et al. [27] isolated and purified lectin from PR, and analysis showed that it contained homotetramers of similar molecular weight and pI 5.8. Wang et al. [28] human screened seven signature enzyme peptides from toxic proteins by a comparative proteogenomic strategy of open-source transcriptomic data on PR and its *Typhonii Rhizoma* (TR), *Arisaematis Rhizoma* (AR) and tubers of *Typhonium flagelliforme* (TF) and *Pinellia pedatisecta* (PP). Counterfeit species were well identified. Kuarat.K et al. [29] isolated a glycoprotein named 6 KP, one of the major proteins in *Pinellia ternata* bulbs. Fan et al. [30] obtained a nodular product containing *Pinellia ternata* proteins consisting of various amino acids such as cystine, arginine, aspartic acid and alanine from *Pinellia ternata* tubers.

Polysaccharide is a macromolecular saccharide composed of multiple monosaccharide molecules connected by glycosidic bonds. Plant polysaccharides are widely distributed in nature and are one of the basic substances to maintain the normal operation of life.



Flavonoid (158–168)

Fig. 7. Structures of Flavonoids isolated from *Pinellia ternata* (Thunb.) Breit.

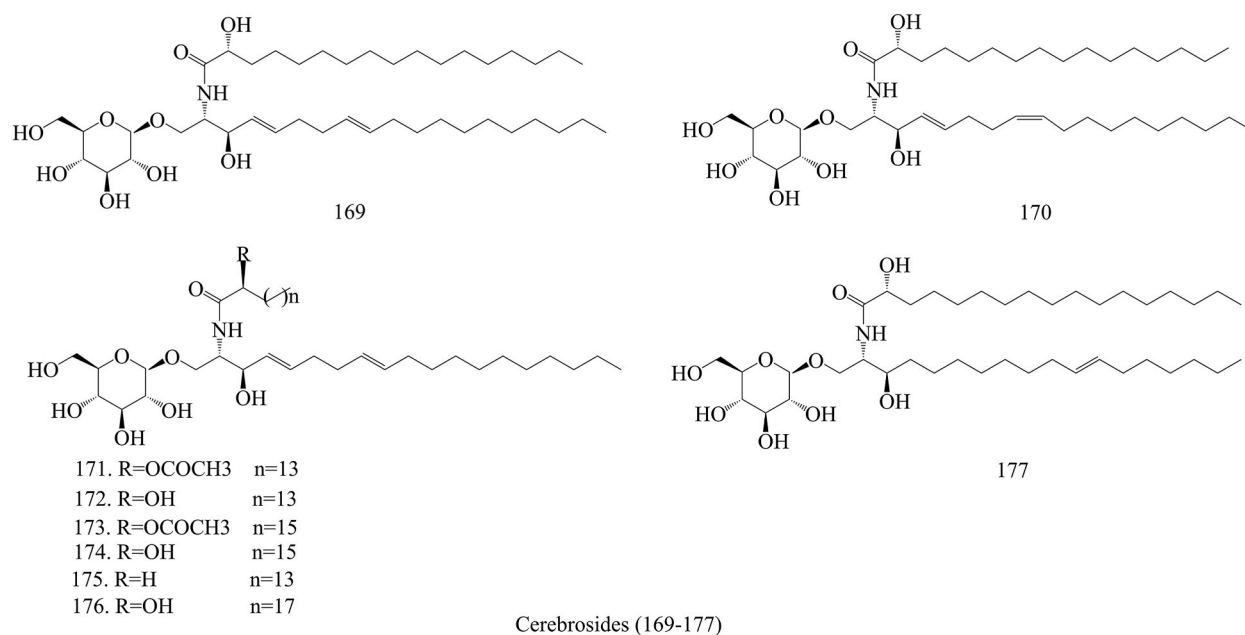


Fig. 8. Structures of Cerebrosides isolated from *Pinellia ternata* (Thunb.) Breit.

With the extraction and separation of various effective components in PR, *Pinellia ternata* polysaccharide has been gradually recognized by researchers. PT-F2-I is a polysaccharide with a molecular weight of about 850,000 isolated from the aqueous extract of PR, consisting of ribose, rhamnose, galactose, glucose, fucose, and arabinose in a molar ratio of 0.05: 0.05: 0.09: 0.10: 0.12: 1.00 [31]. Heteropolysaccharides with a molecular weight of about 10,000 were also extracted from PR, while the acidic polysaccharides obtained consisted of D-galacturonic acid, D-glucuronic acid, L-arabinose, D-galactose, and L-rhamnose (3:3:5:15:1), which had a molecular weight of 118,104, and the main chain consisted of -(1 → 3)-linked D-galactose units, and the side chain consisted of -(1 → 6)-linked D-galactose, while some of the sugar units were connected to the acetyl group and peptide fragments. From *Pinellia ternata* tubers, -(1 → 4) glucan was also isolated, consisting of D-glucans with some sugar units attached to acetyl groups, containing branched chains, with -(1 → 4)-linked D-glucans in the main chain, and partially -(1 → 3)- and -(4 → 6)-linked, which are straight-chained amylopectin with molecular weight of 4100 [32].

6. Extraction method

At present, the research on extraction methods mainly focuses on flavonoids, alkaloids, polysaccharides, and volatile oils in PR. Most of them use the response surface method to optimize the extraction process, but the extraction time varies considerably. When extracting one of the effective parts, the extraction rate of the other effective parts is not fully considered. The extracted components are relatively simple, but the optimization process of phenylpropanoids, organic acids, and other components is more complex. In the future, more consideration should be given to the comprehensive extraction of various components and the optimization of the PR extraction process. A summary of how the PR methods are extracted is provided in Table 3 [33–42].

7. Pharmacological effects

Extracts and certain constituents of PR have progressively exhibited diverse pharmacological properties, among which, antitumor, anticonvulsant, analgesic, and sedative properties are associated with traditional uses. Additionally, several new pharmacological effects have been discovered, including hypolipidemic, anti-gastric ulcer, antidepressant, and other functions. These pharmacological findings are discussed in the following sections and summarized in (Figs. 11–12) and Table 4.

7.1. Respiratory pharmacological effects

7.1.1. Cough suppressant effects

Xiong et al. [71] evaluated the antitussive effect of PR on a mouse cough model induced by ammonia. The results showed that the number of coughs in mice was decreased, and the white blood cell (WBC), lymphocyte (LYM), and monocyte (MON) indices of blood cells was significantly increased. Later research also proved that PR has an antitussive effect through similar experiments also found that PR had an antitussive effect that persisted for more than 5 h by injecting iodine into the chest cavity or electrically stimulating the superior laryngeal nerve of cats [51,72,73]. Bai et al. [74] found that the antitussive effect of wild PR was obviously better than that of

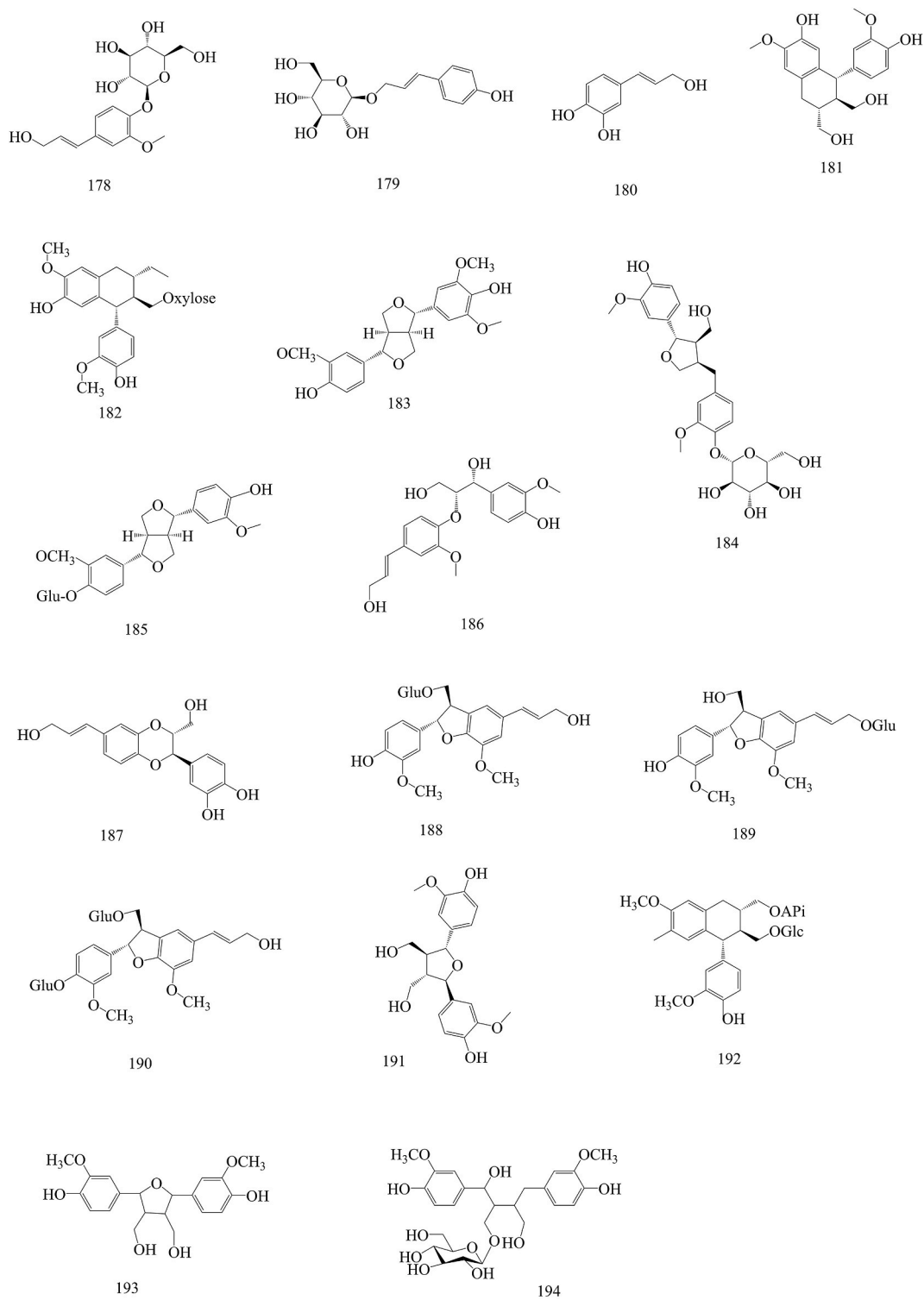


Fig. 9. Structures of Phenylpropanoids isolated from *Pinellia ternata* (Thunb.) Breit.

Table 2
Chemical constituents of *Pinellia ternata* (Thunb.) Breit.

No.	Chemical component	reference
Alkaloids		
1	Choline	[5]
2	Guanosine	[5]
3	Thymidine	[5]
4	Inosine	[5]
5	Trigonelline	[5]
6	Uridine	[5]
7	Adenine	[6]
8	Adenosine	[6]
9	3 α -amino-5 α -pregnan-20-one	[6]
10	2-Pentylpyridine	[6]
11	(2R,3S,4S,6S)-2-(hydroxymethyl)-6-(2-hydroxytridecyl)-3,4-Piperidinediol	[6]
12	N-Benzylidenemethylamine	[6]
13	N-Ethylaniline	[6]
14	Cytidine	[7]
15	Cyclo-(Phe-Tyr)	[8]
16	Cyclo-(Leu-Tyr)	[8]
17	Cyclo-(Val-Tyr)	[8]
18	2'-deoxyuridine	[8]
19	Noopept	[9]
20	Cyclo-pro-ile	[9]
21	Cyclo-pro-val	[4]
22	L-ephedrine	[10]
23	Cavidine	[7]
24	9-(5-methoxypyridin-2-yl) methyl)-9 H-purin-6-amine	[11]
25	4-(2-(2,5-dioxopyrrolidin-1-yl) ethyl) phenyl acetate	[11]
26	N-(9-((5-methoxypyridin-2-yl) methyl)-9 H-purin-6-yl) acetamide	[11]
27	Guanine	[12]
28	Nicotine	[12]
29	Uracil	[12]
30	Nicotinamide	[12]
31	tryptophan	[12]
Volatile oil		
32	n-Butyl vinyl ether	[13]
33	Methyl alpha-chloroacrylate	[13]
34	Ethyl palmitate	[13]
35	Benzaldehyde	[13]
36	2-Methylpiperazine	[13]
37	2-Undecanone	[13]
38	Cis-Anethol	[13]
39	Citral	[13]
40	Octene	[13]
41	Beta-elemene	[13]
42	Valeraldehyde oxime	[13]
43	Beta-Eudesmol	[13]
44	2-Amylfuran	[13]
45	3,4-Dihydro-2-Methoxy-2H-Pyran	[13]
46	Nonan-3-one	[13]
47	Dibutyl phthalate	[13]
48	Butylbenzene	[13]
49	2,4-dimethylfuran	[13]
50	Dodecane	[13]
51	Cis-4-decenal	[13]
52	Vinylcyclohexane	[13]
53	Anisic acid	[13]
54	Furfural	[13]
55	Octadecane	[13]
56	(+)-Aromadendrene	[13]
57	Cyclohexanol,5-methyl-2-(1-methylethenyl)-	[13]
58	Butylated Hydroxytoluene	[13]
59	Cyclohexane	[13]
60	Bisabolene	[13]
61	2,6,10-Trimethyldecane	[13]
62	Dipentene	[13]
63	Citronellal	[13]
64	2-Methylnonane	[13]
65	Allyl 2-ethylbutyrate	[13]
66	6-Methyl-2-heptanone	[13]

(continued on next page)

Table 2 (continued)

No.	Chemical component	reference
67	3-Nonyne	[13]
68	2,5-Dimethyltetradecane	[14]
69	Pulegone	[14]
70	Octahydro-4 α -5-dimethyl-3-isopropyl-naphthalene	[14]
71	1,5-Pentadiol	[14]
72	3-Methyleicosane	[14]
73	Heptadecanoic acid	[17]
74	Terpineol	[20]
75	Octadeca-9,12-dienoic acid ethylester	[21]
76	(E)- β -farnesene	[21]
77	5-methyl-1,3-dimethoxybenzene	[25]
78	3,4,5-trimethoxytoluene	[25]
79	2-pentyl furan	[25]
80	2-acethyl-3-methyl-pyrazine	[25]
81	trimethyl pyrazine	[25]
82	2,3,5,6-tetramethylpyrazine	[25]
83	nopinone	[25]
84	borneol	[25]
85	7-isopropylidene norcarane	[25]
86	cyclosativene	[25]
87	α -ylangene	[25]
88	β -cubebene	[25]
89	α -gurjunene	[25]
90	β -caryophyllene	[25]
91	β -cedrene	[25]
92	α -humulene	[25]
93	β -selinene	[25]
94	α -neocallitropsene	[25]
95	9H-fluorene	[25]
96	β -caryophyllene oxide	[25]
Amino acids		
97	DL-Threonine	[15]
98	Serinic acid	[15]
99	L-glutamic acid	[15]
100	Glycine	[15]
101	Alanine	[15]
102	Cystine	[15]
103	Valine	[15]
104	L-Methionine	[15]
105	D-tert-Leucine	[15]
106	Boc-D-Tyr-OH	[15]
107	L-Lysine	[15]
108	L-Histidine	[15]
109	Argininic acid	[15]
110	Proline	[15]
111	L-isoleucine	[15]
112	Phenylalanine	[15]
113	Magnesium 2-aminosuccinate hydrate	[15]
114	N-[(tert-Butoxy) carbonyl]-D-tryptophan	[15]
115	DL-3-aminobutyric acid	[15]
116	N-dodecanoyl-L-serine	[16]
117	3-Amino-2-naphthoic acid	[16]
118	N- [(dodecyloxy] carbonyl] valine	[16]
119	Glutathione	[16]
120	p-hydroxycinnamic acid	[25]
Organic acids		
121	Nonanoic acid, 9-oxo-	[17]
122	Pentadecanoic acid	[17]
123	7-Hexadecenoic acid	[17]
124	Hexadecanoic acid	[17]
125	9-Hexadecenoic acid	[17]
126	Hexadecenoic acid	[17]
127	8-Octadecenoic acid	[17]
128	Oleic acid	[17]
129	Octadecanoic acid	[17]
130	Linoleic acid	[17]
131	11-Eicosenoic acid	[17]
132	Eicosanoic acid	[17]
133	10,13-Eicosadienoic acid	[17]

(continued on next page)

Table 2 (continued)

No.	Chemical component	reference
134	Docosanoic acid	[17]
135	Heptacosane	[17]
136	Ethyl stearate	[17]
137	Pentacosane	[17]
138	Succinic acid	[18]
139	9(S),12(S),13(S)-Trihydroxy-10(E)-Octadecenoic acid	[19]
140	N-Acetyl-L-glutamic acid	[18]
141	3-Amino-2-naphthoic acid	[12]
142	Gondoic acid	[12]
143	Dicarboxylic Acid	[12]
144	E-P-coumarol	[20]
145	Homogentisic acid	[21]
146	Caffeic acid	[21]
147	Vanillic acid	[21]
148	3-Phenylpropionic acid	[21]
149	12-Octadecadienoic acid	[22]
150	Palmitic acid	[22]
151	Protocatechualdehyde	[21]
152	6-Shogaol	[21]
153	Ferulic acid	[21]
154	Chrysophanic acid	[21]
155	Oleyl glycine	[16]
156	6-gingerol	[25]
157	α -tripalmitin	[25]
Flavonoids		
158	Daidzein	[12]
159	(3R)-2,3-Dihydro-5,7-dihydroxy-3-[(4-methoxyphenyl) methyl]-6,8-dimethyl-4H-1-benzopyran-4-one	[12]
160	Apiin	[12]
161	7- Methyl apigenin	[12]
162	6-Aldehydo-isoophipogonone B	[23]
163	Baicalin	[24]
164	Baicalein	[23]
165	6C- β -D-Xylopyraose-8C- β -D-galactopyranosyl-5,7,4'-three hydroxyl flavone	[23]
166	6C- β -D-Galactopyranosyl-8C- β -D-xylopyraose-5,7,4'-three hydroxyl flavone	[23]
167	6C- β -Galactose-8C- β -arabinose-5,7,4'-three hydroxyl flavone	[23]
168	6C- β -Arabinose-8C- β -galactose-5,7,4'-three hydroxyl Flavone	[23]
Cerebrosides		
169	Soyacerebroside I	[24]
170	Soyacerebroside II	[24]
171	1-O-glucosyl-N-2'-acetoxypalmitoyl-4,8-sphingodienine	[23]
172	1-O-glucosyl-N-2'-hydroxypalmitoyl-4,8-sphingodienine	[23]
173	1-O-glucosyl-N-2'-acetoxystearoyl-4,8-sphingodienine	[23]
174	1-O-glucosyl-N-2'-hydroxystearoyl-4,8-sphingodienine	[23]
175	1-O-glucosyl-N-2'-palmitoyl-4,8-sphingodienine	[23]
176	1-O-glucosyl-N-2'-hydroxyeicosanoyl-4,8-sphingodienine	[23]
177	Pinelloside	[23]
Phenylpropanoids		
178	(E)-Coniferin	[20]
179	Sachalaside 1	[20]
180	3,4-Dihydroxycinnamyl alcohol	[20]
181	(+)-Isolaricresinol	[20]
182	Tiliamuroside A	[20]
183	Wheat sterol	[20]
184	Laricresinol 4-O- β -D-glucopyranoside	[20]
185	Terpineol -4-O- β -D- glucoside	[20]
186	Erythro-guaiacylglycerol- β -O-4'-sinapyl ether	[20]
187	Americanol A	[20]
188	Dehydrodocosanol-9-O- β -D-glucopyranoside	[20]
189	Dehydrodocosanol-9'-O- β -D-glucopyranoside	[20]
190	Dehydrodocosanol-4,9-di-O- β -D-glucoside	[20]
191	Neoolivil	[20]
192	cyclolignanyingoside A	[25]
193	Neo-olivil	[25]
194	Cinnacassoside A	[25]
Others		
195	Isochrysin 9-O- β -D- glucopyranoside	[20]
196	Dehydrodocosanol 4-O- β -D- glucopyranoside	[20]
197	erythritol	[25]
198	gingerol	[25]

(continued on next page)

Table 2 (continued)

No.	Chemical component	reference
199	ammonium glycyrrhizinate	[25]
200	Cinnamon A	[20]
201	Verti-cillatoside A	[20]
202	Daucosterol	[25]
203	Campesterol	[25]
204	Stigmasta-5,22-dien-3-ol	[25]
205	Stigmasta-5,24-dien-3-ol	[25]
206	Cycloartanol	[25]
207	5-Hydroxymethylfurfural	[21]
208	Beta-sitosterol	[21]
209	Eleutheroside A	[22]
210	1,3,12-Nonadecatriene	[22]
211	α -monpalmitin	[22]
212	Pyrrolidine,1-(1-oxo-7,10-hexadecadienyl)	[22]

Table 3

Pinellia ternata (Thunb.) Breit. extraction methods.

Active ingredients	Extraction method	Extraction reagent	Extraction temperature (°C)	Extraction time (h)	Material to liquid ratio (mL/g) Material-to-liquid ratio (mL/g)	Number of extractions	Extraction rate (%) extraction rate	References	
Polysaccharide	Two-phase extraction method	PEG 6000, (NH ₄) ₂ SO ₄	\	44 min	1:1.77	\	44.76 %	[33]	
Alkaloids	Chloroform extraction	Chloroform, 12 % ammonia water	60 °C	25 h	18.00	6	4.56 %	[34]	
Alkaloids	Ultrasonic Assisted Extraction	Chloroform, 12 % ammonia water	80 °C	4 h	18.00	6	4.51 %	[34]	
Total flavonoids	ethanol extraction	62.54 % ethanol	62.72 °C	2.61 h	1:47.10	\	8.91 %	[35]	
Polysaccharide	Water extraction and alcohol precipitation	70 % ethanol	70 °C	1 h	1:30	3	13.68 %	[36]	
Guanosine	Ultrasonic extraction	water	\	2.25 h	1:10	3	16.4 %	[37]	
Polysaccharide	Compound Enzyme Extraction		complex enzyme	54 °C	57 min	1:27	\	27.98 %	[38]
Polysaccharide	Cellulase method		95 % ethanol	55 °C	35 h	The amount of enzyme added is 4 %	\	71.75 %	[39]
Total free organic acids	heating reflow method		75 % ethanol	\	1 h	1:10	2	0.19 %	[40]
Polysaccharide	Ultrasonic extraction		water	\	\	1:12	3	33.3 %	[41]
Total flavonoids	Ultrasonic extraction		50 % ethanol	\	\	1:30	\	1.84 %	[42]

cultivated PR.

Yang [43] studied the antitussive effect of the chemical components of PR and its processed products. Based on the mouse cough model induced by concentrated ammonia water, the antitussive titer of PR and its processed products was determined using the dose-response parallel method, and its efficacy value was determined. Combined with the quantitative determination results of total organic acids, the correlation between total organic acids and biological titer was analyzed. The results showed that the antitussive potency of PR and its processed products was related to the amount of total organic acids. Zhang et al. [18] extracted and separated total free organic acids with 95 % ethanol, and found that total organic acids have an antitussive effect. Zeng et al. [44] used grey correlation analysis to show that the total alkaloids were active constituents that play an antitussive role.

7.1.2. Expectorant effect

Chen et al. [45] evaluated the expected effect of PR by the phenol red secretion in the respiratory tract of mice model. The results showed that the secretion of phenol red in the mouse trachea was increased by PR water extract gavage for seven days. Several studies have also proved that PR has an expectorant effect using similar experiments [44,75]. Deng et al. [46] studied the intervention effect of

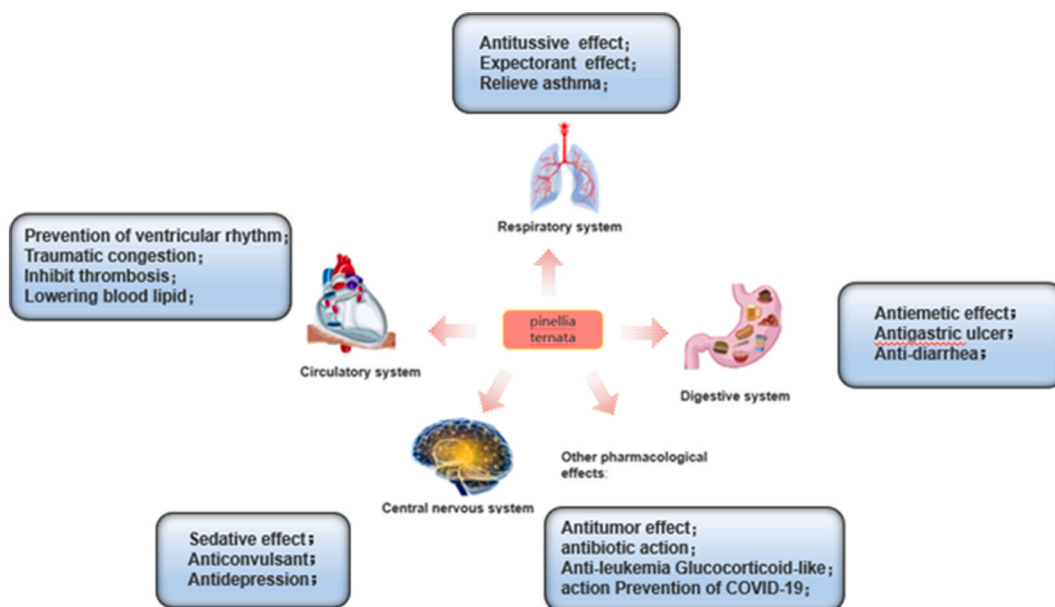


Fig. 11. Pharmacological action diagram of *Pinellia ternata* (Thunb.) Breit.

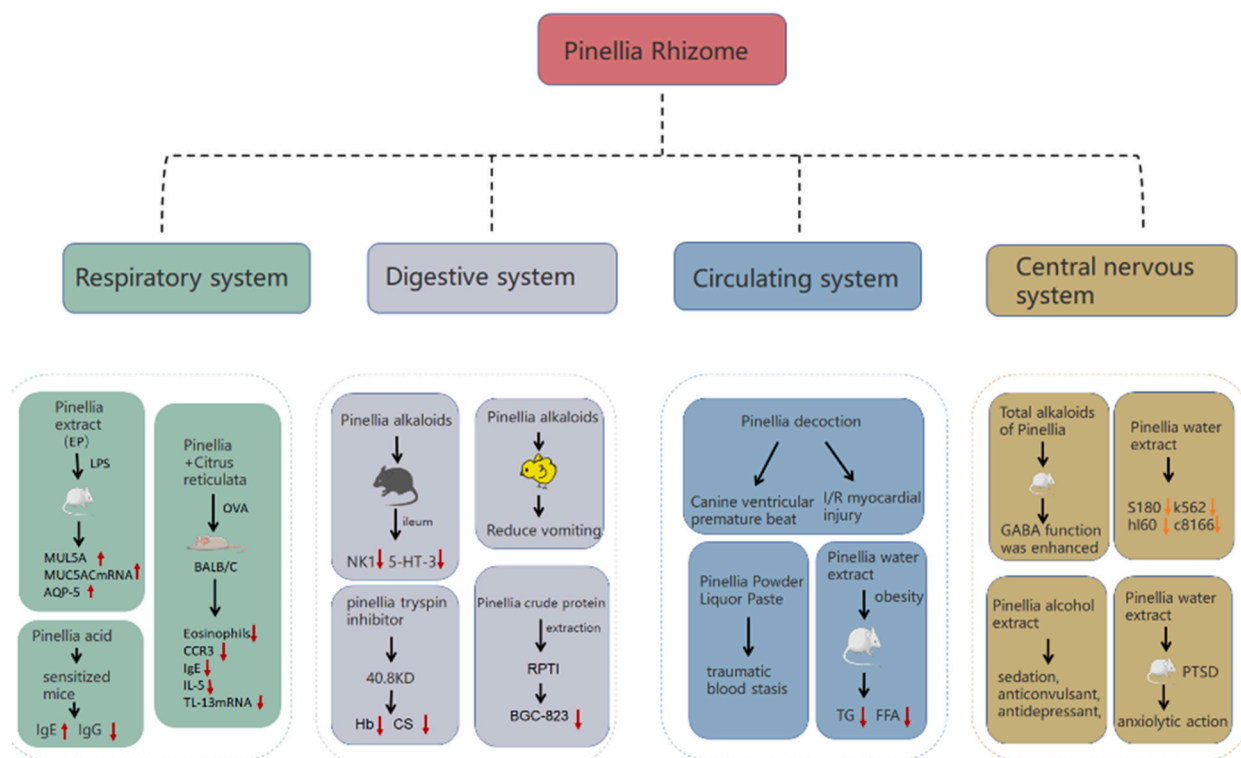


Fig. 12. Pharmacological effect of *Pinellia ternata* (Thunb.) Breit. **Note:** Mucin 5AC messenger RNA (MUC5AC mRNA), Aquaporin-5 (AQP-5), Ovalbumin (OVA), Serum CC chemokine receptor 3 (CCR3), Immunoglobulin E (IgE), Immunoglobulin G (IgG), Interleukin-5 (IL-5), Interleukin-13 (IL-13), Thyroglobulin (TG), Post traumatic stress disorder (PTSD), 5-HT receptor 3 (5-HT-3), natural killer cell 1 (NK1), a trypsin inhibitor (RPTI).

PR extract on a rat airway mucus hypersecretion model induced by lipopolysaccharide (LPS). One hour before LPS injection every day, rats were given PR extract for four consecutive days. The results showed that the expression of MUC5AC protein in the airway epithelium and MUC5AC mRNA in lung tissue were significantly lower than those in the model group, while AQP-5 in the airway

Table 4
Pharmacological research on *Pinellia ternata* (Thunb.) Breit.

system	effect	Element	dose	inside/ outside	references
Respiratory system	Antitussive	Total organic acids	0.41, 0.82 g/kg	In Vivo	[43]
		Total alkaloids	1 mL/0.15 g	In Vivo	[44]
	Apectorant	Pinellia decoction	1.5, 3 g/kg	In Vivo	[45]
		Decoction and alcohol precipitation extract of Pinellia sinensis	10, 30, 60 g/kg	In Vivo	[46]
	Inhibition of ERK activation protects the airway	Pinellia decoction	0.3 g/100 g	In Vivo	[47]
	Protects against allergic airway inflammation	Pinellia Water Extract	13.5, 23.3 mg/kg	In Vivo	[48]
Digestive system	Asthma	Pinellia acid	50 mg/kg	In Vivo	[49]
		Pinellia alkaloids	30 mg/kg	In Vivo	[50]
	Anti-vomit	Pinellia suspension	50, 100 g/kg	In Vivo	[51]
		6 kD globulin	10, 20, 50 mg/kg	In Vivo	[52]
	Fights vomiting caused by apomorphine	Pinellia polysaccharide PT-F2-1		In Vivo	[53]
	Can combat vomiting caused by copper sulfate	Methionine		In Vivo	[54]
	Can combat vomiting caused by cedilan-D	Glycine and D-glucuronic acid		In Vivo	[54]
	Anti-stomach ulcer	5 % ethanol extract of Pinellia chinensis	5, 15 g/kg	In Vivo	[55]
		Pinellia decoction and alcohol precipitation	10, 20 g/kg	In Vivo	[56]
	Stimulate gastric emptying	Pinellia decoction	1, 2.5 g/kg	In Vivo	[57]
		Pinellia micron powder decoction	0.75, 1.5, 3 g/kg	In Vivo	[58]
	Circulatory system	Gastrointestinal propulsion	Ginger Pinellia Powder Suspension	2.5 g/kg	In Vivo
Prevention of ventricular arrhythmias		Qingpinxia decoction	53 g/kg	In Vivo	[60]
traumatic blood stasis		Pinellia powder white wine paste	0.15, 0.25 g/mL	In Vitro	[61]
Central nervous system	Inhibit thrombosis	95 % Ethanol Extract	100 mg/kg	In Vivo	[62]
	blood lipid lowering	Pinellia hot water extract	400 mg/kg	In Vivo	[63]
	Calm down	75 % ethanol extract	8, 12 g/kg	In Vivo	[64]
	anticonvulsant	Pinellia supercritical CO2 ethanol extract		In Vivo	[65]
	Can improve GABAergic nerve function	Pinellia total alkaloids	0.5, 1.0 g/kg	In Vivo	[66]
Others	antidepressant	Pinellia alcohol extract	100, 300, 500 mg/kg	In Vivo	[67]
	Anxiety	Pinellia no-fried granules suspension	3.15 g/kg	In Vivo	[68]
	Improve Parkinson's disease	Pinellia total alkaloids	1, 0.5, 0.25 mg/kg	In Vivo	[69]
	Inhibit tumor growth in the body	Pinellia Water Extract	100 mg/kg	In Vivo	[70]

epithelium was significantly higher than that in the model group. Moreover, Du et al. [47] treated COPD rats with budesonide inhalation for two weeks, and then orally administered PR at a dosage of 3 g/kg for four weeks. The results showed that PR could protect the airway from ICS withdrawal-induced mucus hypersecretion and airway inflammation by inhibiting extracellular signal regulated kinase (ERK) activation.

7.1.3. Asthma calming effect

Ok et al. [76] evaluated the asthma calming effect of PR in an ovalbumin (OVA) induced asthma mice model. A combination of PR and citrus reticulata was used for oral administration. The results showed that eosinophil infiltration, chemokine receptor-3, histamine, and OVA-specific IgE production in serum were reduced, while IL-5 and IL-13 mRNA in lung tissue were inhibited. Lee et al. [48] administered PR water extract at 13.5 mg/kg and 23.3 mg/kg for 25 days and found that PR water extract had a protective effect on allergic airway inflammation. Shan et al. [75] gavaged guinea pigs at 0.15, 0.3, and 0.6 g/kg of PR water extract, and found that the water extract of PR had a certain preventive effect on asthma. Subsequently, Nagai et al. [49] found that Pinellia acid was the active ingredient of PR against allergic airway inflammatory asthma, and gavage of Pinellia acid 50 mg/kg to mice decreased the titer of ovalbumin specific immunoglobulin E (IgE) antibody in the bronchoalveolar lavage fluid of sensitized mice. Moreover, the titer of antiviral immunoglobulin G (IgG) antibody in serum and bronchoalveolar lavage fluid increased by three times.

7.2. Digestive system pharmacological effects

7.2.1. Antivomiting effect

Tang et al. [51] found the antivomiting effect of Hemerocallis by gavage with 50, 100 g/kg of PR suspension through CuSO₄-induced vomiting of domestic pigeons. Zhao et al. [77] similarly demonstrated the antivomiting effect of PR through a mink locomotor

vomiting model. Zhang et al. [50] studied the underlying mechanism of PR in preventing and treating chemotherapy-induced nausea and vomiting by observing the effects of alkaloids in PR on the contraction of isolated guinea pig ileum under the intervention of 5-hydroxytryptophan (5-HT), 2-Methyl-5-HT, substance P, and the selective NK1 receptor agonist GR73632 and measured the peak of contraction force of three-dimensional intestinal tube of guinea pig with an isolated thermostatic bath. The results showed that PR alkaloids had an obvious inhibitory effect on the contraction tension of the guinea pig ileum. The results also showed a certain dose dependence, indicating that PR alkaloids had a certain blocking effect on 5-HT receptor 3 (5-HT₃) and natural killer cell 1 (NK1) receptors in the ileum, that is, PR alkaloids were the main effective part of PR for stopping vomiting. Similarly, it was later demonstrated that PR alkaloids are one of the active components of PR antiemetic [45–50,75–80].

Kurata et al. [52] isolated a water-soluble globulin with a molecular weight of 6 kD from PR. Moreover, when its content was between 5.75 % and 8.30 %, it had an antiemetic effect. Furthermore, by taking the efferent activity of the gastric branch of the vagus nerve in rats as an index. Ao [81] found that the water-soluble and fat-soluble components of PR have antiemetic effects. Maki et al. [53] found that filling the stomach of chickens with PR polysaccharide PT-F2-1 can prevent vomiting caused by apomorphine. Additionally, Ho et al. [54] found that methionine contained in PR can resist vomiting caused by copper sulfate, while glycine and D-glucuronic acid contained in PR can resist vomiting caused by Cedilanid-D.

7.2.2. Anti-gastric ulcer and improvement in gastric function

Shen et al. [55] found that PR had a strong anti-gastric ulcer effect in a gastric ulcer mouse model following oral administration of 5 g/kg and 15 g/kg of crude drugs from PR with 75 % ethanol. Subsequently, Liu et al. [56] and others used two doses (10, 20 g/kg) of PR decoction and alcohol precipitation solution for intragastric administration, which also proved the anti-gastric ulcer effect of PR. Wu et al. [59] gavaged mice with 2.5 g/kg suspension of raw PR and Jiang-Banxia powder for three consecutive days and found that raw PR had no significant impact in gastric emptying, while Jiang-Banxia inhibited it. In previous studies [57,82], mice were given PR decoction (1, 2.5 g/kg) by intragastric administration, which could promote gastric emptying. Li et al. [58] found that gastric emptying could be dose-dependently promoted by intragastric administration of 0.75, 1.5, and 3 g/kg of Pinellia micro-rice flour decoction to mice.

7.2.3. Antidiarrheal and gastrointestinal propulsive motility modulating effects

Zhang et al. [83] gavaged mice with two doses (5, 15 g/kg) of 75 % ethanol extract of PR and found that the number of instances of diarrhea caused by castor oil and senna leaves were reduced within 4 h, while the inhibition time could last for more than 8 h, thereby showing antidiarrhea effects. Wu et al. [59] found that Jiang-Banxia powder suspension (2.5 g/kg) could inhibit the gastrointestinal propulsion of mice by gavage for three days. Oshio et al. [14] found that both methanol and water extracts of PR showed relaxing and antihistamine-like effects on isolated quail rectum. Liu et al. [60] gavaged rabbits with 60 g/kg of Qing-Banxia decoction for four days and found that there was no obvious correlation between the effect of PR on gastrointestinal propulsion and its antidiarrhea effect.

7.2.4. Other pharmacological effects of the digestive system

Wang et al. [84] isolated a trypsin inhibitor (RPTI) with a molecular weight of approximately 14 kD from an extract of crude PR protein. The results showed that the mass inhibition ratio of RPTI to trypsin was approximately 1:4.72, and it could inhibit the cell proliferation of the human poorly differentiated gastric adenocarcinoma cell line BGC-823, with an IC₅₀ of 121.53 µg/mL; thus, RPTI is a type of anti-nausea drug. Wu et al. [85] found a PR trypsin inhibitor with a molecular weight of 40.8 kD, which could inhibit the hydrolysis of amide, ester, hemoglobin and casein by trypsin. Li et al. [86] found that PR decoction (10 %) had no significant effect on the dissolution of gallstones in test tubes when they studied the dissolution of gallstones from 43 kinds of TCM in vitro.

7.3. Role of the circulatory system

7.3.1. Cardiovascular system

Liu et al. [60] proved that Qing-Banxia water extract (53 g/kg) administered to rats prevents ventricular arrhythmia. Teng et al. [87] intravenously injected mixed dogs with PR aqueous solution (0.2, 0.3 g/kg) and found that it had an obvious curative effect on canine ventricular premature beats caused by barium chloride. Moreover, Li et al. [88] adopted the model of myocardial ischemia-reperfusion in rats, and orally administered 2.5 g/kg of Jiang-Banxia water extract to rats for 14 days. The results showed that PR had a certain protective effect on I/R myocardial injury. Huang et al. [89] found that PR water extract could stimulate the secretion of vascular repair factors and reendothelialization of blood vessels, and inhibit the proliferation of neointima, thus playing a role in the vascular repair of carotid artery injury in rats. Zhou et al. [90] found that PR could inhibit the secretion of inflammatory factors in mouse aortic endothelial cells. PR was injected intravenously into rats, dogs, rabbits and cats, which had a short-term antihypertensive effect and was quickly tolerated; however, intramuscular injection had no significant effect on blood pressure and respiration. PR also has a certain cardiac inhibitory effect, inhibiting isolated frog and rabbit hearts and increasing the coronary flow and amplitude of the cardiac contraction curve of isolated rabbit hearts Liu et al. [91] Hong et al. [92] gave PR (1.2 mL/day/200 g) to normal rats, and the experiment proved that PR could prevent or delay the formation of food-induced hyperlipidemia, and had a certain therapeutic effect on hyperlipidemia. Kim et al. [63] fed obese Zucker rats with hot water extract of PR 400 mg/kg every day for six weeks and found that it could reduce the levels of triglyceride and free fatty acids in the blood of such obese rats, and slightly reduce their body weight.

7.3.2. Hematological systems

Jiang et al. [93] gavaged rats with PR decoction 5 g/kg for seven days and found that it could increase the whole blood viscosity at

high shear rate and decrease the erythrocyte aggregation index and erythrocyte deformation index. Lu et al. [61] used a quantitative heavy object to hit the soft tissue of rats' right hind limbs, and wet applied PR powder and Chinese liquor paste of 0.15 and 0.25 g/mL (dosage of 0.5 mL/cm²) every day for 6 h and 5 d and found that PR for external use had a good curative effect on traumatic blood stasis. Shi et al. [62] adopted the mouse model of Agkistrodon acutus poisoning, and orally administered PR powder suspension 1 g/kg or PR 95 % ethanol extract 100 mg/kg every day for seven days. The research found that PR not only inhibited thrombosis but also prevented the exhaustion of coagulation factors. Zhang et al. [94] used 75 % ethanol extract of PR (3 g/kg) and 10 g/kg to gavage rats continuously for three days, the results of which showed a significant increase in the time required for electrical stimulation of the common carotid artery to thrombosis, as well as a slightly prolonged coagulation time.

7.4. Central nervous system

7.4.1. Sedation

Liu et al. [60] injected PR water extracts of 30 and 60 g/kg into the abdominal cavity of mice and found that it could significantly reduce the number of independent activities of mice and slightly prolong the sleep time of mice. Zhan et al. [95,64] gavaged mice with 75 % ethanol extract of PR (8, 12 g/kg), and found that it can significantly increase the number of mice sleeping with a subthreshold dose of pentobarbital sodium, and 12 g/kg can also prolong the sleeping time of mice with a subthreshold dose of pentobarbital sodium. You et al. [96] gavaged mice with raw PR decoction of 1.2, 3.6 g/kg for seven days. The results showed that both of them could increase the sleeping rate caused by subthreshold dose of pentobarbital sodium, although they did not cause mice to fall asleep directly. Fang et al. [97] found that raw PR had a good sedative effect in mice following gavage for seven days with 4, 8, and 16 g/kg. Zhou et al. [98] found that fresh PR decoction had an inhibitory effect on the central nervous system by gavage of 10 g/kg for 0.5 and 1.0 h.

7.4.2. Anticonvulsant

Yang et al. [65] found that the supercritical CO₂ ethanol extract of PR could resist the convulsion induced by maximal electroconvulsive and pentylenetetrazole and reduce the mortality of convulsed mice. Cheng et al. [99] found that the total alkaloid of PR is the anticonvulsant active part. Gu et al. [66] gavaged mice with 0.5, 1.0 g/kg of total alkaloids of PR for 13 days, and found that total alkaloids of PR could improve GABA nerve function. Deng et al. [100] also confirmed that the total alkaloids of PR have a certain therapeutic effect on epilepsy.

7.4.3. Antidepressant

Zhang et al. [67] gavaged mice with 100, 300, and 500 mg/kg of PR alcohol extract, and the results showed that it could shorten the immobility time during forced swimming and tail suspension; thus, PR had an antidepressant effect. Fang et al. [68] used single-prolonged stress method to establish a posttraumatic stress disorder rat model. PR powder mixture (3.15 g/kg) was administered orally for seven days, and the behavioral tests of open field test and forced swimming test were conducted. The results showed that PR had an antianxiety effect, and its effect was similar to that of 1 mg/kg alprazolam.

7.5. Anti-tumor effects

PR can be used to treat various cancers, such as cervical cancer, ovarian cancer, breast cancer, leukemia, liver cancer, cholangiocarcinoma, and gastric cancer [22]. Chen et al. [70] found that the concentration of PR water extract was 100 mg/kg in the ascites of S180 sarcoma tumor-bearing mice, which suggests that PR could inhibit tumor growth in vivo. Total protein extracts of PR have a significant inhibitory effect on ovarian cancer cell line SKOV3 by inducing cell apoptosis in a dose- and time-dependent manner. Another recombinant PR agglutinin exhibits anti-proliferative activity on hepatoma cells in a dose dependent manner [101]. Wu et al. [102] found that PR extract could induce apoptosis in tumor cell K562, prolong the G0/G1 phase of K562 cells, and interfere with DNA synthesis, confirming the antitumor properties of PR. Xiong et al. [103] using network pharmacology and molecular docking techniques, found that PR has the prevention and treatment of lung cancer as a potential pharmacological effect. Trypsin inhibitor isolated from PR significantly inhibited the proliferation of human gastric cancer cell line BGC-823 in a concentration- and dose-dependent manner [104]. Xia Lei et al. [105] found that the mechanism by which PR and ginger synergize against SKOV3 in ovarian cancer may be related to the induction of ROS generation, iron death, and inhibition of the P13K/AKT/mTOR signaling pathway. PR fat-soluble extracts combined with *cis*-dichlorodiammineplatinum-II (CDDP) acted on human cervical cancer cells (Si Ha line and Ca Ski line) to exert antitumor effects by arresting the Si Ha line and Ca Ski line at the cellular G0/G1 and G2/M phases, respectively [106]. Baicalein, the active component of PR, can inhibit tumor angiogenesis by down-regulating the expression of VEGF, fibroblast growth factor receptor-2 (FGFR-2) and up-regulating the expression of RB-1 (a tumor suppressor gene that regulates cell growth and differentiation) [107]. PR extract showed significant growth inhibition and pro-apoptotic effects on cervical cancer HeLa cells, as well as increased the sensitivity of HeLa cells to cisplatin [108]. Moreover, Zhao [109] and Li [110] confirmed that the PR polysaccharide is its antitumor active ingredient. Addition to proteins, various types of secondary metabolites are reported to be involved in various antitumor processes. A water-soluble polysaccharide (RAP-W1) has inhibitory effect on human breast cancer cell line MCF-7 [111].

7.6. Other pharmacological effects

Zhou et al. [69] gavaged MPTP rats with Parkinson's disease with total alkaloids of PR of 1, 0.5, and 0.25 mg/kg for eight weeks and found that total alkaloids of PR could improve the learning and memory function of Parkinson's disease rats. Chen et al. [112] Pinellia

glycosides extracted from PR can also inhibit the growth of *Candida albicans*. Moreover, it has been speculated that 3,4-dihydroxyformaldehyde in PR may be an effective component with an antibacterial effect [113]. Liu [114] found that PR extract could inhibit the proliferation of myeloid leukemia K562 and HL60 and lymphocytic leukemia C8166 cells, and was the most stable at a concentration of 500 $\mu\text{g}/\text{mL}$. Feng et al. [115] found that the anti-leukemia mechanism of PR extract may be related to its regulation of Bax/Bcl-2 and Caspase-3 protein expression. It was later reported that PR had a glucocorticoid-like effect, which was speculated to be an underlying mechanism responsible for the anti-inflammatory effect of PR [116]. It was also reported that PR has certain pharmacological effects in treating COVID-19 [117]. The lysophosphatidylcholine in PR is also known to cause demyelination, degeneration, and inflammatory reactions of neurons to varying degrees [118].

8. Toxicology

In the Chinese Pharmacopoeia (2020 edition), PR is listed as a toxic TCM, and its toxicity has been recorded in the medical books of successive dynasties. The manifestations and mechanisms of its toxicity have gradually been clarified through widespread research. Here, we comprehensively describe the research progress on the toxicology of *Pinellia ternata* (Fig. 13 and Table 5).

8.1. Acute toxicity

Wu et al. [119] found obvious acute toxicity after intraperitoneal injection of PR in mice, with an LD_{50} of 5.381 g/kg. Zhang et al. [120] gavaged 1 mL of PR for seven days in mice and found obvious acute toxicity with LD_{50} of 397.24 g/kg. Increasing evidence has shown that the powder of PR has obvious toxicity, while its water extract shows almost no toxicity.

8.2. General toxicity

Xu et al. [133] found that raw PR suspension (36 g/kg) had high acute toxicity, while 6 g/kg dose had significant maternal toxicity and embryo toxicity. Zhong et al. [121] found that the stimulating component of PR may be calcium oxalate needle crystal, which is mainly composed of calcium oxalate and protein, with a protein content exceeding 6%. Zhao [136] and Pan [123] confirmed that toxic needle crystals and lectin proteins of PR can cause cell membrane damage and cell death. Lu et al. [137] found that the toxic components of PR mostly exist in the alcohol-soluble part, with few toxic components in the water-soluble part. Lv et al. [138] found that the toxicity of PR was related to the content of total organic acids and alkaloids. Zhang et al. [125] found that PR water extract (62.5 g/kg) and acid water percolate (1.77 g/kg) had hepatotoxicity. The water extract of PR (0.4 g/mL) could significantly increase the contents of creatine kinase (CK), creatine kinase isozyme (CKMB), and lactate dehydrogenase (LDH) in SD rats, while raw PR could cause cardiotoxicity by blocking the mTOR signal pathway and activating transforming growth factor- β 1 (TGF- β 1) signaling pathway [136,139]. Additionally, raw PR significantly increased the content of serotonin (5-HT) in serum. It has also been reported that 5-HT can induce cell apoptosis by activating the TGF- β 1 signaling pathway and upregulating the expression of TGF- β 1 protein, which ultimately results in cardiotoxicity [129,140]. Studies have shown that raw PR (2.25, 4.5, 9 g/kg) can cause compensatory kidney growth and even death in mice [141,131]. It has been reported that PR decoction (25 g/kg) can cause focal infiltration of lymphocytes scattered in the renal parenchyma of mice, resulting in a tubular formation [132].

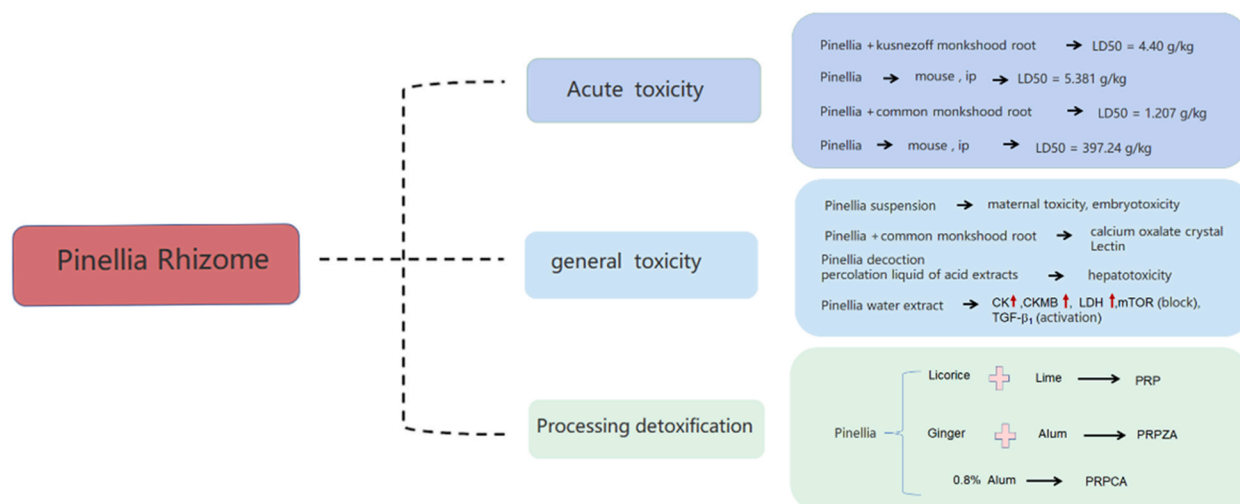


Fig. 13. Toxicological effect of *Pinellia ternata* (Thunb.) Breit. Note : Pinelliae Rhizoma Praeparatum Cum Alumine (PRPCA), Pinelliae Rhizoma Praeparatum Cum Zingibere et Alumine (PRPZA), and Pinelliae Rhizoma Praeparatum (PRP). Creatine kinase (CK), Creatine kinase Isozyme (CKMB), Lactate dehydrogenase (LDH), Mammalian target of rapamycin (mTOR), Transforming growth factor- β 1 (TGF- β).

Table 5
Toxic effects of the *Pinellia ternata* (Thunb.) Breit.

Toxic effects	Animal/cells	Extracts/compounds	Detail effects	References
Causing death	Mice	Born Pinellia (i.p.)	LD50 = 5.381 g/kg	[119]
	Mice	Born Pinellia (i.g.)	LD50 = 397.24 g/kg	[120]
	Mice	Suspension of PR powder (i.g.)	LD50 = 3.359 g/kg	[121]
	Mice	Water extracts of PR (i.g.)	No obvious death	[121]
	Mice	Suspension of PR powder (i.g.)	LD50 = 0.553 g/kg	[122]
	Mice	Suspension of PRPZA powder (i.g.)	LD50 = 1.23 g/kg	[122]
	Mice	Suspension of PR powder (i.g.)	LD50 = 5.38 g/kg	[119]
	Mice	Needle-like calcium oxalate crystal and PR Lectin (12 kD) (i.g.)	LD50 = 15.94 mg/kg	[121]
Inflammation causing effect	Macrophage	Different Concentrations of Poisonous Needle Crystals of Pinellia pedatisecta	Increasing the TGF- α , IL-1 β	[123]
	Mice	Suspension of PR powder (0.2 g/kg, i.g.)	Inducing writhing response and celiac inflammation.	[119]
	Mice	Suspension of PR powder (0.4 g/kg, i.g.)	Increasing capillary permeability, PGE 2 and histamine in abdominal cavity; Inducing celiac inflammation	[121]
Conjunctival irritation	Rabbit	Needle-like calcium oxalate crystal (o.a.), 2 drops/rabbit	Tissue swelling and hyperemia	[121]
Inflammation causing effect	Rats	PR Lectin (12kD, 0.15, 0.3, 0.6, 1.2, 2.4 mg/kg, i.g.)	Increasing the contents of protein and PGE2 in peritoneal exudate; Inducing celiac inflammation	[124]
	Mice	Needle-like calcium oxalate crystal and PR Lectin (12kD, i.g.)	Stabbing into the mesenteric surface of mice and causing tissue swelling and inflammation	[121]
Hepatotoxicity	Mice	pinellia water extraction (62.5 g/kg, i.p.)	Increasing the ALT, AST and liver tissue damage within 2 h	[125]
	Mice	Pinellia acid water percolation liquid (1.77 g/kg, i.p.)	Increasing the ALT, AST and liver tissue damage within 2–4 h	[125]
Cardiotoxicity	HepG2	Water extracts of PR (10–20 μ g/mL)	Inhibiting cell proliferation, and increasing ALT and AST	[126]
	Mice	PR powder (25 g/kg, for 10 days, i.g.)	Inducing edma of hepatic cells and steatosis	[127]
	Mice	Water extracts of PR (2.275 g/kg, crude herb mass equivalent, for 14 days, i.g.)	Inducing cardiomyocyte degeneration	[128]
	Rats	PR powder (6 g/kg, for 14 days, i.g.)	Increasing the LDH, CK, CK-MB in serum	[129]
Cardiotoxicity	Rats	PR powder, PRPZA powder (3 g/kg, i.g., for 14 days)	Causing cardiotoxicity via inhibition of mTOR signaling; and activation of the TGF- β pathway, and processing reduced the toxicity via free radical scavenging	[130]
Nephrotoxicity	Mice	PR powder (2.275 g/kg/day, i.g.)	Inducing obvious pathological changes of kidney; Inducing obvious pathological changes of heart and kidney in pregnant mice after PR administration in gestation 6.5–15.5 days	[131]
	Mice	PR powder (25 g/kg, i.g., for 10 days)	Inducing scattered focal lymphocytic infiltration in the renal parenchyma, and tubular formation in the renal tubules	[127]
	Mice	Water extracts of PR (2.275 g/kg, crude herb mass equivalent, i.g., for 14 days)	Inducing degeneration of renal tubular cells	[128]
Inducing vomiting	Pigeon	PR powder (i.g.)	ED50 = 0.74 g/kg	[132]
Conjunctival irritation	Rabbit	Suspension of PR powder (27 %), Ophthalmic administration (o.a.), 2 drops/rabbit	Tissue swelling and hyperemia	[121]
	Rabbit	Raw Pinellia prepared into 30 % suspension with normal saline	100 % positive rate	[78]
		Suspension of PR powder (20 %), o.a., 0.05 mL/rabbit	Serious conjunctival irritation	[128]
Effect of Pinellia extract on airway mucus hypersecretion	Rat	The extract of PR was given 10,30,60 g/kg by gavage for 4 consecutive days.	Increased MUC5AC content; Significant reduction of AQP-5 mRNA	[46]
Reproductive-embryonic toxicity	Mice	Suspension of PR powder (36 g/kg)	Mortality 50 %	[133]
	Mice	Suspension of PR powder (6 g/kg)	Mortality 30 %	[133]
	Mice	PR Lectin (4.4 kD, 30 mg/kg, s.c.)	Anti-early pregnancy rate was 100 %; decreasing plasma progesterone level; decreasing endometrial thickness and decidual reaction; inducing embryo arrest and abortion	[3]
Mutagenic effect	Mice	Raw Pinellia and PRPCA decoction 10 d (ip)	Equally increased the incidence of chromosomal abnormalities in cells	[134]
	Pregnant mice	PR and PRPCA (1.434 g/kg)	Glycerophospholipid metabolism, amino acid and carbohydrate metabolism have different degrees of interference and produce toxic effects	[5]
		PRPCA (10 g/kg)	Can cause DNA damage, leading to maternal cell genetic material changes, resulting in teratogenic effects	[135]

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Table 5 (continued)

	Mice	PR decoction (10 g/kg)	embryotoxicity	[134]
	Mice	PRPCA (10 g/kg, 20 g/kg, 30 g/kg)	PRPCA can cause changes in maternal cell genetic material; mutagenic effect on fetal cells through placental barrier	[134]
Reproductive-embryonic toxicity	Rabbit	PR Lectin (4.4kD, 500 µg/rabbit, intrauterine injection)	Inhibitory rate of the rabbit embryo implantation was 100 %	[3]
	Mice	PR Lectin (4.4kD, 250 µg/mice, s.c.)	Inducing abortion in 50 % mice	[3]

8.3. Irritant toxicity

In a rabbit eye irritation experiment, Hu et al. [78] found that the positive rate of 30 % PR powder and 0.9 % sodium chloride suspension on rabbit eyelid conjunctiva reached 100 %. Wu et al. [127] found that soaking in 8 % alum water or alkaline water with a pH > 12 could reduce the irritating toxicity of raw PR. Moreover, Zhu et al. [142] found that PR agglutinin can significantly increase PGE 2 and protein content in rat peritoneal exudate and aggravate the irritation of PR poison needle crystal to rabbit conjunctiva. PR poison needle crystal could significantly induce neutrophil migration after stimulating macrophages, while pure PR poison needle crystals or macrophages themselves had no such effect; thus, PR lectin protein has a strong inflammatory effect.

8.4. Mutagenic toxicity

Wang et al. [143] used three doses (10, 20, 30 g/kg) of Jiang-Banxia for 15 consecutive days and conducted micronucleus analysis of the sternum bone marrow of the mother mouse and the liver blood of the fetal mouse and made Single Cell Gel Electrophoresis (SCGE) test of blood lymphocytes. The results showed that Jiang-Banxia may have some mutagenic effects. Xiong et al. [144] administered mice the decoction of PR and Jiang-Banxia for 10 days continuously and found that they all increased the incidence of abnormal chromosome structure cells to the same extent, which was close to that of the 1 mg/kg mitomycin C group.

It has been reported that PR and Jiang-Banxia (1.434 g/kg) have toxic effects on glycerophospholipid metabolism, amino acid, and carbohydrate metabolism in pregnant rats, with varying degrees of interference [145]. Jiang-Banxia (10 g/kg) can cause DNA damage, resulting in the alteration of maternal cell genetic material and teratogenic effects [5]. Moreover, PR decoction administered at 10 g/kg has been shown to be embryotoxic to mice [134].

8.5. Concoction to reduce toxicity

The proper use of PR requires processing using concoctions and related methods before clinical use. Knowledge of empirical practice suggests that processing has a considerable impact on the safety of PR. A logical way to demonstrate detoxification is to check whether the content of toxic components changes significantly after processing. Tao et al. [135] reported that soaking in lime water (pH > 12) caused irreversible denaturation of lectin proteins, resulting in a significant decrease in the inflammation-causing toxicity of PR, which played a key role in the detoxification of the concoction. Ge et al. [146] reported that the use of alum can completely destroy the needle crystal structure and composition of the toxic needle crystal, resulting in a significant reduction in the toxicity of PR. It has also been shown that ginger and licorice can reduce the inflammatory reaction caused by the poisonous needle crystals of PR, thus reducing the irritation induced by PR [122,124,126,128,130,147].

9. Quality control

9.1. Origins

PR is the tuber of the *Pinellia ternata* genus in the family Araceae, which is composed of about six species worldwide and five species in China. It can be confirmed that the original plant of the *Pinellia ternata* herb is consistent with The Ch.P (2020 edition). Tu Jing Ben Cao (《图经本草》): “February born seedlings, a stem, stem end out of the three leaves, light green, rather like bamboo leaves and light, Jiangnan people like peony leaves.” The “Zhi Wu Ming Shi Tu kao” (《植物名实图考》): “where all have, have long leaves, round leaves two kinds, the same place.” That is to say, it describes the different leaf shape variations of PR. The former describes that the leaf shape of PR is divided into bamboo leaf shape and peony leaf shape, while the latter is divided into long and round leaf shape. In fact, the leaf shape variations of PR are even more diverse than those mentioned above, and the ratio between the length and width can be from 2:1 to 30:1, which is also significantly different between cultivated and wild *Pinellia ternata*.

9.2. Cultivation technology

Pinellia ternata root shallow, like mild, humid climate, afraid of drought, avoid high temperature. In recent years, due to changes in land use and cover changes as well as changes in farming practices such as pesticide and herbicide use, which have led to changes in the wild microenvironment of PR, wild resource populations have been greatly reduced or depleted, and cultivation has become the main source of PR. Many factors such as sowing density and depth, seed stem specification, shading intensity, and planting and harvesting

Table 6
Summary of different methods and representative sample preparation procedures for analysis of markers in *Pinellia ternata* (Thunb.) Breit.

Method	Analytes	Sample preparation	Column	Mobile phase	Reference
UV	Beta-Sitosterol	0.4 g of PR powder was mixed with 20 mL ethyl acetate, and cold soak overnight, take the filtrate. The filtrate was extracted twice, the ethyl acetate was recovered, and the residue was diluted to 10 mL with ethyl acetate.			[148]
TLC	<i>Pinellia ternata</i> Pinellia pedatisecta	1 g PR powder was mixed with 20 mL of ethanol and then subjected to refluxed extraction for 1 h and evaporated to dryness. The residue was dissolved in 1 mL of ethanol.	Silicone G Thin Layer Plates	Trichloromethane-methanol-water (6:4:0.5)	[149]
ELISA	Pinellia ternata lectin	1 g PR powder was mixed with 20 mL of ultrapure water and shaking for 2 h, and centrifuged at 8000 r/min for 15 min. The residue was re-extracted twice under the same conditions and supernatants were combined.			[150]
ELISA	PTL	1 g PR powder was mixed with 20 mL of PBS and shaking for 1 h, and centrifuged at 8000 r/min for 15 min. The residue was re-extracted twice under the same conditions and supernatants were combined.			[151]
UPLC-MS/MS	Lysophosphatidylcholines Sanedrine Trigonelline Choline Protocatechuic acid Protamine sulfates Homogentisic acid Chrysophanic acid	5 g of PR, PRPCA, PRPZA and PRP powder were mixed with 50 mL of methanol and 10 L of internal standard solution, and reaction was extracted twice of 30 min each time, centrifuged at 10000 r/min for 15 min, and then the supernatants were combined.	Waters Acquity UPLC HSST3 (100 mm × 2.1 mm, 1.8 μm)	methanol (A)-water (B) with gradient elution	[152]
UPLC-Q-TOF-MS/MS	Alkaloids Flavonoids Amino acids Others	2 g PR powder was immersed in 70 % ethanol (20 mL) for 0.5 h, then extracted under reflux for 1 h, filtered, extracted with 70 % methanol (10 mL) for 0.5 h, combined filtrate.	shim-pack xR-ODSIII column (2.1 mm × 75 mm, 1.6 μm)	acetonitrile (A)-0.1 % formic acid in water (B) with gradient elution	[153]
HPLC	Uracil 6-Hydroxypurine Uridine Guanosine Thymidine	1 g of PR powder was mixed with 50 mL of water, weigh the mass, sonicate for 30 min, filter and take the filtrate.	Agilent Zorbax SB C18 column (4.6 mm × 250 mm, 5 μm)	methanol (A)-water (B) with gradient elution	[154]
HPLC	Uracil Cytidine Uridine Inosine Guanosine Thymidine Adenosine	0.2 g of PR powder was mixed with 10 mL of water, ultrasonic extraction for 1 h, centrifuged at 3000 r/min for 10 min, and the supernatant was taken.	Agilent Zorbax SB Cs (4.6 mm × 250 mm, 5 μm)	water (A)-methanol (B) with gradient elution	[155]
HPLC	Inosine Guanosine Adenosine Succinic acid Ephedrine Hydrochloride	2 g of PR powder was mixed with 20 mL of ultrapure water, ultrasonic extraction for 45 min, 10000 r/min ⁻¹ centrifugation for 5 min, take the supernatant 10 mL, recover the solvent to dry, add the appropriate amount of ultrapure water to make the dissolution, transferred to a 10 mL measuring flask, with the use of purified water to the gradient of the volume, shaking well, and the extract was then extracted.	Agilent Eclipse XDB C18 column (4.6 mm × 250 mm, 5 μm)	acetonitrile (A)- water (B) with gradient elution	[156]
HPLC	Inosine Guanosine Thymidine Adenosine Trigonelline	1 g of PR powder was mixed with 50 mL ultrapure water, ultrasonic extraction was performed 3 times, each time for 45 min. 12000 r/min centrifugation was performed for 10 min, and the supernatants of the 3 extractions were combined.	C18 column (150 mm × 4.6 mm, 5 μm)	methanol and water (3:97)	[157]
UPLC	Calcium oxalate	Precisely weigh the appropriate amount of PR powder, add ultra-pure water vortex mixing, set to 60 °C aqueous	Acquity UPLC BEH C18 column	0.5 % (NH ₄) H ₂ PO ₄	[158]

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Table 6 (continued)

		solution, set to 60 °C water bath heating and stirring, centrifuged at 8000 r/min for 5 min, aspirate the supernatant, the same method for 2 times: combined supernatant and transferred to a 10 mL measuring flask, add water to set volume.	(50 mm × 2.1 mm, 1.7 μm)		
RP-HPLC	Oxalic acid Citric acid Malic acid Succinic acid	2 g of PR powder was mixed with 40 mL ultrapure water, ultrasonic extraction 2 times, each time 2 h, filtration, combined filtrate, with ultrapure water to 100 mL, precision measurement of 20 mL, add concentrated ammonia to adjust pH 11.5, with 3 times the amount of extract of ethyl acetate (60 mL) extraction for 3 times, collection of alkaline solution, acidified with phosphoric acid to pH 2.0, and then 3 times the amount of ethyl acetate extraction for 5 times. Then the extract was extracted with 3 times amount of ethyl acetate for 5 times, collected the ethyl acetate, dried by rotary evaporation, dissolved in ultrapure water and concentrated to 25 mL.	Gemini-C18 column (4.6 mm × 250 mm, 5 μm)	methanol and 0.03 % ammonium dihydrogen phosphate buffer (97:3)	[159]
Potentiometric titration	Total acid	5 g PR powder was mixed with 95 % ethanol and then subjected to refluxed extraction for 1 h, extracted three times, filtered and 0.1 mol/L NaOH aqueous solution (10 mL), and then subjected to ultrasonic extraction for 30 min.	NaOH, HCL titration solution		[160]
microchip electrophoresis with electrochemical detection	Guanosine Methionine Glycine 3,4-dihydroxybenzaldehyde Homogentisic acid	2 g PR powder was mixed with 6 mL of the extraction solvent containing C ₂ H ₅ OH/DI H ₂ O (1:1, v/v) and then subjected to ultrasonic extraction for 20 min.			[161]
HPLC	Uridine Adenine Guanosine Adenosine	1 g PR powder was mixed with 25 mL of water, sonicate for 30 min, cool to room temperature, shake well and centrifuge at 12000 r/min for 10 min, take the supernatant.	Shim-pack Scepter C18-120 column (250 mm × 4.6 mm, 5 μm)	10 % acetonitrile (A)- water (B) with gradient elution	[162]
GC-MS	Fat-soluble ingredients	500 g of PR powder, 3 times with 3 L methanol osmosis drip extraction, each 4 d, respectively, combined extracts, 38 concentrated under reduced pressure into a crude extract. The crude extract was dispersed into 600 mL of distilled water, and then extracted with 600 mL of petroleum acyl (60 ~ 90 °C) for 3 times, concentrated at 38 °C under reduced pressure, and then freeze-dried by freeze-dryer to obtain the extract. 1 mg of each extract was dissolved in 10 mL of methanol and sonicated.	VARIAN VF-5 ms column (30 m × 0.25 mm × 0.25 μm)	carrier gas: N ₂	[163]
MLPA	PR Pinellia pedatisecta Pinellia cordata	The surface of the herbs was scrubbed with 75 % ethanol and the surface cortex was scraped off, 30–50 mg of the dried samples were placed in 2 mL EP tubes and 2 small steel beads were added, and then the samples were ground into powder for 2 min in a high-throughput tissue grinder, and then the samples were extracted by using the Plant Genomic DNA Extraction Kit, and the concentration and purity of the DNA were determined by using the NanoDrop-2000 Ultra-Micro Spectrophotometer.			[10]
PCR-RFLP	PR Arisaema erubescens	By comparing the rbcL sequences of Arisaema erubescens, PR and their mixed pseudo-products, the specific			[164]

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Table 6 (continued)

ATR-FTIR	Pinellia ternata of different origins	cleavage sites <i>HaeIII</i> and <i>DraI</i> were selected for <i>Arisaema erubescens</i> and PR, respectively, and were identified by polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) The powder of <i>pinellia ternata</i> was finely ground in an agate mortar and pestle under dry conditions.	[165]
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patterns have an important effect on *Pinellia ternata* yield during artificial planting, with sowing density having the greatest impact on *Pinellia ternata* yield. Sowing density is too small then it will cause land and fertilizer waste, resulting in low yields too high density is prone to nutrient deficiencies, poor ventilation and air permeability, less light, and low photosynthetic products. High temperature and rainy season are serious, only reasonable dense planting to achieve high yield. In addition, the sowing depth should also be appropriate, sowing depth is too shallow, half-summer growth is susceptible to surface temperature and dry early influence, thus inhibiting tuber expansion and plant growth and development, depth is too deep, the soil permeability is poor, half-summer seedling late, development is not complete, low yield. Be careful to keep the indoor temperature not more than 10 °C, to avoid high temperatures to break the dormancy of the seed stem germination. *Pinellia ternata* seed sources are best from areas of similar ecology and geographic proximity.

9.3. Agricultural management

In the past 10 years (2011–2020), the international trade of *Pinellia ternata* herbs in China is mainly dominated by export trade, with a total export volume of 15,642.06 tons and a total export value of 22,888.40 million US dollars, while the import trade accounts for a very small proportion. In the past 10 years, our *Pinellia ternata* herbs have been exported to 33 countries and regions, mainly in East and Southeast Asia. At present, there are more problems in the development of international trade and industrialization of PR medicinal materials, such as limited export targets, difficulties in standardization, decline of wild high-quality resources, many pests and diseases, primitive and crude planting patterns, imperfect industrial chain, and insufficient protection of Taoist brands. We should strengthen the scientific research of *Pinellia ternata* and establish an internationally unified quality standard system for *Pinellia ternata* herbs; rely on scientific and technological innovation to empower the development of the *Pinellia ternata* herb industry; shape the Taoist *Pinellia ternata* brand, expand and extend the *Pinellia ternata* industry chain; standardize the international business of Chinese herbal medicines and boost the development of international trade of *Pinellia ternata* herbs.

9.4. Determination of the content of active ingredients

Developing a quality evaluation system for TCM is necessary to improve the quality standards of TCM. Over-collection of wild and endangered herbs can lead to the depletion of wild medicinal resources, while the global demand for endangered herbs continues to increase, especially in Asian countries. In this context, quality control of herbal medicines is particularly important. With the continuous development and progress of modern science and technology, many analytical tools, such as Thin-layer chromatography (TLC), Ultraviolet-visible spectrometry (UV), High-performance liquid chromatography (HPLC), Ultra-performance liquid chromatography-quadrupole optical-fluorescence mass spectrometry (UPLC-Q-TOF-MS) and Gas chromatography-mass spectrometry (GC-MS) coupling techniques have been used for the qualitative and quantitative analyses of the chemical compositions in the PR, and the relevant analytical methods are summarized in Table 6.

TLC is a chromatographic separation technique for the separation, identification and quantification of mixed samples with support coated on support plate as stationary phase and suitable solvent as mobile phase. The Ch.P (2020 edition) identifies arginine, alanine, valine and leucine, the characteristic components of PR, mainly by TLC. Chen et al. [162] found that the TLC profiles were clearly different between the PR and *Pinellia pedatisecta*. PR showed only one yellow-green spot on TLC while *Pinellia pedatisecta* showed two yellow-green spot.

HPLC method is a powerful tool for qualitative and quantitative analysis of PR and its adulterants. Most of chemical profiling and the main chemical component's contents in PR were carried out by using HPLC. Researchers developed an HPLC method for the simultaneous determination of five representative components in PR, which can be used as a rapid and reliable method for the quantitative analysis of active components in PR [150,155]. Liu et al. [151] established a content determination method for simultaneous determination of seven nucleoside constituents in PR, and found that the relative contents of different nucleoside constituents in the same origin of PR also differed considerably. Wang et al. [152] established a method for the determination of uridine, adenine, guanosine and adenosine content in PR and its mixed pseudo-products, *Arisaema erubescens*, *Typhonium flagelliforme* and *Pinellia pedatisecta* by one-measure-multiple-assessment method, and it was found that, except for *Arisaema erubescens*, the results of the determination of the content of nucleosides based on nucleosides combined with the stoichiometric analysis can well differentiate between *Pinellia ternata*, *Typhonium flagelliforme* and *Arisaema erubescens*. He et al. [158] developed a UPLC method for the determination of calcium oxalate in *Pinellia ternata* herbs and their concoctions from different origins, which is accurate and reliable, and can provide a reference for the quality control of *Pinellia ternata* herbs.

UPLC-Q-TOF-MS technology, due to its advantages of rapidity, high resolution and high sensitivity, has been widely used in the quantitative analysis of Chinese medicine ingredients with the advancement of technology, providing more possibilities for quality control. Zhai et al. [10] using UPLC-Q-TOF-MS were isolated and identified 80 compounds, which can be used for basic research on PR. Cui et al. [16] used UPLC-Q-TOF-MS to analyze the chemical composition of multi-material, multi-processed PR and found significant differences in the chemical composition of PR before and after processing. Lu et al. [149] used UPLC-MS/MS to determine the contents of eight potentially toxic components in PR and artillery products, combined with PCA and PLS-DA multivariate statistical analyses, found that choline, ephedrine hydrochloride, and protocatechuic acid were the main differential components. In addition, Xu et al. [154] used GC-MS to analyze the fat-soluble components in PR and identified 27 compounds, which can provide a reference for the standardization of quality standards for PR.

Other analytical methods including microchip electrophoresis, MLPA, UV, PCR-RFLP, ATR-FTIR and ELISA have also been employed to determine the chemical constituents of PR. Shih et al. [164] used microchip electrophoresis to determine five representative ingredients in PR. The method was rapid, accurate and sensitive, and provided a promising alternative analytical platform for rapid analysis of PR. Mo et al. [160] found that PR and its common mixed forgeries (*Pinellia pedatisecta* and *Pinellia cordata*) could be clearly identified by using the multiple ligation probe amplification technique. Zhang et al. [156] established a UV method to determine the content of total alkaloids in PR. The results showed that there were significant differences in the alkaloids content of PR from different origins. Xiao et al. [165] used PCR-RFLP technology to identify *Arisaematis Rhizoma* and PR. Qiao et al. [161] realized rapid identification of PR from different origins based on infrared spectroscopy.

The Chinese Pharmacopoeia (2020 edition) identifies arginine, alanine, valine and leucine, the characteristic components of PR, mainly by TLC, and specifies that the leachate should not be less than 7.5 %, the moisture should not be more than 13.0 %, and the total ash should not be more than 4.0 %. Which detailed description of the nature of the flavour attribution, function and main treatment, usage and dosage, contraindications and storage measures, concoctions and processing methods are also included in the standard. The Ch.P (2015 edition) specifies that the total acids content in PR calculated as succinic acid equivalent should not be less than 0.25 %. However, controlling the total acid content does not reflect the traditional medicinal effects of PR, nor does it control its toxicity. The Ch.P (2020 edition) is a lack of quality standards for quantitative analysis. And the search for quality marker for PR is particularly important for quality control. However, the quality of PR is affected by many factors such as origin, harvesting season, processing, storage method and storage time, as well as climatic and environmental changes, which make the myriad of chemical components contained in PR contribute differently to the clinical efficacy, and it is difficult to achieve quality control by a single indicator only; therefore, to ensure clinical efficacy, the quality standard of PR should be unified and a PR quality standard system should be developed. Furthermore the processing method is also an important factor affecting the content of ingredients. Therefore, we believe that different quality standards should be established for quality control of different processed products based on multiple bioactive ingredients.

10. Conclusions and future perspectives

To summarize, despite showing a certain toxicity, PR is an important TCM with a long history of more than 2000 years. Many chemical constituents have been isolated and identified from the plant, and many experts continually study PR, with great contributions from many aspects. However, there remain problems and challenges that require further research and exploration to meet the clinical needs.

First, although various chemical constituents have been identified from PR, the substances that exert pharmacological effects are still unclear. Therefore, it is necessary to further study the combination of monomer compounds and its clinical effects. Certain methods combined with experiments were used to verify the mechanisms and components of PR. Second, the mechanism of action of Chinese medicine is a hot research topic. Although the pharmacological effects of PR are continuously reported, they are mostly evaluated on the efficacy of animals, with few studies on the targets and pathways of action of PR. Therefore, studies on the mechanism of action at the cellular level should be conducted in the future. Third, although some progress has been made in the study of the toxicity of PR, the toxic substances remain unclear. The reported calcium oxalate needle crystals are only closely related to irritation. In the future, there is a need to further elucidate the toxic substances of PR along with comprehensive toxicity evaluation to improve the safety of its clinical use to lay the foundation for future drug development and clinical use.

Generally, as a commonly used TCM, PR still needs further research. Here, we have systematically and comprehensively introduced the current status of the research on PR at home and abroad in recent years, including traditional applications, phytochemistry, pharmacology, and toxicology. Although great progress has been made in its research, there are still some problems in various aspects; therefore, continuous efforts to develop and exploit PR are required.

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Data availability statement

No data was used for the research described in the article.

CRediT authorship contribution statement

Ting Zou: Writing – review & editing, Writing – original draft. **Jing Wang:** Supervision, Validation. **Xu Wu:** Validation. **Kai Yang:** Project administration. **Qiao Zhang:** Methodology. **Changli Wang:** Formal analysis. **Xiao Wang:** Data curation, Methodology. **Chongbo Zhao:** Investigation.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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