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Review

The Herba Patriniae (Caprifoliaceae): A review on traditional uses, phytochemistry, pharmacology and quality control

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ARTICLE INFO

Keywords:
Herba patriniae
Traditional uses
Phytochemistry
Pharmacology
Quality control

ABSTRACT

Ethnopharmacological relevance: Herba Patriniae has been used for thousands of years in China as a traditional Chinese medicine with heat-clearing and detoxicating effects. It is applied widely for the treatment of rheumatoid arthritis, diarrhea, acute hepatitis, pelvic inflammatory disease and ulcerative colitis in clinic. Two species, namely Patrinia scabiosaefolia Fisch. (PS) and Patrinia villosa Juss. (PV) from the Caprifoliaceae family, are considered as Herba Patriniae in the pharmaceutical industry.

Aim of the review: This paper aims to comprehensively outline the traditional uses, botanical description, phytochemistry, pharmacology, toxicology, quality control, pharmacokinetics and patents of Herba Patriniae, and elaborate the same/different characteristics between PS and PV.

Materials and methods: Detailed information of Herba Patriniae was collected from various online databases (Pubmed, Web of Science, Google Schola, China National Knowledge Infrastructure Database, National Intellectual Property Administration, PRC National Medical Products Administration), and those published resources (M.Sc. Thesis and books).

Results: A total of 233 compounds have been identified in Herba Patriniae, including triterpenoid saponins, flavonoids, organic acids, iridoids, and volatiles. A very distinct difference was observed, that PS is rich in triterpenoid saponins and volatiles, while PV contains more flavonoids. Two source species of Herba Patriniae gave similar pharmacological effects on anti-cancer, anti-inflammatory, antioxidant, antimicrobial, sedative and hypnotic effects. But there were no reports were on antipruritic, proangiogenic and anti-diarrheal effects for PS, and no studies on anti-diabetic effects for PV. Generally, Herba Patriniae showed non-toxic in the clinical dose, but mild side effects, such as temporary leukopenia, dizziness and nausea, could be found when large and excessive dosage is used. A variety of compounds have been quantified for the quality control of PS and PV. The variety, growth environment, growth time, and harvest time not only affected the contents but also the pharmacological activities of the bioactive compounds. In the past year, patents for compositions containing PV and PS have been filed, mainly involving human health, hygiene, agriculture, and animal husbandry. Unfortunately, the research on pharmacokinetics is insufficient. Only the prototype components and metabolites were reported after intragastric administration of total flavonoids extract from PV in rats.

Conclusion: Herba Patriniae has displayed a significant medicinal value in clinic, but the differences in phytochemistry, pharmacological effects and the content of compounds have been found between two official recorded species. About side effects and pharmacokinetic characteristics, the differences between two species have not been well studied. For a better clinical use of Herba Patriniae, it is urgent to establish systematic pharmacology, quality control, pharmacokinetics, and clinical researches on the same/different characteristics between PS and PV.

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https://doi.org/10.1016/j.jep.2020.113264
Received 25 March 2020; Received in revised form 21 July 2020; Accepted 6 August 2020
Available online 23 August 2020
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List of abbreviations

3T3-L1 preadipocytes
5-FU/HCT-8 human ileocecal adenocarcinoma cells
A2780 human ovarian cancer cells
A375-S2 human melanoma cells
A498 human renal carcinoma cells
AS49 human lung cancer cells
ABTS\textsuperscript{+} 2,2′-azino-bis(3-ethylbenzothiazoline-6-sulphonic acid)
AGS human gastric cancer cells
AKT protein kinase B
ALT alanine aminotransferase
AP acute pancreatitis
AP3 polysaccharide mixture
AST aspartate aminotransferase
BAX Bel-2-associated X protein
Bcl-2 B-cell lymphoma-2
Bcl-xL B cell lymphoma factor X\textsubscript{L}
BEL-7402 human hepatoma cells
BV-2 mouse microglia cells
Caco2 human colon cancer cells
COX-2 cyclooxygenase-2
CRC colorectal cancer
dAI disease activity index
dPPH 2,2-diphenyl-1-picrylhydrazyl
eG\textsubscript{50} half maximal effective concentration
EMT epithelial-mesenchymal transition
FAK focal adhesion kinase
GC-MS gas chromatography-mass spectrometer
GLUT4 glucose transporter 4
GSH glutathione
H\textsubscript{2}O\textsubscript{2} hydrogen peroxide
HeLa human cervical cancer cells
HepG2 human hepatoma cells
HL-60 human promyelocytic leukemia cells
HO-1 heme oxygenase-1
HPLC high performance liquid chromatography
HSP 60 heat shock proteins 60
HSP 72 heat shock proteins 72
HT1080 human fibrosarcoma cells
HT-29 human colon carcinoma cells
HUVECs human umbilical vein endothelial cells
IC\textsubscript{50} 50% inhibitory concentration
ICAM-1 intercellular adhesion molecule 1
ICR institute of cancer research
IL-1\textbeta interleukin-1 beta
IL-6 interleukin 6
IL-8 interleukin 8
iNOS inducible nitric oxide synthase
IRS insulin receptor substrate
K562 human malignant myeloid cells
LDH lactate dehydrogenase
LPS lipopolysaccharides
MCF-7 human breast cancer cells
MDA malondialdehyde
MDA-MB-231 human breast cancer cells
MPO myeloperoxidase
mRNA messenger ribonucleic acid
NF-\kappa B nuclear factor \kappa B
NGF nerve growth factor
NO nitric oxide
NQO-1 quinine oxidoreductase 1
Nrf2 nuclear factor erythroid 2-related factor 2
O2\textsuperscript{−} superoxide anion
OH hydroxyl radical
PCNA proliferating cell nuclear antigen
PID pelvic inflammatory disease
PS Patrinia scabiosaefolia Fisch
PV Patrinia villosa Juss
R RAW264.7 mouse leukemic monocyte macrophage
ROS reactive oxygen species
RSV respiratory syncytial virus
SARS severe acute respiratory syndrome
SD sprague dawley
SGC-7901 human gastric cancer cells
SMCC-7721 hepatocellular carcinoma cells
STAT3 signal transducer and activator of transcription 3
SW480 human colon carcinoma cells
T\textsubscript{C} half toxic concentration
TCM traditional Chinese medicine
TGF-\beta transforming growth factor beta
TI drug treatment index
TNF-\alpha tumor necrosis factor alpha
T-AOC total antioxidant capacity
T-SOD total superoxide dismutase
U14 mice cervical cancer cells
U937 human lymphoma cells
UC ulcerative colitis
UV ultraviolet.

1. Introduction

Herba Patriniae, as known as “Bai Jiang Cao” in Chinese, is a traditional Chinese medicine (TCM) originally recorded in “Shen Nong’s Herbal Classic” as a “middle grade” medicinal material, which has been used for thousands years. Besides, Korean ancient pharmacopoeiae “Donguibogam” also record its medical value, and it has been used for more than 400 years in Korea (Jeon et al., 2010). It possesses the TCM properties of pungent and bitter in flavor and slightly cold in nature, and has been classified to the stomach, large intestine, and liver meridians (Xiao, 1995). Two official species of Patrinia scabiosaefolia Fisch. (PS) and Patrinia villosa Juss. (PV) (Fig. 1) were considered as Herba Patriniae in Chinese Pharmacopoeia (1977 edition) and Chinese provincial pharmacopoeias. These two plants have been widely used for more than 2000 years with good biological activities of clearing heat and detoxification, eliminating carbuncle and expelling pus, dispelling blood stasis, and relieving pain. Through an analysis of ancient and modern literatures, Herba Patriniae was mostly used in intestinal carbuncle, lung carbuncle, gynecological epigastric pain, postpartum blood stasis, and eczema in ancient times (Chen and Han, 2017). Modern pharmacological studies have found that it has effects of anti-cancer, anti-inflammation, anti-pathogenic microorganisms, anti-oxidation, sedation, and hypnosis (Wang et al., 2019a). Nowadays, Herba Patriniae is widely used in the respiratory system, digestive system, gynecology, dermatology and other multi-disciplinary diseases in clinical practice (Zhu and Jiang, 2015), and the number of applied patents increases every year (http://ps-system.cnipa.gov.cn). In view of its high content of amino acids, vitamins, minerals and other nutrients, Herba Patriniae is not only regarded as a potherb with healthy value, but also processed into tea products (Su et al., 1999; Zeng et al., 2019; Zhong et al., 2001).

In the past decades, an increasing number of scholars have studied the chemical constituents and pharmacological effects of Herba Patriniae. Interestingly, based on these studies, we found that there are many
different/same characteristics between $PS$ and $PV$. Both of them are official species for Herba Patriniae, but differentiated clinical uses of them in different diseases may be better for the clinical outcome. Unfortunately, we cannot found a comprehensive and updated review on the same/different characteristics of the two sources of Herba Patriniae, and actually, these two species also have not been differentiated in clinical uses. Therefore, this review aims to systematically summarize the similarities and differences from the aspects of the traditional uses, botanical description, phytochemistry, pharmacology, and quality control of these two species of Herba Patriniae, as well as being evidences for their clinical application and further research.

2. Traditional uses

Herba Patriniae has a wide geographical distribution, mainly in East Asia and North America (He et al., 2017). Some plants, such as Sonchus Arvensis L., Sonchus Asper Vill, Sonchus oleraceus L. etc, may be confused as Herba Patriniae (Lu, 1996), and hence, these adulterants of Herba Patriniae should be exclude when clinical use. Traditionally, according to records of “Shen Nong’s Herbal Classic” (神农本草经), “Compendium of Materia Medica” (本草纲目), and “Synopsis of the Golden Chamber” (金匮要略), “Tai Ping Sheng Hui Fang” (太平圣惠方), “Pu Ji Fang” (普济方), “Sheng Ji Zong Lu” (圣济总录), “Qian Jin Yi Fang” (千金翼方) and “Qian Jin Fang” (千金方), ancient doctors have used the whole herbs and roots of Herba Patriniae for disease treatment, such as the stomach, intestine, liver, gallbladder, and gynecological diseases (Tian and Tian, 2003; Zhu and Jiang, 2015). Herba Patriniae was recorded in Chinese Pharmacopoeia (1977 edition) for the treatments of appendicitis, dysentery, enteritis, hepatitis, conjunctivitis, postpartum blood stasis abdominal pain, swollen welling-absces, and cleft sores (Pharmacopoeia Committee of the Ministry of Health of P. R. China, 1978). In addition, Herba Patriniae is also recorded in the standards of traditional Chinese medicine in many provinces of China (Table 1). In Miao nationality, Herba Patriniae is also called “Jia jiang le” and used to treat rheumatoid arthritis, colds, and diarrhea (Qiu, 2005; Wang, 2002). In Dong medicine (Lu, 1992), Yi medicine (Drug Control Institute of Yunnan Chuxiong Health Bureau, 1983), and Dai medicine (Shi, 1983), $PS$ is called “Nyangt ngec liongc baij lajng”, “She wei long”, and “Pa hong”, respectively. Its whole herb is used to treat infantile diarrhea, schizophrenia, and infantile tinea capitis, respectively. $PV$ is also called “Ba gai bao” in Zhuang medicine, and its root is used to treat icteric hepatitis, furuncles, and snakebites (Shi, 1983). $PV$ is called “Bitter vegetable” by She nationality (Biological Products Identification Institute of the Ministry of Health, 1990) and “Pao zi tong” by Tujia nationality (Peng and Guan, 1994). Its whole herb can be used to treat appendicitis, intestinal febrile symptoms constipation, mammary abscess, blister carbuncle, and Qi stagnation. $PV$ is also called “Ba gai lan” and “Hong pa” in Zamuang medicine (Biological Products Identification Institute of the Ministry of Health, 1990) and Dai medicine (Shi, 1983), respectively, and its root is used to treat jaundice hepatitis, furuncle, local ulceration caused by snake injury, and infantile convulsion. Moreover, in Korea, people usually use the roots or whole plants of $PS$ as a traditional herbal medicine to treat appendicitis, inflammation, wound healing, edema, abscesses, endometritis, and abdominal pain after childbirth (Kang et al., 1997; Yang et al., 2001).

In recent years, Herba Patriniae has been extensively applied in clinical practice in China, especially in gynecology, such as postpartum pain, mastitis, dysmenorrhea, and tubal obstructive infertility (Liu, 2019a). It is noteworthy that Herba Patriniae is one of the most important ingredients in many prescriptions of TCM which is effective in diarrhea (He, 1991), acute hepatitis (Song, 1987), pelvic inflammatory disease (Zhang, 1997a), typhoid fever, paratyphoid fever (Sun, 2000), ulcerative colitis (Liu, 2011), anal cryptitis (Shi, 2012), pelvic endometriosis (Yan and Qiu, 2013), acute pancreatitis (He et al., 2019b).
Shuan and Yifei Qinghua Gao are used to treat gynecological diseases, benign prostatic hyperplasia, rhinosinusitis, mumps, and phlebitis and respiratory diseases, respectively, while Longqing Pian, Nankang prescriptions containing Herba Patriniae, among which Kangfu Xiaoyan macopoeia (2015 edition), there are 6 Chinese herbal medicine pre

Table 1
The information of Herba Patriniae in national and local standards in China.

| Standards | Application | Dosage | Standard-setting Department |
|-----------|-------------|--------|-----------------------------|
| Standard of traditional Chinese medicine in Hunan Province | Acute appendicitis, diarrhea, enteritis, hemorrhagic leucorrhea, red eye, pterygium, postpartum abdominal pain, boils and carbuncles | 9-15 g | Hunan Food and Drug Administration (2010) |
| Standard of traditional Chinese medicine in Shandong Province | Appendicitis, dysentery, enteritis, hepatitis, conjunctivitis, postpartum blood stasis abdominal pain, boils and carbuncles | 9-15 g | Shandong Medical Products Administration (2002) |
| Standard of traditional Chinese medicine in Heilongjiang Province | Acute appendicitis, diarrhea, hemorrhagic leucorrhea, postpartum blood stasis abdominal pain, swelling and pain of eye, hepatitis, boils and carbuncles | 9-15 g | Heilongjiang Medical Products Administration (2001) |
| Standard of traditional Chinese medicine in Liaoning Province | Acute appendicitis, diarrhea, dysentery, postpartum blood stasis abdominal pain, conjunctivitis, boils and carbuncles | 9-15 g | Liaoning Food and Drug Administration (2009) |
| Standard of traditional Chinese medicine in Sichuan Province | Acute appendicitis and its abdominal pain, postpartum blood stasis abdominal pain, boils and carbuncles | 9-15 g | Sichuan Food and Drug Administration (2011) |
| Standard of traditional Chinese medicine in Guizhou Province | Appendicitis, dysentery, enteritis, hepatitis, conjunctivitis, postpartum blood stasis abdominal pain, boils and carbuncles | 9-15 g | Guizhou Medical Products Administration (2003) |
| Chinese Pharmacopoeia (1977 edition) | Appendicitis, dysentery, enteritis, hepatitis, conjunctivitis, postpartum blood stasis abdominal pain, boils and carbuncles | 9-15 g | Pharmacopoeia Committee of the Ministry of Health of P. R. China (1978) |

itching (Wang and Wang, 2002), gastroesophageal reflux disease, benign prostatic hyperplasia, rhinosinusitis, mumps, and phlebitis (Kong and Zhao, 2008; Zhu and Jiang, 2015). A powder composed of Coicos Semen, Radix Aconiti Lateralis Preparata, and Herba Patriniae, is a classic prescription for treating intestinal carbuncle in the “Synopsis of the Golden Chamber”, which is clinically used to treat chronic appendicitis, chronic pelvic inflammatory disease, and chronic prostatitis (Ji, 2006). In addition, a powder containing Herba Patriniae in the prescription is also used to treat sinustitis, acute purulent tonsillitis, and recurrent upper respiratory tract infection (Qin and Diao, 2018; Zhu and Jiang, 2015). Moreover, it showed significant efficacy in the treatment of psoriasis vulgaris (Yan et al., 2015), Keshan disease (Qian Jin Yi Fang ©千金方 Volume 6 (Sun, 1952)), and chronic pelvic inflammation (Jia, 2010) in the form of tablets. In the Chinese Pharmacopoeia (2015 edition), there are 6 Chinese herbal medicine prescriptions containing Herba Patriniae, among which Kangfu Xiaoyan Shuan and Yifei Qinghua Gao are used to treat gynecological diseases and respiratory diseases, respectively, while Longqing Pian, Nankang

Table 2
Traditional and clinical preparation of Herba Patriniae in China.

| Preparation name | Formulation | Main compositions | Reference |
|------------------|-------------|-------------------|-----------|
| Baijiang Tang    | Decoction   | Coicos Semen, Aconitii Lateralis Radix, Herba Patriniae | Jin Gui Yao Lue ©金匮要略 (Zhang, 1997b) |
| Aiye San         | Powder      | Herba Patriniae, Angelicae Sinensis Radix, Chuanxiong Rhizoma, Paeoniae Radix Alba, Siphonostegiae Herba | Pu Ji Fang ©普济方 Volume 251 (Zhu, 1959) |
| Baijiang San     | Powder      | Herba Patriniae, Angelicae Sinensis Radix, Chuanxiong Rhizoma, Paeoniae Radix Alba, Siphonostegiae Herba | Tai Ping Sheng Hui Fang ©太平圣惠方 Volume 80 (Wang, 1958) |
| Baijiang Tang    | Decoction   | Herba Patriniae, Angelicae Sinensis Radix, Chuanxiong Rhizoma, Paeoniae Radix Alba, Siphonostegiae Herba | Sheng Ji Zong Lu ©圣济总录 Volume 160 (Zhao, 1982) |
| Baijiang Yin     | Decoction   | Herba Patriniae, Angelicae Sinensis Radix, Chuanxiong Rhizoma, Paeoniae Radix Alba, Siphonostegiae Herba | Sheng Ji Zong Lu ©圣济总录 Volume 161 (Zhao, 1982) |
| Changyong Tang   | Decoction   | Moutan Cortex, Siphonostegiae Herba, Radix Alba, Rehmanniae Radix, Bambusae Caulis in Taenias, Angelicae Sinensis Radix, Bidentatae Radix, Forsythiae Cortex | Qian Jin Fang ©千金方 Volume 23 (Sun, 1998) |
| Chure Jili Wan   | Pills       | Tribuli Fructus, Rhei Radix et Rhizoma, Herba Patriniae, Angelicae Sinensis Radix, Siphonostegiae Herba | Qian Jin Fang ©千金方 Volume 23 (Sun, 1998) |

(continued on next page)
## Table 2 (continued)

| Preparation name | Formulation | Main compositions                                                                 | Reference                                                                 |
|------------------|-------------|-----------------------------------------------------------------------------------|--------------------------------------------------------------------------|
| Gualou San       | Decoction   | Radix, Angelicae Sinensis, Rhizoma, Moutan, Bupleuri Radix, Arctii Caulis, Isatidis Radix | Beijing Chinese Traditional Patent Medicine specification (1982)          |
| Pu Yao           | Powder      | Rhizoma, Moutan, Bupleuri Radix, Arctii Caulis, Isatidis Radix                    | Beijing Chinese Traditional Patent Medicine specification (1982)          |
| Gualou San       | Decoction   | Radix, Angelicae Sinensis, Rhizoma, Moutan, Bupleuri Radix, Arctii Caulis, Isatidis Radix | Be Beijing Chinese Traditional Patent Medicine specification (1982)        |
| Pu Yao           | Powder      | Rhizoma, Moutan, Bupleuri Radix, Arctii Caulis, Isatidis Radix                    | Beijing Chinese Traditional Patent Medicine specification (1982)          |
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## Table 2 (continued)

| Preparation name | Formulation | Main compositions                                                                 | Reference                                                                 |
|------------------|-------------|-----------------------------------------------------------------------------------|--------------------------------------------------------------------------|
| Gualou San       | Decoction   | Radix, Angelicae Sinensis, Rhizoma, Moutan, Bupleuri Radix, Arctii Caulis, Isatidis Radix | Be Beijing Chinese Traditional Patent Medicine specification (1982)        |
| Pu Yao           | Powder      | Rhizoma, Moutan, Bupleuri Radix, Arctii Caulis, Isatidis Radix                    | Beijing Chinese Traditional Patent Medicine specification (1982)          |
| Gualou San       | Decoction   | Radix, Angelicae Sinensis, Rhizoma, Moutan, Bupleuri Radix, Arctii Caulis, Isatidis Radix | Be Beijing Chinese Traditional Patent Medicine specification (1982)        |
| Pu Yao           | Powder      | Rhizoma, Moutan, Bupleuri Radix, Arctii Caulis, Isatidis Radix                    | Beijing Chinese Traditional Patent Medicine specification (1982)          |
| L. Gong et al.   |             |                                    |                                                                          |
### Table 2 (continued)

| Preparation name | Formulation | Main compositions | Reference |
|-------------------|-------------|-------------------|-----------|
| **Lidan** | Decoction | | |
| **Tuihuang Tang** (利胆退黄汤) | | | |
| **Neibu Wuxiang Wan** (内补五香丸) | Pills | | |
| **Qumai Wan** (囊丸) | Capsules | | |
| **Yinjiao Hongjiang Jiedu Tang** (银翘红酱解毒汤) | Capsules | | |
| **Danhuang Quyu Jionang** (丹黄祛瘀胶囊) | Capsules | | |

### Table 2 (continued)

| Preparation name | Formulation | Main compositions | Reference |
|-------------------|-------------|-------------------|-----------|
| **Qianlieping Jiaonang** (前列腺平胶囊) | Capsules | | |
| **Fuping Jiaonang** (妇平胶囊) | Tablets | | |
| **Fuyan Kangfu Pian** (妇炎康复片) | Capsules | | |
| **Fuyan Kangfu Jiaonang** (妇炎康复胶囊) | Tablets | | |
| **Keli Granules** (妇科消炎颗粒) | | | |
| **Fuyan Xiao Jionang** (妇科消胶囊) | | | |

(continued on next page)
## Table 2 (continued)

| Preparation name | Formulation | Main compositions | Reference |
|------------------|-------------|-------------------|-----------|
| Xiaoer Reke (小儿热咳口脹) | Oral liquid | Rhizoma, Alismatis Rhizoma, Ephedrae Herba, Armeniaca Semen Amaranum, Forsythiae Fructus, Rhei Radix et Rhizoma, Trichosanthis Fructus, Mori Cortex, Herba Patriniae, Caryophyllaceae Flos, Glycyrrhizae Radix et Rhizoma | [https://www.yaozh.com/NMPA](https://www.yaozh.com/NMPA) |
| Kangfu suppository | | Sophorae Flavescentis Radix, Violae Herba, Herba Patriniae, Andrographis Herba, Suis Fellis Pulvis, Trachycarpus fortunei Fructus, Rhei Radix et Rhizoma, Forsythiae Armeniacae Semen Rhizoma, Flos, Glycyrrhizae Radix et Rhizoma | [State Pharmacopoeia Commission of P. R. China, 2015](https://www.yaozh.com/NMPA) |
| Kangfu Capsules | | Taraxaci Herba, Herba Patriniae, Paeoniae Radix Rubra, Coicis Semen, Angelicae Sinensis Radix, Astragali Radix, Atractylodis Rhizoma, Chuanxiong Rhizoma, Scutellariae Alismatis Rhizoma, Radix Herba Patriniae, Moutan Cortex, Leonuri Herba Patriniae, Moutan Radix, Herba Rhizoma, Scutellariae Radix, Poria, Alismatis Asini Corii Colla, Rehmanniae Radix, Epimedii Folium, Cinnamomi Ramulus, Epimedium Cumini, Rehmanniae Radix, Spatholobi Caulis, Herba Eriobotryae, Herba, Sicyonos, Scutellariae Barbatae Herba, Sedi Herba, Ardisiae Japonicae Rhizoma et Radix, Bistortae Rhizoma, Spatholobi Caulis, Herba, Magnoliae Scutellariae Barbatae Herba, Herba Patriniae, Poria, Coicis Semen, Curcumae Radix, Sappan Lignum, Ostreae Concha, Artemisiae Scopariae Herba, Cyperi Rhizoma | [https://www.yaozh.com/NMPA](https://www.yaozh.com/NMPA) |
| Nankang Pian (男康片) | Tablets | Paroniale Radix Rubra, Rehmanniae Radix Praeparata, Cistanthes Herba, Glycyrrhizae Radix et Rhizoma, Taraxaci Herba, Pyrolae Herba, Phellodendri Chinensis Cortex, Caryophyllaceae Flos, Houttuyniae Herba, Epimedi Foliun, Fubi Fructus, Atractylodis Macrocephala Radix, Atractylodis Radix, Cuscutae Semen, Violae Herba, Herba Patriniae, Chrysanthemi Indici Flos, Angelicae Sinensis Radix Sophorae Fructus, Notoginseng Radix et Rhizoma, Sophorae Flavescentia Radix, Bietiliae Rhizoma, Cnidii Fructus, Artemisiae Argyi Foliun, Herba Patriniae, Lonicerae Japonicae Flos, Portulaceae Herba, Saposnikoviae Radix, Alumen, Borneolum Syntheticum, | [State Pharmacopoeia Commission of P. R. China, 2015](https://www.yaozh.com/NMPA) |
| Zhishihua Xiye (痔舒洗液) | Lotion | Sophorae Fructus, Notoginseng Radix et Rhizoma, Sophorae Flavescentia Radix, Bietiliae Rhizoma, Cnidii Fructus, Artemisiae Argyi Foliun, Herba Patriniae, Lonicerae Japonicae Flos, Portulaceae Herba, Saposnikoviae Radix, Alumen, Borneolum Syntheticum, | [https://www.yaozh.com/NMPA](https://www.yaozh.com/NMPA) |
| Gao (益肺清化膏) | Ointment | | [https://www.yaozh.com/NMPA](https://www.yaozh.com/NMPA) |
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## Table 3 (continued)

| Preparation name | Formulation | Main compositions | Reference |
|------------------|-------------|-------------------|-----------|
| Baijiang Granules | | Glycyrrhizae Radix et Rhizoma, PV, Sucrose, dextrin | [https://www.yaozh.com/NMPA](https://www.yaozh.com/NMPA) |
| Yifei Qinghua Gao | | Astragali Radix, Codonopsis Radix, Glehniae Radix, Liriopes Radix, Agrimoniae Herba, Bistortae Rhizoma, Fritillariae Cirrhosae Bulbus, Asteris Radix et Rhizoma, Platycodonis Radix, Armeniaca Semen Amaranum, Herba Patriniae, Glycyrrhizae Radix et Rhizoma | [State Pharmacopoeia Commission of P. R. China, 2015](https://www.yaozh.com/NMPA) |
| Ganfu Pian (肝复乐片) | Tablets | Codonopsis Radix, Trionycis Carapax, Paridis Rhizoma, Atractylodis Macrocephala Radix, Astragali Radix, Citri Reticulatae Pericarpium, Eupolyphaga Steleopsga, Rhei Radix et Rhizoma, Persicae Semen, Scutellariae Barbarae Herba, Herba Patriniae, Poria, Coicis Semen, Curcumae Radix, Sappan Lignum, Ostreae Concha, Artemisiae Scopariae Herba, Cyperi Rhizoma | [https://www.yaozh.com/NMPA](https://www.yaozh.com/NMPA) |
| Gandujing Keli (肝毒净颗粒) | Granules | Polygonyi Cupidati Radix, Rhizoma et Radix, Ardisiae Japonicae Herba, Sedi Herba, Scutellariae Barbatae Herba, Magnoliae Officinalis Cortex, Herba Patriniae, Arnebiae Radix, Wenyujin Rhizoma Concium | [https://www.yaozh.com/NMPA](https://www.yaozh.com/NMPA) |
| Lanwei Xiaoyan Wan (阑尾消炎丸) | Pills | Lonicerae Japonicae Flos, Ixitis Foliun, Herba Patriniae, Taraxaci Herba, Spatholobi Caulus, Toosendan Fructus, Rhei Radix et Rhizoma, Aucklandiae Radix, Persicae Semen, Paeoniae Radix Rubra, Scutellariae Radix | [https://www.yaozh.com/NMPA](https://www.yaozh.com/NMPA) |
| Lanwei Xiaoyan Pian (阑尾消炎片) | Tablets | Lonicerae Japonicae Flos, Ixitis Foliun, Herba Patriniae, Taraxaci Herba, Spatholobi Caulus, Toosendan Fructus, Rhei Radix et Rhizoma, Aucklandiae Radix, Persicae | [https://www.yaozh.com/NMPA](https://www.yaozh.com/NMPA) |

(continued on next page)
| Preparation name | Formulation | Main compositions | Reference |
|------------------|-------------|-------------------|-----------|
| Shuangshi Tongli  | Capsules    | Atractylodis Rhizoma, Tatarinowii Rhizoma, Plantaginis Semen, Indigo Naturalis, Phellodendri Amurensis Cortex, Talcum, Herba Patriniae, Salviae Miltiorrhizae Radix et Rhizoma | https://www.yaozh.com/ | NMPA |
| Yigong Keli       | Granules    | Herba Patriniae, Salviae Miltiorrhizae Radix et Rhizoma, Leonuri Herba, Codonopsis Radix, Dipsaci Radix, Angelicae Sinensis Radix, Scutellariae Radix, Coptidis Rhizoma, Salviae Miltiorrhizae Radix et Rhizoma | https://www.yaozh.com/ | NMPA |
| Lianqi           | Capsules    | Aquilariae Lignum Resinatum, Coptidis Rhizoma, Akebiae Caulis, Artemisiae Scopariae Herba, Ostreae Concha, Sappan Lignum, Carcumaee Radix, Coicis semen, Poria, Herba Patriniae, Scutellariae Barbatae Herba, Rhei Radix et Rhizoma, Persicae semen, Eupolyphaga Steleophaga, Citri Reticulatae Pericarpium, Astragalii Radix, Atractylodis Macrocephalae, Rhizoma, Paeoniae Radix Rubra, Salviae Miltiorrhizae Radix et Rhizoma, Trionycis Radix, Codonopsis Radix, Bupleuri Radix Fructus, Ginseng Fructus, Rhei et Rhizoma, Angelicae Sinensis Radix, Astragali Radix, Hircudi, Coicis semen, Atractylodis Macrocephalae, Rhizoma, Fritillariae Thunbergii Bulbus, Sparagami Rhizoma, Carcumaee Rhizoma, Herba Patriniae, Scutellariae Barbatae Herba, Glycyrrhizae Radix et Rhizoma | https://www.yaozh.com/ | NMPA |

**Table 2 (continued)**

| Preparation name | Formulation | Main compositions | Reference |
|------------------|-------------|-------------------|-----------|
| Niaosaitong      | Granules    | Vaccariae Semen, Alismatis Rhizoma, Citri Reticulatae Pericarpium, Paeoniae Radix Rubra, Carthami Flora, Persicae Semen, Herba Patriniae, Lycopi Herba, Salviae Miltiorrhizae Radix et Rhizoma, Angelicae Dahuarii Radix | https://www.yaozh.com/ | NMPA |
| Jinma Gantai Keli | Granules    | Verbeae Herba, Stephaniae Tetrandrae Radix, Herba Patriniae, Epimedi Folium, Astragali Radix, Paeoniae Radix Rubra, Salviae Miltiorrhizae Radix et Rhizoma, Glycyrrhizae Radix et Rhizoma | https://www.yaozh.com/ | NMPA |
| Shufeng Jiedu     | Capsules    | Polygioni Cuspidati Rhizoma et Radix, Forsythiae Fructus, Isatidis Radix, Bupleuri Radix, Herba Patriniae, Verbeae Herba, Phragmitis Rhizoma, Glycyrrhizae Radix et Rhizoma | https://www.yaozh.com/ | NMPA |
| Longqing Pian     | Tablets     | Alismatis Rhizoma, Plantaginis Semen, Herba Patriniae, Lonicerae Japonicae Flox, Moutan Cortex, Paeoniae Radix Rubra, Agrimoniae Herba, Coptidis Rhizoma, Phellodendri Chinensis Cortex | (State Pharmacopoeia Commission of P. R. China, 2015) | |
| Qianliexin        | Capsules    | Persicae Semen, Salviae Miltiorrhizae Radix et Rhizoma, Carthami Flora, Vaccariae Semen, Herba Patriniae, Toosendan Fructus, Pyroloae Folium, Myrrhae, Paeoniae Radix Rubra, Lycopi Herba, Angelicae Dahuarii Radix, Taraxaci Herba, Gleditsiae Spina, Lycii Fructus | (State Pharmacopoeia Commission of P. R. China, 2015) | |

*NMPA was cited from the website: http://www.nmpa.gov.cn/WS04/CL2042/.

*PV: Patrinia villosa Juss.; Herba Patriniae: not indicate species.*
Pian, Nioasaitong Pian and Qianlixin Jiaonang are used to treat genitourinary diseases (State Pharmacopoeia Commission of P. R. China, 2015). A summary of the traditional and Traditional and clinical preparation of Herba Patriniae in China is given in Table 2.

The tender stems and leaves of Herba Patriniae are rich in nutrients, fresh in taste, and grow in the mountains without environmental pollution. It is a high-quality vegetable that urban and residential like to eat. PV tea is also abundant in Hubei Province and Fujian Province (Jiang, 2019a; Xu et al., 2018). Herba Patriniae is not only used in human health, but also in agriculture, fishery, and animal husbandry. Interplanting Herba Patriniae in the newly reclaimed tea garden can increase the natural vegetation and reduce soil erosion and surface runoff caused by rainstorm erosion in the rainy season (Chen, 2001). The combination of Herba Patriniae and other medicinal plants can be used to treat poisoned wounds of cattle by Aγkstrodon acutus biting, crawling bee disease, liver and skin diseases of turtle and fish, and postpartum abdominal pain in cattle (Chen, 2006; Li, 2002; Shi, 2010; Zhao, 2003).

3. Botany

*Patrina villosa* Juss often grows in roadsides, grassy areas, thickets, forest margins, or forests, with an altitude of 100–2000 m. It is a perennial herb with a height of 50–120 cm. Its rhizomes are long and laterally, rarely stoloniferous. The stems are yellowish green with antratopous white coarse hairs, rarely uniformly glabrous or glabrescent. The corolla is campanulate; the tube is 1.5 × 1.1 mm. The 4 stamens of *P. villosa* are subsessile; it is bright green or dark green on the upper surface, white-hirsute. The campanulate corolla appears yellow and its tube is 1.5 × 1.5 mm. Flowering from July to September, fruiting from September to October (Fig. 1B) (Flora of China Editorial Committee, 1986).

Table 3

| NO. | Compound Name | Molecular Formula | Species | Reference |
|-----|---------------|-------------------|---------|----------|
| 1   | 3-O-β-D-xylopyranosyl-(1 → 3)-α-L-rhamnopyranosyl-(1 → 2)-α-L-arabinopyranosyl oleanolic acid | C₄₀H₅₂O₁₃ | PS | Li and Lou (2007) |
| 2   | Gigantesiade D | C₁₅H₂₀O₁₁ | PS | Li and Lou (2007) |
| 3   | 3-O-β-D-glucopyranosyl-(1 → 3)-α-L-rhamnopyranosyl-(1 → 2)-α-L-arabinopyranosyl oleanolic acid | C₂₄H₃₅O₁₆ | PS | Choi and Woo (1987) |
| 4   | Patrinia-glycosides B-II | C₂₄H₃₅O₁₆ | PS | Ren et al. (2013) |
| 5   | Conformer of Patrinia-glycoside B-II | C₂₄H₃₅O₁₆ | PS | Ren et al. (2013) |
| 6   | 3-O-β-D-glucopyranosyl-(1 → 3)-α-L-arabinopyranosyl oleanolic acid | C₂₄H₃₅O₁₁ | PS | Jiang et al. (2003) |
| 7   | 3-O-α-L-rhamnopyranosyl-(1 → 2)-α-L-arabinopyranosyl oleanolic acid | C₂₄H₃₅O₁₁ | PS | Nakanishi et al. (1993) |
| 8   | 3-O-α-L-rhamnopyranosyl-(1 → 2)-α-L-arabinopyranosyl oleanolic acid | C₂₄H₃₅O₁₁ | PS, PV | (Li et al., 2002; Xu et al., 1985) |
| 9   | Scabiosides B | C₁₅H₂₀O₁₂ | PS | Bukharov et al. (1970) |
| 10  | 3-O-β-D-xylopyranosyl oleanolic acid | C₂₃H₃₇O₇ | PS | Li et al. (2002) |
| 11  | 3-O-α-L-rhamnopyranosyl-(1 → 2)-β-D-xylopyranosyl oleanolic acid | C₁₅H₂₀O₁₁ | PS | Gao et al. (2011b) |
| 12  | 3-O-β-D-glucopyranosyl-(1 → 3)-α-L-rhamnopyranosyl-(1 → 2)-α-L-arabinopyranosyl oleanolic acid 28-O-β-D-glucopyranosyl ester | C₅₀H₄₆O₂₅ | PS | Gao et al. (2011a) |
| 13  | 3-O-β-D-glucopyranosyl-(1 → 4)-β-D-xylopyranosyl-(1 → 3)-α-L-rhamnopyranosyl-(1 → 2)-β-D-xylopyranosyl oleanolic acid 28-O-β-D-glucopyranoside | C₅₀H₄₆O₂₅ | PS | Gao et al. (2011b) |
| 14  | 3-O-β-D-xylopyranosyl oleanolic acid 28-O-β-D-glucopyranosyl ester | C₂₃H₃₇O₁₂ | PS | Gao et al. (2011b) |
| 15  | 3-O-α-L-rhamnopyranosyl-(1 → 2)-β-D-xylopyranosyl oleanolic acid 28-O-G-glucopyranosyl ester | C₂₃H₃₇O₁₆ | PS | Gao et al. (2011b) |
| 16  | 28-O-β-D-glucopyranosyl oleanolic acid | C₂₃H₃₇O₁₉ | PV | Yang et al. (2000) |
| 17  | 3-O-β-D-xylopyranosyl-(1 → 3)-α-L-rhamnopyranosyl-(1 → 2)-β-D-xylopyranosyl oleanolic acid 28-O-β-D-glucopyranoside | C₅₀H₄₆O₂₅ | PS | Gao et al. (2012) |
| 18  | 3-O-β-D-glucopyranosyl-(1 → 3)-α-L-rhamnopyranosyl-(1 → 2)-α-L-arabinopyranosyl oleanolic acid 28-O-β-D-glucopyranosyl-(1 → 6)-β-D-glucopyranosyl ester | C₅₀H₄₆O₂₅ | PS | Choi and Woo (1987) |
| 19  | Oleanolic acid 28-O-β-D-glucopyranosyl-(1 → 6)-β-D-glucopyranosyl ester | C₂₃H₃₇O₁₃ | PS | Gao et al. (2011b) |
| 20  | 3-O-β-D-glucopyranosyl-(1 → 3)-α-L-rhamnopyranosyl-(1 → 2)-β-D-xylopyranosyl oleanolic acid 28-O-β-D-glucopyranosyl-(1 → 6)-β-D-glucopyranoside | C₂₃H₃₇O₂₅ | PS | Gao et al. (2011b) |
| 21  | C₄₆H₅₄O₂₁ | PS | (continued on next page) |
| NO. | Compound Name                                      | Molecular Formula | Species | Reference                  |
|-----|---------------------------------------------------|-------------------|---------|----------------------------|
| 22  | 3-O-β-D-glucopyranosyl(1 → 4)-β-D-xylpyranosyl(1 → 3)-α-L-rhamnopyranosyl(1 → 2)-β-D-xylpyranosyl oleic acid 28-O-β-D-glucopyranosyl(1 → 6)-β-D-glucopyranoside | C₆₅H₁₀₅O₃₀        | PS      | Gao et al. (2011a)         |
| 23  | Scabiosides F                                     | C₅₇H₇₂O₃₄        | PS      | Bukharov and Karlin (1970a) |
| 24  | Scabiosides G                                     | C₅₈H₁₀₂O₂₉        | PS      | Bukharov and Karlin (1970b) |
| 25  | Sulfapatrinosides II                              | C₄₉H₇₀NaO₁₇S      | PS, PV  | (Inada et al., 1988; Zou, 1994) |
| 26  | Patrinovilosides A                                | C₄₈H₇₂O₁₇        | PV      | Lee et al. (2013)          |
| 27  | 2α,6-hydroxyoleanolic acid                        | C₃₀H₄₀O₄        | PS      | Li et al. (2002)           |
| 28  | 2α, 3β, 23-trihydroxyolean-12-en-28-oic acid      | C₃₀H₄₀O₅        | PS      | Xia et al. (2010)          |
| 29  | 2α, 3β, 19α, 23-tetrahydroxyolean-12-en-28-oic acid | C₃₀H₄₀O₆       | PS      | Xia et al. (2010)          |
| 30  | 3β, 12α-dihydroxyolean-13β, 28-olide              | C₃₀H₄₀O₄        | PS      | Gao et al. (2011b)         |
| 31  | 3-O-α-L-rhamnopyranosyl(1 → 2)-β-D-xylpyranosyl(12)-30-dihydroxy-olean-28, 13β-olide | C₃₀H₄₀O₁₃        | PS      | Gao et al. (2011a)         |
| 32  | 3-O-β-D-xylpyranosyl(1 → 3)-α-L-rhamnopyranosyl(1 → 2)-β-D-xylpyranosyl(12)-30-dihydroxy-olean-28, 13β-olide | C₃₀H₄₀O₁₇        | PS      | Gao et al. (2011a)         |
| 33  | 3-O-β-D-xylpyranosyl(1 → 3α-L-rhamnopyranosyl(1 → 2)-β-D-xylpyranosyl(12)-12β, 30-dihydroxy-olean-28, 13β-olide | C₃₀H₄₀O₁₄        | PS      | Gao et al. (2011a)         |
| 34  | Patrinolide A                                     | C₃₀H₄₀O₅        | PS      | Yang et al. (2001)         |
| 35  | 11α, 12α-epoxy-3-O-β-D-xylpyranosyl-olean-28, 13β-olide | C₃₀H₄₀O₆        | PS      | Gao et al. (2012)          |
| 36  | 11α, 12α-epoxy-3-O-β-D-xylpyranosyl-olean-28, 13β-olide | C₃₀H₄₀O₁₆        | PS      | Gao et al. (2012)          |
| 37  | 3-Oxooleanolic acid                               | C₃₀H₄₀O₃        | PS      | Choi and Woo (1984)        |
| 38  | 3-oxo-29-hydroxy-olean-12-en-28-oic acid          | C₃₀H₄₀O₄        | PS      | Gao et al. (2011b)         |
| 39  | 3, 11-dioxoolean-12-en-28-oic acid                | C₃₀H₄₀O₄        | PS      | Gao et al. (2011b)         |
| 40  | 3-hydroxyolean-11-oxo-12-en-28-oic acid           | C₃₀H₄₀O₁₀        | PS      | Gao et al. (2011b)         |
| 41  | Prosapogenin CP                                   | C₃₀H₄₀O₁₀        | PS      | Li and Lou (2007)          |
| 42  | Kalopanaxaxaponin B                              | C₃₀H₄₀O₂₀        | PS      | Kim (1997)                 |
| 43  | Patrinia saponin H₁                                | C₃₀H₄₀O₁₁        | PS      | Kang et al. (2017)         |
| 44  | Hederagenin                                       | C₃₀H₄₀O₃        | PS      | Kim (1997)                 |
| 45  | Sapindoside A                                     | C₃₀H₄₀O₁₂        | PS      | Li and Lou (2007)          |
| 46  |                                                   | C₃₀H₄₀O₃        | PS      |                            |

Table 3 (continued)
| NO. | Compound Name | Molecular Formula | Species | Reference |
|-----|---------------|-------------------|---------|-----------|
| 5  | 5-hydroxy-7, 4'-dimethoxy flavone | C16H14O5 | PV | Peng et al. (2006a) |
| 69 | 8-(7'R-3', 4'-dihydroxyphenyl)-ethyl)-3', 4', 5, 7-tetrahydroxyflavone | C25H18O7 | PV | Peng et al. (2018) |
| 70 | 7-O-β-D-glucuronide methyl ester-8-(7'R-3', 4'-dihydroxyphenyl)-ethyl)-3', 4', 5-trihydroxyflavone | C25H18O7 | PV | Peng et al. (2018) |
| 71 | 7-O-β-D-glucuronide methyl ester-8-(7'R-3', 4'-dihydroxyphenyl)-ethyl)-3', 4', 5-trihydroxyflavone | C25H18O7 | PV | Peng et al. (2018) |
| 72 | 7-O-β-D-glucuronide methyl ester-6-(7'R-3', 4'-dihydroxyphenyl)-ethyl)-3', 4', 5-trihydroxyflavone | C25H18O7 | PV | Peng et al. (2018) |
| 73 | 7-O-β-D-glucuronide methyl ester-6-(7'R-3', 4'-dihydroxyphenyl)-ethyl)-3', 4', 5-trihydroxyflavone | C25H18O7 | PV | Peng et al. (2018) |
| 74 | Luteolin-7-O-rutinoside | C27H20O16 | PV | Peng et al. (2018) |
| 75 | Luteolin | C15H10O6 | PS, PV | (Jang, 2017; J. Y. Peng et al., 2006b) |
| 76 | Luteolin-7-O-β-D-glucuronide methyl ester | C25H18O7 | PV | Peng et al. (2018) |
| 77 | Luteolin-7-O-β-D-glucuronide ethyl ester | C25H18O7 | PV | Peng et al. (2018) |
| 78 | Apigenin | C15H10O6 | PV | Peng et al. (2018) |
| 79 | Apigenin-7-O-β-D-glucuronide methyl ester | C25H18O7 | PV | Peng et al. (2018) |
| 80 | Scutellarin | C15H10O6 | PV | Han et al. (2020) |
| 81 | 8-C-glucosylprunetin | C22H20O10 | PV | Peng et al. (2006a) |
| 82 | Isoorientin | C22H20O12 | PV | Peng et al. (2006a) |
| 83 | Isovitrinin | C22H20O10 | PV | Peng et al. (2006a) |
| 84 | 5-hydroxyl-7, 3', 4'-trimethoxy flavone | C18H10O6 | PV | Peng et al. (2006a) |
| 85 | Rutin | C22H18O16 | PS, PV | (Kim, 1997; Li et al., 2006) |
| 86 | Quercetin | C15H10O7 | PS, PV | (Jang, 2017; Peng et al., 2006a) |
| 87 | 3-O-methylquercetin | C16H12O3 | PV | Song et al. (2018) |
| 88 | Kaempferol | C15H10O6 | PS, PV | (Han et al., 2016; Jang, 2017) |
| 89 | Kaempferol-3-O-arabinoside | C20H14O10 | PV | Song et al. (2016) |
| 90 | Kaempferol-3-O-α-L-rhamnosopyranosyl-(1→3)-(4'-O-acytyl)-O-L-rhamnosopyranosyl-(1→6)-(O-β-D-galactopyranoside | C27H22O11 | PV | Huang et al. (2007) |
| 91 | Kaempferol-3-O-β-D-glucopyranoside | C21H18O11 | PV | (Zou, 1994) |
| 92 | Kaempferol-3-O-β-D-trihaminoside | C23H18O18 | PV | Peng et al. (2006a) |
| 93 | Flavonolside | C24H18O20 | PV | Peng et al. (2006a) |
| 94 | Patrivilosides I | C24H18O20 | PV | Peng et al. (2006a) |
| 95 | Catharticin | C24H18O10 | PV | Peng et al. (2006a) |

| NO. | Compound Name | Molecular Formula | Species | Reference |
|-----|---------------|-------------------|---------|-----------|
| 96 | Patrivilosides 2 | C24H18O25 | PV | Peng et al. (2006a) |
| 97 | Kaempferol-3-O-β-D-glucopyranoside | C27H22O15 | PV | Peng et al. (2006a) |
| 98 | 3, 7-dimethoxy-5, 3', 4'-trihydroxyflavanone | C15H12O4 | PV | Peng et al. (2006a) |
| 99 | Patriniaflavonone A | C23H18O6 | PV | Peng et al. (2006a) |
| 100 | (2S)-5, 7, 2', 6'-tetrahydroxy-6, 8-di(γ, γ-dimethylallyl) flavanone | C25H20O6 | PV | Peng et al. (2006a) |
| 101 | (2S)-5, 7, 2', 6'-tetrahydroxy-6-lavandulylated flavanone | C25H20O6 | PV | Peng et al. (2006a) |
| 102 | (2S)-5, 7, 2', 6'-tetrahydroxy-4'-lavandulylated flavanone | C25H20O6 | PV | Peng et al. (2006a) |
| 103 | Bolusanthol B | C20H18O6 | PV | Peng et al. (2006a) |
| 104 | Tetrapetrol I | C23H18O4 | PV | Peng et al. (2006a) |
| 105 | Orotinin | C23H18O6 | PV | Peng et al. (2006a) |
| 106 | Orotinin-5-methyl ether | C23H18O6 | PV | Peng et al. (2006a) |
| 107 | (2S)-5, 2', 6'-trihydroxy-2', 2'-dimethylpyrano[5', 6'; 6, 7] flavanone | C25H20O6 | PV | Peng et al. (2006a) |
| 108 | (2S)-5, 2', 6'-trihydroxy-3', 3'-γ, 7-dimethylallyl-1', 2', 2'-dimethyl-3', 4'-dihydropyrano[5', 6'; 6, 7] flavanone | C25H20O6 | PV | Peng et al. (2006a) |
| 109 | Licoagrochalcone B | C24H22O4 | PV | Peng et al. (2006a) |

| NO. | Compound Name | Molecular Formula | Species | Reference |
|-----|---------------|-------------------|---------|-----------|
| 110 | Chlorogenic acid | C13H18O3 | PS, PV | (Han et al., 2020; Liu et al., 2013a) |
| 111 | Caffeic acid | C6H8O4 | PS, PV | (Han et al., 2020; Xia et al., 2010) |
| 112 | Iso-chlorogenic acid A | C24H22O12 | PS, PV | (Liu and Lei, 2019) |
| 113 | Iso-chlorogenic acid C | C24H23O12 | PS, PV | (Liu and Lei, 2019) |
| 114 | Ferulic acid | C13H18O4 | PS, PV | (Li et al., 2008; Zhao and Yang, 2016) |
| 115 | Protocatechuic acid | C7H6O3 | PS | Peng et al. (2006a) |
| 116 | Gallic acid | C7H6O3 | PS | Peng et al. (2006a) |
| 117 | trans-caffic acid | C7H6O3 | PV | Peng et al. (2006a) |
| 118 | Hydrocaffeate | C13H22O4 | PS, PV | (Han et al., 2016) |
| 119 | Palmitic acid | C15H25O2 | PS, PV | (Liu et al., 2015; Xu et al., 1985) |
| 120 | Linoleic acid | C18H32O2 | PV | Peng et al. (2005a) |
| 121 | n-dotriacontanoic acid | C33H56O2 | PV | Peng et al. (2005a) |
| 122 | Cryptochlorogenic acid | C13H18O3 | PS | Peng et al. (2006a) |

**Organic acids**

| NO. | Compound Name | Molecular Formula | Species | Reference |
|-----|---------------|-------------------|---------|-----------|

**Iridoids**

(continued on next page)
| NO. | Compound Name | Molecular Formula | Species | Reference |
|-----|---------------|-------------------|---------|-----------|
| 123 | Valerosidate C | C_{19}H_{24}O_{11} | PV | Lee et al. (2013) |
| 124 | Patrinoside A | C_{19}H_{24}O_{11} | PS | Liu et al. (2016a) |
| 125 | Patrinoside A | C_{19}H_{24}O_{11} | PS | Liu et al. (2016a) |
| 126 | Scalbrasside J | C_{19}H_{24}O_{11} | PS | Liu et al. (2016a) |
| 127 | Villosol C | C_{19}H_{24}O_{11} | PV | Liu et al. (2016a) |
| 128 | Villosolide C | C_{19}H_{24}O_{11} | PV | Liu et al. (2016a) |
| 129 | Patricrabinol | C_{19}H_{24}O_{11} | PS | Liu et al. (2016a) |
| 130 | Patricrabinoside | C_{19}H_{24}O_{11} | PS | Liu et al. (2016a) |
| 131 | Logatin | C_{19}H_{24}O_{11} | PS, PV | Liu et al. (2016a) |

**Volatiles**

| NO. | Compound Name | Molecular Formula | Species | Reference |
|-----|---------------|-------------------|---------|-----------|
| 132 | Loganic acid | C_{19}H_{24}O_{11} | PV | Lee et al. (2013) |
| 133 | Isopatrinoside | C_{19}H_{24}O_{11} | PS | Liu et al. (2016a) |
| 134 | Isopatrinoside | C_{19}H_{24}O_{11} | PS | Liu et al. (2016a) |
| 135 | Scabroside C | C_{19}H_{24}O_{11} | PS | Liu et al. (2016a) |
| 136 | Morrotrioside | C_{19}H_{24}O_{11} | PV | Liu et al. (2016a) |
| 137 | Villosate | C_{19}H_{24}O_{11} | PV | Liu et al. (2016a) |
| 138 | Patroescallosid | C_{19}H_{24}O_{11} | PV | Liu et al. (2016a) |
| 139 | Jatamamin J | C_{19}H_{24}O_{11} | PS | Liu et al. (2016a) |
| 140 | Scalbrasside K | C_{19}H_{24}O_{11} | PS | Liu et al. (2016a) |
| 141 | Jatamamin A | C_{19}H_{24}O_{11} | PS | Liu et al. (2016a) |
| 142 | 8-Epideoxyloganic acid | C_{19}H_{24}O_{11} | PS | Liu et al. (2016a) |
| 143 | 7-Deoxyloganic acid | C_{19}H_{24}O_{11} | PS | Liu et al. (2016a) |

**Continued on next page**
Table 3 (continued)

| NO. | Compound Name                  | Molecular Formula | Species | Reference                      |
|-----|--------------------------------|-------------------|---------|-------------------------------|
| 200 | Tetradecanoic acid              | C_{14}H_{26}O_{2}  | PS      | Liu et al. (2016a)            |
| 201 | Nonanoic acid                   | C_{10}H_{18}O_{2}  | PS      | Liu et al. (2016a)            |
| 202 | 3-Methylpentanoic acid          | C_{10}H_{20}O_{2}  | PS      | Liu et al. (2016a)            |
| 203 | Hexanoic acid                   | C_{10}H_{18}O_{2}  | PS      | Liu et al. (2016a)            |
| 204 | 5-Methyl-2-acetylfuran          | C_{9}H_{16}O_{2}   | PS      | Xue et al. (2016)             |
| 205 | 2-Pentylfuran                   | C_{8}H_{14}O_{2}   | PS, PV  | Liu et al. (2016a)            |
| 206 | Anethofuran                     | C_{10}H_{18}O      | PV      | Liu et al. (2016a)            |
| 207 | 1, 8-Cineole                    | C_{10}H_{18}O      | PS      | Liu et al. (2016a)            |
| 208 | 2H-chromene                     | C_{9}H_{18}O       | PV      | Liu et al. (2016a)            |
| 209 | Dehydro-ar-irone                | C_{13}H_{16}O      | PV      | Liu et al. (2016a)            |
| 210 | α-Ionene                        | C_{13}H_{18}O      | PS, PV  | Liu et al. (2016a)            |
| 211 | Propofol                        | C_{13}H_{18}O      | PV      | Liu et al. (2016a)            |
| 212 | Phenanthrene                    | C_{14}H_{10}O      | PS      | Liu et al. (2016a)            |
| 213 | β-sitosterol                    | C_{20}H_{32}O      | PS, PV  | Liu et al., 2008; Zuo, 2013   |
| 214 | β-daucosterol                   | C_{20}H_{32}O      | PV      | Li et al. (2008)              |
| 215 | 7β-hydroxyisotestosterone       | C_{18}H_{30}O      | PS, PV  | Peng et al., 2005a; Zhao and Yang, 2016 |
| 216 | Stigmasterol                    | C_{20}H_{32}O      | PV      | Peng et al. (2005a)           |
| 217 | 2, 6, 2′, 6′-tetramethoxy-4, 4′- bis (1, 2-trans-2, 3-epoxy-1- hydroxypropyl) biscarbonyl | C_{20}H_{32}O      | PV      | Yan et al. (2016)             |
| 218 | 2, 6, 2′, 6′-tetramethoxy-4, 4′- bis (2, 3-epoxy-1-hydroxy- propyl) biscarbonyl | C_{20}H_{32}O      | PV      | Yan et al. (2016)             |
| 219 | (7S, 8R)-3, 4, 9-trihydroxy-4- methoxy-9α-O-shikyl-acetyl-7, 8-dihydroprenoulan-1′- propyl ligana | C_{20}H_{32}O      | PS      | Jing (2017)                   |
| 220 | Lariciresinol                   | C_{18}H_{30}O      | PS      | Jing (2017)                   |
| 221 | 1H-O-[H]-glucopyranosyl-15- O-(p-hydroxyphenylacetyl)-5S, 6βH-eudesma-3-en-12, 6α- oleide | C_{22}H_{32}O_{11} | PV | Peng et al. (2005b)           |
| 222 | Aurantiamide acetate            | C_{17}H_{32}N_{2}O_{4} | PV | Peng et al. (2005b); Zhong et al. (2017) |
| 223 | Patricicabratine                | C_{17}H_{32}N_{2}O_{4} | PS | Peng et al. (2005b)           |
| 224 | trans-cafeic acid methylate     | C_{10}H_{20}O_{4}  | PV      | Xiang et al. (2016)           |
| 225 | Chlorogenic acid n-butyl ester  | C_{10}H_{20}O_{4}  | PV      | Yang et al. (2016)            |
| 226 | Caffeic acid ethyl ester        | C_{11}H_{18}O_{4}  | PV      | Liu et al. (2016)             |
| 227 | Caffeic acid n-butyl ester      | C_{11}H_{18}O_{4}  | PV      | Liu et al. (2016a)            |
| 228 | p-hydroxyphenylacetic acid      | C_{8}H_{16}O_{4}   | PV      | Xiang et al. (2016)           |
| 229 | methyl ester                    | C_{12}H_{20}O_{12} | PV      | Yang et al. (2016)            |

Table 3 (continued)

| NO. | Compound Name                  | Molecular Formula | Species | Reference                      |
|-----|--------------------------------|-------------------|---------|-------------------------------|
| 230 | 3, 4, 5-tri-O-p-hydroxophenylacetylquinic acid methyl ester | C_{30}H_{32}O_{12} | PV | Yang et al. (2016)             |
| 231 | methyl ester                    | C_{10}H_{18}O_{4}  | PS      | Xiang et al. (2016)            |
| 232 | Insitol                         | C_{12}H_{20}O_{5}  | 'Herba Patriniae' | Wang et al. (2002)          |
| 233 | Impelonye A                     | C_{14}H_{20}O_{5}  | PV      | Liu et al. (2019b)            |

Patrinia villosa Juss. (PV); Patrinia scabiosofolia Fisch. (PS). * Not indicate species.

4. Phytochemistry

Up to now, 233 compounds have been reported from Herba Patriniae, including 66 triterpenoid saponins, 43 flavonoids, 13 organic acids, 21 iridoids, 69 volatile oils, and 21 miscellaneous compounds. Among them, 153 components are discovered in PS, with triterpenoid saponins and volatile components as the main components, while 102 components, mainly including flavonoids, are from PV. The detailed information for these compounds is summarized in Table 3.

4.1. Triterpenoid aglycones and triterpenoid saponins

Triterpenoid aglycones and triterpenoid saponins are one of the main active constituents in Herba Patriniae. To date, more than 66 compounds (1-66) have been isolated from Herba Patriniae. It’s worth noting that 62 compounds are in PS, 7 compounds are in PV, and only 3 compounds are in both PS and PV. According to the aglycone, all of them were divided into oleanane type (1–57) and ursane type (58–66). Further, the oleanane type is divided into 5 different types, including oleanolic acid type (1–29), 13, 28-epoxy-oleanolic acid type (30–34), 11, 12 epoxy-13, 28-cycloxy-oleanolic type (35–36), 3-carbonyl oleanolic acid type (37–40), and hederagenin type (41–57) according to their structures. Their chemical structures were draw by ChemBioDraw Ultra 14.0 and described in Fig. 2.

Oleanolic acid (8), hederagenin (44) and ursolic acid (62) are typical representatives of triterpenoid aglycones in Herba Patriniae. An increasing number of studies have proved that oleanolic acid (8) possesses antitumour (Mbaeng et al., 2020), antimicrobial (Zhou et al., 2020), and antiviral (Meng et al., 2019) activities. Hederagenin (44) gave anti-inflammatory and anti-oxidative activities to alleviate ethanol-induced liver damage (Kim et al., 2017). Ursolic acid (62) has been reported with antioxidant and antiproliferative activities (Zhang et al., 2020), as well as protective effects against cisplatin-induced otoxicity (Di et al., 2020) and alleviates hypercholesterolemia (Hao et al., 2020). In addition, giganteaside D (2) was found with the induction effect on ROS-mediated apoptosis (Liu et al., 2016b). Alpha-hederin (50) showed acute anti-inflammatory activities in carrageenan-induced rat paw edema (Gepdiremen et al., 2005). But the biological activities of most triterpenoid aglycones and triterpenoid saponin were still unclear.

4.2. Flavonoids

Flavonoids is a class of famous natural products with widely biological activities, such as anti-oxidation, anti-inflammation and anti-tumor. There are 43 flavonoids were identified in Herba Patriniae. They are mainly classified into five groups according to the structure of aglycone, including flavones (67–84), flavonols (85–98), flavanones (99–102), isoflavonones (103–104), and other types (105–109). Luteolin (75), apigenin (78) and scutellarin (80) were blong to flavones. All of
Fig. 2. Chemical structures of triterpenoid aglycones and triterpenoid saponins in Herba Patriniae.
Fig. 3. Chemical structures of flavonoids in Herba Patriniae.
them have been widely studied in cardiovascular and tumor fields (Park et al., 2020; Xu et al., 2020; Bao et al., 2020). Isoorientin (82) and iso-vitexin (83) were two specific compounds in Herba Patriniae due to C-6 forming a C–C bond. Quercetin (86) and kaempferol (88) are two of the most common flavonols in dicotyledons. Compounds 85, 87 and 93 were derived from quercetin, while compounds 89, 90, 91, 92, 94, 95, 96, 97 and 98 were derived from kaempferol. It is interesting to note that more than 43 flavonoids (67–109) have been identified from PV, but are rarely

Fig. 4. Chemical structures of organic acids in Herba Patriniae.

Fig. 5. Chemical structures of iridoids in Herba Patriniae.
found in PS (75, 85, 86, 88). Their chemical structures are prescribed in Fig. 3.

4.3. Organic acids

To date, only 13 organic acids (110–122) have been identified from Herba Patriniae. The contents of chlorogenic acid (110), caffeic acid (111) and protocatechuic acid (115) are higher. These phenolic compounds possess many health-promoting properties, including antioxidant, antiinflammatory, antidiabetic, and antihypertensive activities (Al-Megrin et al., 2020; Paciello et al., 2020; El-Sonbaty et al., 2019; Li et al., 2020). For example, protocatechuic acid administration for

Fig. 6. Chemical structures of volatile in Herba Patriniae.
twelve-week could improves insulin-induced vasorelaxation in aging spontaneously hypertensive rats. Of these, 10 organic acids (110–114 and 117–121) are in PV, 9 organic acids (110–116, 119 and 122) are in PS. Among them, 6 compounds are in both PS and PV. Their chemical structures are shown in Fig. 4.

4.4. Iridoids

Iridoids are a kind of very important natural products in plant kingdom, structurally characterized with bicyclic cis-fused cyclopentane-pyran or cleavage of a bond in the cyclopentane ring (secoiridoid). Clinically, iridoids extract or traditional Chinese medicine rich in iridoids have been proved with anti-inflammatory, antiviral and anti-tumor effects, as well as protection of cardiovascular and immunomodulatory activities (Wang et al., 2020; Jie et al., 2015; Ji et al., 2019; Luan et al., 2019). To date, 21 iridoids (123–143) have been isolated in Herba Patriniae. Of these, loganin (131), loganic acid (132) and morroniside (136) are the compounds with more reported biological activities. Loganin has been proved with inhabitation effect on inflammatory response (Wen et al., 2020; Wei et al., 2013a) and mitigative effect on osteoarthritis (Hu et al., 2020). Morroniside has shown protective effect against \( \text{H}_2\text{O}_2 \)-induced damage in human neuroblastoma cells (Zhong et al., 2017). It is worth pointing out that 8 iridoids were obtained from PV, and 14 iridoids were isolated from PS. Only 1 compound (131) was a common constituent of the two plants. Their chemical structures were prescribed in Fig. 5.

4.5. Volatiles

The volatile constituent is one of the most abundant compounds in Herba Patriniae with many biological activities, such as antioxidant, antiinflammatory and anti-tumor effects, and it also proved with sedative and hypnotic effects (Lin et al., 2018; Luo et al., 1986). Approximately 69 volatile compounds (144–212) have been isolated from Herba Patriniae. All the volatiles were obtained by GC-MS method and list here for reference. Of these, 57 volatiles were isolated from PS, and 17 volatiles were separated from PV. Their chemical structures were prescribed in Fig. 6. These two sources of plants have 5 common volatile constituents.

4.6. Other compounds

In addition to the above compounds, Herba Patriniae also contains steroids (213–216), lignans (217–220), sesquiterpene lactone glycosides (221), amides (222–223), and other compounds (224–233). Of these, 17 compounds were isolated from PV, and 7 compounds were obtained from PS. Compounds 213 and 215 are common components of the two plants. Their chemical structures were prescribed in Fig. 7.

5. Pharmacology

“Heat” is a conception in traditional Chinese medicine, which is the synonym of “fire” and is the predominant pathogenic factor of summer. Excessive “heat” consumes Yin fluid and results in imbalance between
| Model | Experimental subject and administration | Results | Species | Reference |
|-------|----------------------------------------|---------|---------|-----------|
| CRC cell line SW480 (negative control: culture solution) | total saponin extract (PV was crushed and immersed in 1000 mL 70% ethanol for 12 h, refluxed and extracted at 40 °C, and concentrated under reduced pressure to remove ethanol and purified to obtain the total saponin extract); 1/16, 1/32, 1/64 and 1/128 mL/mL for 48 h | The total saponin of PV significantly inhibited TGF-β-induced EMT, and up-regulated the expression of E-cadherin and down-regulated the expression of N-cadherin and NF-kBp65 in CRC SW480 cell. | PV | Xia et al. (2018) |
| CRC mouse xenograft model (negative control: saline), HT-29 and HUVECs cells (negative control: culture solution) | ethanol extract (500 g PS was extracted by refluxing with 5000 mL 85% ethanol and filtered. The ethanol solvent was concentrated by rotary evaporation to a relative density of 1.05. The dry powder was obtained by spray drying. Mouse: the powder was dissolved in saline with a working concentration of 250 mg/mL; cells: the powder was dissolved in 50% DMSO with a stock concentration of 250 mg/mL); mouse: intragastric administration, 1.93 g/kg/day, 5 days a week for 21 days; cells: 0.5, 1, 2 mg/mL for 24 h | After treatment with the ethanol extract of PS, the tumor volume of CRC xenograft mice (0.65 ± 0.15 cm³) was significantly suppressed compared with the control group (1.20 ± 0.31 cm³), the tumor angiogenesis of CRC xenograft mice and HUVECs were suppressed in a dose-dependent manner (0.5–2 mg/mL), and the VEGF-A expression of CRC xenograft mice and HT-29 cells were obviously decreased. | PS | Chen et al. (2013) |
| CRC mouse xenograft model (negative control: saline), HT-29 cells (negative control: culture solution) | ethanol extract (500 g PS was extracted by refluxing with 5000 mL 85% ethanol and filtered. The ethanol solvent was concentrated by rotary evaporation to a relative density of 1.05. The dry powder was obtained by spray drying. Mouse: the powder was dissolved in saline with a working concentration of 250 mg/mL; cells: the powder was dissolved in 50% DMSO with a stock concentration of 250 mg/mL); mouse: intragastric administration, 1.93 g/kg/day, 5 days a week for 21 days; cells: 0.5, 1, 2 mg/mL for 24 h | The ethanol extract from PS treatment increased apoptosis and the ratio of pro-apoptotic Bax/Bcl-2 in HT-29 cells and CRC tumor tissues. It also induced a decrease in mitochondrial membrane potential in HT-29 cells and activated caspase-9 and -3. | PS | Liu et al. (2013b) |
| SMMC-7721 cells (negative control: 0.1% (v/v) DMSO culture solution; positive control: 5-Flavonouracil) | Patriniaflavanone A (The air-dried leaves of PV (15 kg) were extracted with 70% ethanol reflux for 3 times. After purification, 16.5 mg of Patriniaflavanone A was obtained.) | Patriniaflavanone A exhibited a moderate cytotoxic effect on SMMC-7721 cells with an IC₅₀ value of 61.27 μM. | PV | Xiang et al. (2016) |
| A375-S2, A549, HeLa; HepG2, HT1080, K562, HL-60 and U937 cells (negative control: culture solution; positive control: 5-Flavonouracil) | Patrinia-glycosides B-II (Patrinia-glycosides B-II was synthesized by linear 11-step sequence 11 with an overall yield of 9.4%); administration 48 h | Patrinia-glycosides B-II showed powerful inhibitory activity against eight tumor cell lines at micromolar concentrations (3.4–28.7 μM). | PS | Ren et al. (2013) |
| AGS, SGC-7901, BV-2, S-FU/HCT-8, HepG2, HT-29, HeLa and MDA-MB-231 cells (negative control: culture solution) | essential oil extract (The dried whole plant of PS (500 g) was distilled with double distilled water of 5000 mL for 4 h, and the yellow essential oil of 0.2 mg/g (w/w) was obtained); 50–200 μg/mL for 24 h | The essential oil of PS exhibited remarkable dose-dependent growth inhibition in the dilution range of 50–200 μg/mL. | PS | Lin et al. (2018) |
| A498, A549, BEL-7402, HT-29, MCF-7, K562 and SGC-7901 cell lines | six flavonoids isolated from PV (A 75% aqueous ethanol extract crude extract (400 mg) of the leaves of PV was separated in one single isolation procedure to obtain 44.9 mg of (25)-5, 7, 2', 6' -tetrahydroxy-6, 8-di (γ′-dimethylallyl) flavanone with 99.1% purity, 35.5 mg of (25)-5, 7, 2', 6' -tetrahydroxy-6-lavandulylated flavanone with 98.8% purity, 79.8 mg of (25)-5, 7', 2', 6' -tetrahydroxy-4'-lavandulylated flavanone with 99.3% purity, and 45.8 mg of (25)-5, 7', 2', 6'-trihydroxy-2', 2'-dimethylallylpyran [5', 6', 7, 8] flavanone with purity 98.6%, 39.8 mg of (25, 3'S)-5, 2', 6'-trihydroxy-3'-γ, γ'-dimethylallyl-2', 2'-dimethyl-3', 4'-dihydropyran [5', 6', 7] flavanone with purity 98.6%, 9.6 mg of licoriceglucocane B with 97.5% purity.); administration 3 day | (25)-5, 7, 2', 6'-tetrahydroxy-6, 8-di (γ′-dimethylallyl) flavanone, (25)-5, 7, 2', 6' -tetrahydroxy-6-lavandulylated flavanone and (25)-5, 7', 2', 6'-tetrahydroxy-4'-lavandulylated flavanone exhibited high anticancer activities (IC₅₀ < 7 μg/mL) in a dose-dependent manner, and when the concentration of these compounds exceeded 15 μg/mL, the proliferation of cancer cells were completely inhibited, especially for K562 cancer cells (IC₅₀ < 3.1 μg/mL). | PV | Peng et al. (2006c) |
| U14 mice of cervical cancer (negative control: distilled water; positive control: cyclophosphamide) | ethanol extract (100 g PV was refluxed and extracted with 1000 mL 70% ethanol for 2 h, extracted twice, and the solid crude extract was obtained by vacuum drying.); intragastric administration, 10, 15 mg/kg/day, 14 days | The ethanol extract of PV increased the tumor inhibition rate of U14-bearing mice with the inhibitory rate of 49.19% and 54.23% at the dosage of 10 g/kg and 15 g/kg, respectively. | PV | Chen et al. (2019c) |
| SMMC-7721 cell lines (negative control: culture solution) | total flavonoids extract (50 g PS was refluxed and extracted with 750 mL 60% ethanol for 1 h, extracted for 3 times, then evaporated and purified to obtain total flavonoids with a purity of 91.32%); 0.125–2 mg/mL. | The total flavonoids extract suppressed the growth of SMMC-7721 cells in a dose-dependent manner (0.125–2 mg/mL). | PS | Zhao et al. (2019) |
| SMMC-7721 cell lines (negative control: culture solution) | total flavonoids extract (10 g PS was refluxed and extracted with 100 mL70% ethanol for 1.5 h | The total flavonoids extract PS and PV inhibited the growth of SMMC-7721 cells in a dose-dependent manner (0.125–2 mg/mL). | PS, PV | Wei et al. (2013b) | (continued on next page) |
| Model                                                                 | Experimental subject and administration                                                                 | Results                                                                                                                                                                                                 | Species | Reference          |
|----------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------|--------------------|
| A375, A549, MCF-7, HepG2 and PC-3 cell lines (negative control: 0.5% (v/v) DMSO culture solution) | h, extracted for 3 times, then combined and dried to obtain 0.094 g extract. The extraction method of PS was the same as PV, the extract was 0.115g, 1–10 mg/mL for 24 h. Ethyl acetate extract (100 g PS was immersed in 1000 mL methanol for 3 days at room temperature, immersed twice. The combined methanol was rotary evaporated for 2 h, dried in a dryer for 1 day (0.5 g), then dissolved in 10 mL distilled water, extracted with ethyl acetate and dried (0.05 g), and the dry powder was dissolved in DMSO (100 mg/mL), filtered and blown dry; 0.8–400 µg/mL for 48 h. Ethanol extract (500 g PS was extracted by refluxing with 5000 mL 85% ethanol and filtered. The ethanol solvent was concentrated by rotary evaporation to a relative density of 1.05. The dry powder was obtained by spray drying and dissolved with DMSO to 200 mg/mL; 0.25–1 mg/mL for 24 h. | The extract has the most significant growth inhibitory effect on MCF-7 cells (IC₅₀ → 112.3 µg/mL), which is through activation of caspase-independent mitochondrial cell death pathway. | PS      | Chiu et al. (2006) |
| U266 cells (negative control: 0.5% (v/v) DMSO culture solution)       | Ethanol extract dose-dependently reduced proliferation and promoted the apoptosis of cancer cells via inhibition of the STAT3 pathway at the dosage of 0.25–1 mg/mL. |                                                                                                                                           | PS      | Peng et al. (2011) |
| U14 mice of cervical cancer (negative control: distilled water; positive control: cyclophosphamide) | The saponin extract remarkably inhibited the tumour growth of mice bearing the U14 cervical cancer cells in a dose-dependent manner (50, 100 mg/kg). Which induced the apoptosis of tumour cells and reduced the ratio of tumour cells in the G0/G1 phase, and decreased the expression of PCNA and Bcl-2, mutant p53 protein. | PV      | Zhang et al. (2008) |
| HepG2, A549 and A2780 cell lines (negative control: culture solution)  | Impeclonone A (The air-dried leaves of PV (15 kg) were refluxed and extracted with 70% ethanol for 2 h, extracted for three times, and evaporated under reduced pressure to obtain an ethanol extract. By separating the ethanol extract, 25.2 g of dry saponin extract was obtained; intragastric administration, 50, 100 mg/kg/day, 15 days | The Patrinia monoterpenoid iridoid ether esters extract inhibited proliferation and induced apoptosis, down-regulated the expression of Bax and caspase3 in HepG2 and MCF7 cells. | PV      | Liu et al. (2019b) |
| HepG2 and MCF-7 cells (negative control: culture solution; positive control: cisplatin) | Patrinia monoterpenoid iridoid ether esters extract (After immersed Herba Patriniae with 95% ethanol for 48 h, it was extracted with dichloromethane three times and separated, the yield was 1.24%); HepG2 cells: 12.5–50 µg/mL; MCF-7 cells: 1.75–7 µg/mL, 24 h. | The Patrinia monoterpenoid iridoid ether esters extract inhibited proliferation and induced apoptosis, down-regulated the expression of Bcl-2, Cdc2 and Cyclin B1, and up-regulated the expression of Bax and caspase3 in HepG2 and MCF7 cells. | Hebra Patriniae | Ji et al. (2019) |
| HCT-8 and 5-FU/HCT-8 cells (negative control: culture solution)        | Ethanol extract (500 g PS was extracted by refluxing with 5000 mL 85% ethanol and filtered. The ethanol solvent was concentrated by rotary evaporation to a relative density of 1.05. The dry powder was obtained by spray drying. The powder was dissolved in 50% DMSO with a stock concentration of 250 mg/mL; ethanol extract (1 kg PS was immersed in 10 L 95% ethanol for 3 days and filtered. The filtrate was freeze-dried after the relative density was 1.05 in vacuum evaporator. And dissolved in DMSO to form a stock solution with a concentration of 300 µg/mL; 0.2–1 mg/mL for 24 h, 0.6 mg/mL for 0–24 h. | The ethanol extract of PS inhibited the growth and promoted the death of 786-O cells in both dose- (0.2–1 mg/mL) and time-dependent (0–24 h) manner. At the dose of 0.6 or 1 mg/mL, it markedly increased the levels of intracellular ROS and Ca²⁺, and significantly down-regulated the expression of SIRT-1 and reduced the ratio of pmTOR/mTOR. | PS      | Li et al. (2018)   |
| 786-O and HK-2 cells (negative control: culture solution)              | Ethanol extract (500 g PS was extracted by refluxing with 5000 mL 85% ethanol and filtered. The ethanol solvent was concentrated by rotary evaporation to a relative density of 1.05. The dry powder was obtained by spray drying. mouse: the powder was dissolved in saline with a working concentration of 250 mg/mL; cells: the powder was dissolved in 50% DMSO with a stock concentration of 500 µg/mL; mouse: intragastric administration, 1.93 g/kg/day, 5 days a week for 3 weeks; cells: 0.5–3 mg/mL for 24 h. | The ethanol extract of PS (1.93 g/kg) markedly inhibited the tumour volume and the expression of PCNA in CRC mice, and dose-dependently (0.5–2 mg/mL) decreased the proliferation of HT-29 cells by G1/S cell cycle arrest. It also down-regulated the expression levels of CyclinB1 and CDK4 both in vivo and in vitro at the level of mRNA and protein. | PS      | Zhang et al. (2015) |
| CRC mouse xenograft model (negative control: saline), HT-29 (negative control: culture solution) | Ethanol extract (500 g PS was extracted by refluxing with 5000 mL 85% ethanol and filtered. The ethanol solvent was concentrated by rotary evaporation to a relative density of 1.05. The dry powder was obtained by spray drying. mouse: the powder was dissolved in saline with a working concentration of 250 mg/mL; cells: the powder was dissolved in 50% DMSO with a stock concentration of 500 µg/mL; mouse: intragastric administration, 1.93 g/kg/day, 5 days a week for 3 weeks; cells: 0.5–2 mg/mL for 24 h. | The ethanol extract of PS (1.93 g/kg) markedly inhibited the tumour volume and the expression of PCNA in CRC mice, and dose-dependently (0.5–2 mg/mL) decreased the proliferation of HT-29 cells by G1/S cell cycle arrest. It also down-regulated the expression levels of CyclinB1 and CDK4 both in vivo and in vitro at the level of mRNA and protein. | PS      | Zhang et al. (2015) |
| Anti-inflammatory effect                                               | Ethanol extract (30g PV was extracted with 300 mL 70% ethanol under reflux for 1h, extracted twice, filtered and concentrated to 1 g/mL concentration, and then dried; female ICR mice: intragastric administration, 0.08 g/kg for 4 h) | The 70% ethanol extract of PV (0.08 g/kg) was significantly reduced the ear edema thickness induced by arachidonic acid and the writhing response induced by acetic acid in ICR mice (80% and 48%, respectively), and (0.55 g/kg) | PV      | Zheng et al. (2012) |

(continued on next page)
Table 4 (continued)

| Model                                | Experimental subject and administration                                                                 | Results                                                                                     | Species | Reference |
|--------------------------------------|-----------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------|---------|------------|
| AP rat model (negative control: saline) | water extract (Decoction with boiling distilled water for 3 h); intragastric administration, 100 mg/kg/day for 5 days | The water extract of PS (100 mg/kg) reduced the ratio of pancreatic weight/body weight, the levels of serum lipase and amylnase, and suppressed the secretion of IL-1β, IL-6, and TNF-α in AP rats, as well as increasing the levels of HSP60 and HSP72 in pancreas. | PS      | Seo et al. (2006) |
| PID rat model (negative control: saline) | ethanol extract (500 g PS was extracted with 5 L of hot ethanol under reflux for 1 h, extracted twice, filtered and dried to yield 63.9 g); intragastric administration, 600 mg/kg/day for 21 days | After treatment with ethanol extract of PS (600 mg/kg), the infiltration of inflammatory cells and the expression of cytokines in the upper genitral tract of PID rats were significantly decreased. | PS      | Zou et al. (2015) |
| RAW 264.7 cells (negative control: culture solution); BALB/c mice (negative control: saline) | ethyl acetate extract (15 kg PS was extracted with hot ethanol under reflux for 4 h, extracted for four times, and 220 g total extract was obtained by vacuum evaporation. This extract was then dissolved in distilled water, extracted and separated with ethyl acetate, and evaporated in vacuo to yield 5.9 g); cells: 10–100 μg/mL for 24 h; mice: intragastric administration, 300 mg/kg for 24 h | The ethyl acetate extract of PS treatment on RAW 264.7 cells, inhibited the production of NO and IL-6 induced by LPS and the expression of iNOS and COX-2 at the protein and mRNA levels in a concentration-dependent manner (10–100 μg/mL), in which the inhibition was operated by suppressed the level of NF-κB activity. In addition, the ethyl acetate extract of PS inhibited the production of TNF-α and IL-6 in splenocytes of BALB/c mice stimulated by LPS. | PS      | Lee et al. (2012) |
| UC mice model (negative control: saline; positive control: 5-ASA) | methanol extract (206.65 g PS was refluxed and extracted twice with 70% methanol, and evaporated under reduced pressure to obtain a solid extract 22.21 g); intragastric administration, 10, 30, 50 mg/kg for 7 days | The administration of 10, 30 and 50 mg/kg of the methanol extract of PS for 7 days in UC mouse model considerably reduced ulcerative colitis DAI scores and tissue MPO accumulation, prevented enlargement of spleen and shortening of colon length in a dose-dependent manner, and also inhibited the mRNA expression of IL-1β, IL-6 and TNF-α. | PS      | Cho et al. (2011) |
| BV-2 cells (negative control: culture solution; positive control: indomethacin) | essential oil extract (The dried whole plant of PS (500 g) was distilled with double distilled water of 5000 mL for 4 h, and the yellow essential oil of 0.2 mg/g (w/w) was obtained); 100, 150, 200 μg/mL for 24 h | The secretion of IL-1β and IL-6 induced by LPS in BV-2 cells was remarkably inhibited by the essential oil extract of PS treatment in a dose-dependent manner (100–200 μg/mL). Therefore, the essential oil extract of PS has a significant anti-neuroinflammatory activity. | PS      | Lin et al. (2018) |
| Rat models of focal cerebral ischemia-reperfusion (negative control: saline; positive control: nimosipine and Naolautong) | total flavonoids (The content of total flavonoids in Herba Patriniae is 51.76%); intragastric administration, 50, 100, 200 mg/kg/day for 7 days | The total flavonoids (50, 100, 200 mg/kg) significantly reduced the levels of IL-1β, ICAM-1, IL-6, C3, Caspase-3, Bax and enhanced the levels of Bcl-2 and Nrf2 in the brain tissue of rats. Moreover, the total flavonoids (100, 200 mg/kg) significantly suppressed the percentage of cerebral infarction area, the production of NF-κB p65 and TNF-α, which showed significant neuroprotective effect. | *Herba Patriniae* | Wei et al. (2019) |
| Antioxidant effect | eleven phenethyl flavonizes (PV was extracted with ethanol under reflux for 2 h, extracted twice, and 8.2 g crude extract was separated and purified to yield 8-(7″R-(3″,-4″)-dihydroxyphenyl)ethyl)-3′, 4′, 5, 7-tetrahydroxystilbene (2.7 mg), 7-O-β-D-glucuronide methyl ester-8-(7″R-(3″,-4″)-dihydroxyphenyl)ethyl)-3′, 4′, 5-trihydroxyystilbene (9.5 mg), 7-O-β-D-glucuronide methyl ester-8-(7″S-(3″,-4″)-dihydroxyphenyl)ethyl)-3′, 4′, 5-trihydroxyystilbene (21.3 mg), 7-O-β-D-glucuronide methyl ester-6-(7″S-(3″,-4″)-dihydroxyphenyl)ethyl)-3′, 4′, 5-trihydroxyystilbene (10.5 mg), Luteolin-7-O-rutinoside (13.9 mg), Luteolin (11 mg), Luteolin-7-O-β-D-glucuronide methyl ester (12.4 mg), Luteolin-7-O-β-D-glucuronide ethyl ester (7.2 mg), Luteolin-7-O-β-D-glucuronide methyl ester (8-(7″R-(3″,-4″)-dihydroxyphenyl)ethyl)-3′, 4′, 5, 7-tetrahydroxystilbene, 7-O-β-D-glucuronide methyl ester-8-(7″R-(3″,-4″)-dihydroxyphenyl)ethyl)-3′, 4′, 5-trihydroxyystilbene and 7-O-β-D-glucuronide methyl ester-6-(7″R-(3″,-4″)-dihydroxyphenyl)ethyl)-3′, 4′, 5-trihydroxyystilbene isolated from PV (25 μM) reduced the generation of ROS in Caco2 cells induced by H2O2, 8-(7″R-(3″,-4″)-dihydroxyphenyl)ethyl)-3′, 4′, 5, 7-tetrahydroxystilbene and 7-O-β-D-glucuronide methyl ester-6-(7″R-(3″,-4″)-dihydroxyphenyl)ethyl)-3′, 4′, 5-trihydroxyystilbene increased the mRNA levels of NQO-1 and HO-1, and 7-O-β-D-glucuronide methyl ester-6-(7″R-(3″,-4″)-dihydroxyphenyl)ethyl)-3′, 4′, 5-trihydroxyystilbene decreased the expression of mir-144-3p, thus increasing the level of NF-κB protein in Caco2 cells, which was helpful to resist oxidative stress in Caco2 cells. | PV | Feng et al. (2018) |

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Table 4 (continued)

| Model                              | Experimental subject and administration                                                                 | Results                                                                 | Species | Reference           |
|------------------------------------|----------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------|---------|---------------------|
| DPPH and ABTS†                     | Volatiles extract (The volatiles extract of 200 g PV was extracted by supercritical CO2 fluid extraction for 2 h, and the total volatiles was composed of hydrocarbon (49.65%), fatty acid (22.38%), aldehyde (16.60%), terpene (9.04%) and little alcoholic.) 10–150 µg/mL | The IC50 values against DPPH and ABTS+ of the volatiles from PV were 32.01 and 50.90 µg/mL, respectively. | PV      | Xie et al. (2008)   |
| DPPH                               | Essential oil extract (The dried whole plant of PS (500 g) was distilled with double distilled water of 5000 mL for 4 h, and the yellow essential oil of 0.2 mg/g (w/w) was obtained.); 0.5–2 mg/mL | The volatiles extract of PS has a dose-dependent scavenging effect on DPPH radical, with IC50 of 1.455 mg/mL. | PS      | Lin et al. (2018)   |
| mice with acute liver injury (negative control: saline) | 60% ethanol extract (20 g PV powder was refluxed and extracted with 400 mL petroleum ether for 5 h, then dissolved with 400 mL 60% ethanol, refluxed and extracted for 2 h at 70 °C, extracted twice. The extract was centrifuged at 4000 r/min for 10 min, collected the supernatant and dried to obtain crude extract.); intragastric administration, 60, 120, 240 mg/kg/day for 10 days | The 60% ethanol extract of PV had obvious antioxidant activity in mice with acute liver injury by decreasing the activities of ALT and AST in serum, reducing the content of MDA and activity of LDH in liver, and enhancing the activities of T-SOD, T-AOC and GSH in liver. | PV      | Huang et al. (2019b) |
| OH, DPPH and O2−                  | Ethanol and water extract (The ethanol extract: 100 g PS or PV was immersed in 1.5 L 70% ethanol for 30 min, refluxed and extracted for 2 h, filtered, repeated 3 times, combined filtrate, concentrated and freeze-dried. The contents of chlorogenic acid, caffeic acid and total flavonoids in the ethanol extract of PV were 64.37 ± 2.43, 21.19 ± 1.24, and 293.00 ± 2.65 mg/g, respectively, and in the ethanol extract of PS were 83.80 ± 1.15, 1.12 ± 0.09, and 318.00 ± 2.65 mg/g, respectively. The water extract: 100 g PS or PV was immersed in 1.5 L distilled water for 30 min, refluxed and extracted for 2 h, filtered, repeated 3 times, combined filtrate, concentrated and freeze-dried. The contents of chlorogenic acid, caffeic acid and total flavonoids in the water extract of PV were 94.18 ± 1.94, 19.05 ± 0.75, and 334.00 ± 5.20 mg/g, respectively, and in the water extract of PS were 117.29 ± 0.85, 1.52 ± 0.09, and 383.00 ± 3.61 mg/g, respectively.); 5, 10, 15 mg/mL for scavenging OH and DPPH; 0.5, 1, 1.5 mg/mL for scavenging O2− | The water extract exhibited a stronger clearance rate for scavenging DPPH and OH than ethanol extract both in PS and PV. Moreover, the contents of chlorogenic acid and total flavonoids in the extracts are positively correlated with free radical scavenging ability. | PS, PV  | Sun et al. (2018)   |

**Antimicrobial effects**

| Model                              | Experimental subject and administration                                                                 | Results                                                                 | Species | Reference           |
|------------------------------------|----------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------|---------|---------------------|
| HeLa cells (negative control: culture solution; positive control: ribavirin) | Polysaccharide mixture (AP3) (1 kg of Herba patriniae was immersed in 7000 mL distilled water at room temperature for 12 h, filtered, the drug residue was repeatedly extracted with 5000 mL of distilled water, the two extracted filtrates were combined, concentrated under reduced pressure to 1000 mL, and AP3 was obtained after purification.); 0.02–2 mg/mL for 0, 2, 4, 6, 8 h | The polysaccharide mixture (AP3) exerted an obvious dose-dependent anti-RSV effect with TC50 and EC50 values of 11.45 and 0.0986 mg/mL, respectively. Moreover, the therapeutic index (TI = TC50/EC50) was 116.12. | AP3     | Li et al. (2004)    |
| λ-Lysogen (negative control: without water extract and irradiation; positive control: without water extract but irradiated) | Water extract from water at room temperature for 30 min, then boiled slowly for 30 min, and the volume was adjusted to 50 mL, and 750 mg/mL water extract was obtained after filtration.); 93.75, 187.5, 375, 750 mg/mL. | The inhibitory rates of the water extract from Herba Patriniae anti-SARS virus reached 45.0% at the concentration of 750.0 mg/mL. | AP3     | Li et al. (2006)    |
| Staphylococcus aureus, Streptococcus, Pasteurella, Salmonella, Escherichia coli | Ethanol and water extract (The crude drug content in ethanol and water extract are both 1 g/mL); 0.5 g/mL for 20 h | The water extract of PS (0.5 g/mL) has a strong inhibitory effect against Staphylococcus aureus, Streptococcus and Escherichia coli, and it has a weak antibacterial effect on Pasteurella and Salmonella, while the ethanol extract (0.5 g/mL) has a relatively weak antibacterial effect on these five kinds of bacteria. | PS      | Tan et al. (2003)   |
| Staphylococcus aureus, Escherichia coli, Proteus spp., Bacillus subtilis (negative control: without bacteria but have 70% ethanol extract; positive control: without 70% ethanol extract but have bacteria) | 70% ethanol extract (200 g of PV was immersed in 70% ethanol at 60 °C for 2.5 h, repeatedly extracted twice, and the two ethanol extracts were combined, filtered and concentrated to 200 mL by rotary evaporation, and obtained | The minimum inhibitory concentration of the extract was between 125-250 mg/mL. When the temperature was 23–160 °C, and the UV irradiation time was 10–50 min, the extract maintains high antimicrobial activity. | PS      | Dai and Lin (2011)  |

(continued on next page)
### Table 4 (continued)

| Model | Experimental subject and administration | Results | Species | Reference |
|-------|------------------------------------------|---------|---------|-----------|
| **Pseudomonas aeruginosa** (negative control: deionized water) | ethanol extract with a crude drug concentration of 1 g/mL; 125–250 mg/mL | The water extract of *Herba Patriniae* dramatically suppressed the expression of biofilm-associated key genes (algA, algl, bdIA, pell, ppyR and psIM), thus decreased the biofilm formation and changed the structure of the biofilm of *Pseudomonas aeruginosa*. It also reduced exopolysaccharide production and increased swirling motility. | *Herba Patriniae* | Fu et al. (2017) |
| **Suphylococcus aureus, Escherichia coli, Bacillus subtilis, Salmonella typhimurium, Shigella dysenteriae, Aspergillus niger, Aspergillus flavus, Beer yeast** (positive control: potassium sorbate) | tannin extract (1 g of PV powder was added to 60 mL 50% acetone and extracted under 80 W ultrasound for 60 min, the extraction rate was 6.4648%); 1.0 mg/mL for 48 h | The 60% ethanol, volatile oil, and dried ethanol extract of *PS* possessed sedative and hypnotic effect on mice induced by threshold dose of pentobarbital sodium and patients suffered from neurasthenia or neurasthenic syndromes with insomnia. | PV | (Fan, 2004) |
| Sedative and hypnotic effects | ethanol and water extract (The crude drug content in ethanol and water extract are both 1 g/mL); intraperitoneal injection, 0.5 g/mL/10 g | The ethanol extract of PS (0.5 g/mL/10 g) had an obvious sedative effect on mice, its sedative time was longer than water extract and its intensity was similar to that of pentobarbital, while without hypnotic effect. | PS | Tan et al. (2003) |
| Male ICR mice (negative control: physiological saline solution of 20% 1, 2-propanediol) | petroleum ether, chloroform, ethyl acetate and n-butanol extract from 95% ethanol extract: intragastric administration, 0.12 g/kg, 5 h after administration, the number of mouse activity in 10 min was recorded; 95% ethanol extract: intragastric administration, 0.45 g/kg, 5 h after administration, the number of mouse activity in 10 min was recorded | The 60% ethanol, volatile oil, and dried ethanol extract from PS possessed sedative and hypnotic effect on mice induced by threshold dose of pentobarbital sodium. | PS | Xu et al. (2007) |
| Mice (negative control: saline, patients) | 60% ethanol extract, volatile oil and dried ethanol extract (60% ethanol extract: the root of PS was crushed and immersed in 60% ethanol, then distilled under reduced pressure until 20% extract contains 10–15% ethanol); 60% ethanol extract (mice: intragastric administration, 30 g/kg); volatile oil (mice: intragastric administration, 0.2 g/kg; patients: 20 mg/capsule, 1–2 capsules/day, 1 times/day, 10–14 days); dried ethanol extract (mice: intragastric administration, 7.5 g/kg; patients: 1 g/tablet, 2–4 tablets/day, 2–3 times/day, 10–14 days) | The 60% ethanol, volatile oil, and dried ethanol extracts from PS possessed sedative and hypnotic effect on mice induced by pentobarbital sodium. | PS | Luo et al. (1986) |
| Mice (negative control: saline) | water extract (The water extract concentration was 2 g/L); intraperitoneal injection, 20 and 40 mg/kg | The water extract of PV inhibited the spontaneous activity, shortened the time of falling asleep and prolonged the sleeping time induced by pentobarbital sodium in a dose-dependent manner (20 and 40 mg/kg). | PV | Chen et al. (2005) |
| Mice (negative control: saline) | water extract (The crude drug content in water extract was 4.69 g/g); intraperitoneal injection, 40 and 60 mg/kg | The water extract of PV inhibited the spontaneous activity, shortened the time of falling asleep and prolonged the sleeping time induced by pentobarbital sodium in a dose-dependent manner (40 and 60 mg/kg). | PV | Zhong et al. (2004) |
| **Proangiogenic effect** | water extract (600 g PV was boiled in distilled water for 2 h, filtered and evaporated in vacuum, and then freeze-dried to obtain solid extract 52.8 g; cells: 10 and 100 mg/mL for 72 h; mice: intramuscular injection, 2.5 g/L, 20 μL/day, 3 day) | The water extract of PV (10 and 100 mg/L) significantly increased HUVEC cell proliferation and migration as well as the formation of capillary-like structures, induced phosphorylation of FAK and Akt in a time-dependent manner. Furthermore, intramuscular injection of the extract (20 μL of 2.5 g/L) significantly decreased the necrosis probability of ischemic limbs in vivo. | PV | Jeon et al. (2010) |

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5.1. Anti-cancer effect

Cancer is one of the main diseases that endanger human health, and recent studies have shown that Herba Patriniae plays an important role in anti-cancer. Some extracts of Herba Patriniae have been used to study the anti-cancer effect in several human cancer cell lines. Among them, the ethanol extract of PS and PV showed remarkable anti-cancer effects both in vitro and in vivo. Many studies showed the anti-cancer effect of the ethanol extract of PS. Chen et al. (2013) discovered that the ethanol extract of PS suppressed the proliferation, migration, and tube formation of HUVECs (human umbilical vein endothelial cells) at the dose of 0.25–2 mg/mL. According to the studies of Liu et al. (2013b) and Zhang et al. (2015), it also inhibited the angiogenesis and the expression of CyclinD1 and CDK4 in HT-29 (human colon cancer cells), increased the ratio of pro-apoptotic Bax to anti-apoptotic Bcl-2, induced the activation of caspase-3 and -9 in HT-29 cells via the mitochondrial-dependent pathway, and decreased the proliferation of HT-29 cells by G1/S cell cycle arrest. When the ethanol extract of PS was intragastrically administered to colorectal cancer mice at the dose of 1.93 g/kg, the tumor volume was significantly decreased, and the intratumoral microvessel density and the expression of PCNA were reduced in tumor tissues. Huang et al. (2019a) found that the ethanol extract of PS decreased the drug resistance of HCT-8/5-FU (human colorectal cancer cells) by inhibiting AKT pathway and inducing apoptosis. Moreover, in human multiple myeloma U266 cells, it dramatically suppressed proliferation, decreased Cyclin D1 and Bcl-2 mRNA levels, and eventually induced apoptosis in a dose-dependent manner (0.25–1 mg/mL), with a very high, and the extraction process of the extract needs to be further optimized.

The other extracts of Herba Patriniae also showed potential anti-cancer effects, though these effects may have some differences between them. The essential oil extract of PS showed a significant dose-dependent inhibition effect on 8 kinds of tumor cells at dose of 50–200 μg/mL. Lin et al. (2018) found that the ethanol extract of PV increased the tumor inhibition rate of U14-bearing mice with the inhibitory rate 49.19% and 54.23% at the dosage of 10 g/kg and 15 g/kg, respectively. However, the dose level of 10 g/kg and 15 g/kg is the inhibitory rate 49.19% and 54.23% at the dosage of 10 g/kg and 15 g/kg, respectively. However, the dose level of 10 g/kg and 15 g/kg is very high, and the extraction process of the extract needs to be further optimized.

Yin and Yang, which can produce endogenous toxins lurking in the human body (Tu et al., 2016). With activities of heat-clearing and detoxifying, Herba Patriniae exerted anti-cancer, anti-inflammatory, antioxidant, antimicrobial effects, as well as a sedative, hypnotic, proangiogenic, anti-diabetic, antipruritic, and anti-diarrheal effects in vitro and in vivo. There are different pharmacological effects between PV and PS. We have enlisted an overview of the modern pharmacological studies in the following sections (Table 4).

5.2. Anti-diabetic effect

Some extracts of Herba Patriniae have been used to study the anti-diabetic effect and in vivo detoxifying, Herba Patriniae exerted anti-cancer, anti-inflammatory, antioxidant, antimicrobial effects, as well as a sedative, hypnotic, proangiogenic, anti-diabetic, antipruritic, and anti-diarrheal effects in vitro and in vivo. We have enlisted an overview of the modern pharmacological studies in the following sections (Table 4).

Table 4 (continued)

| Model                  | Experimental subject and administration | Results                                                                 | Species | Reference     |
|-----------------------|-----------------------------------------|-------------------------------------------------------------------------|---------|---------------|
| Anti-diabetic         | Mouse ST3-L1 preadipocytes (negative control: culture solution; positive control: Sodium Orthovanadate) | Patrinoside and patrinoside A (5 kg PS powder was extracted in 95% ethanol at room temperature, then concentrated under reduced pressure and purified to obtain Patrinoside and patrinoside A); 6.25–200 μM for 48 h | PS      | Liu et al. (2019c) |
| Anti-diarrheal effect | isolated intestine cramps model, Castor oil-induced diarrhea rats (negative control: distilled water; positive control: Changshu tablet) | 60% ethanol, dichloromethane layer, ethyl acetate layer, N-butanol layer and water layer extract (The 60% ethanol extract: 50 g PV was crushed and refluxed with 500 mL 60% ethanol at 85 °C for 2 h, extracted twice, filtered and concentrated by rotary evaporation under reduced pressure to obtain a solid powder 4.75 g; extracts of different polar parts: 500 g PV was crushed and refluxed with 500 mL 60% ethanol at 85 °C for 2 h, extracted twice, filtered and concentrated by rotary evaporation under reduced pressure to no alcohol rate, and then diluted with 2000 mL water and extracted with dichloromethane, ethyl acetate and N-butanol, extracted twice. After vacuum drying, the extract was 1.77, 2.28 and 10.61 g, respectively, the water layer extract was 23.34 g; isolated intestine cramps model: 0.02–1.28 mg/mL/day in vivo: intragastric administration, 100, 200, 400 mg/kg/day; 7 days | PS      | Zhang et al. (2019a) |

PV indicates Patrinia villosa Juss. (PV); Patrinia scabiosafolia Fisch. (PS).

* Not indicate species.
mitochondrial cell death pathway (Chiu et al., 2006; Ji et al., 2019).

There are many kinds of compounds within Herba Patriniae, which may support the anti-cancer effect of Herba Patriniae, and hence, scholars wish to clarify what kinds of compounds exert this pharmacological effect. After treatment with the saponins extract of PV, the EMT and NF-κB signaling pathways were down-regulated in vitro, which subsequently inhibited the invasion and metastasis of human colorectal cancer cells (Xia et al., 2018). Moreover, at the dose of 50 mg/kg and 100 mg/kg, it also effectively reduced the weight of U14 cervical tumor in vivo (35.1% and 57.1%, respectively), which was closely related to the increase of apoptosis and G0/G1 tumor cells and the decrease of mutant P53 and Bcl-2 protein expression (Zhang et al., 2008). Patrinia-glycoside B-II from PS showed strong cytotoxic activities against HeLa (human cervical carcinoma cells), HepG2, HT1080 (human fibrosarcoma cells), A549 (human lung adenocarcinoma cells), A375-S2 (human melanoma cells), K562 (human erythroleukemic cells), HL60 (human leukemia cells), and U937 (Human leucemic monocyte lymphoma cells) with an IC\textsubscript{50} of 5.4, 4.2, 18.0, 27.9, 15.8, 6.2, 6.6, and 5.5 μM, respectively (Ren et al., 2013). Therefore, terpenoids in Herba Patriniae can be used as an anti-cancer potential component for in-depth research in vivo and in vitro. Flavonoids, as another kind of active compounds rich in Herba Patriniae, have also been proved to have considerable anti-cancer effects. Peng et al. (2006c) carried out the growth inhibition experiments on A498 (human kidney cancer cells), A549, BEL-7402 (human hepatocellular carcinoma cells), HT-29, MCF-7, SGC-7901 (human gastric adenocarcinoma cells), and K562 with 6 flavonoids isolated from PV. The results showed that (2S)-5, 7, 22S(68)-5, 7, showed 8-di-(γ,γ-dimethylallyl) flavanone, (2S)-5, 7, 28-tetrahydroxy-6-lavandulylated flavanone and (2S)-5, 7, 2te 6tetrahydroxy-6-lavandulylated fl flavanone exhibited high anticancer activities (IC\textsubscript{50} < 7 μg/mL) in a dose-dependent manner, and when the concentration of these compounds exceeded 15 μg/mL, the proliferation of cancer cells was completely inhibited, especially for K562 cells (IC\textsubscript{50} < 3.1 μg/mL). Patriniaflavanone A isolated from PV and the total flavonoid extract of PS and PV showed obvious dose-dependent inhibitory effects on SMMC7721 hepatocarcinoma cells (0.125–10 mg/mL). Meanwhile, the total flavonoids extract of PV has a better inhibitory effect on the growth of SMMC-7721 cells than PS (Wei et al., 2013b; Xiang et al., 2016; Zhao et al., 2019). Besides, impetycline A isolated from PV showed an inhibition effect on 2 kinds of tumor cells at the doses of 12.5–50 μM (Liu et al., 2019b).

5.2. Anti-inflammatory effect

Herba Patriniae has been widely used in traditional medicine to treat pelvic inflammatory disease (PID), pancreatitis, colitis, and other inflammatory diseases (Ji, 2006; Qiu, 2005; Zhang, 1997a). Modern pharmacological studies have demonstrated that various effective extracts of Herba Patriniae showed anti-inflammatory effects in different inflammatory-related diseases. In vitro, the ethyl acetate extract (10–100 μg/mL) and essential oil extract (100–200 μg/mL) of PS inhibited the secretion of pro-inflammatory cytokines in RAW 264.7 (murine macrophage cells) or BV-2 (mouse microglia cells) in a dose-dependent manner, respectively (Lee et al., 2012; Lin et al., 2018). In vivo, both the ethanol extract of PS (600 mg/kg) and the 70% ethanol extract of PV (0.55 g/kg) showed strong anti-inflammatory effects in rats with PID, which inhibited the infiltration of inflammatory cells and the production of cytokines in the upper genital tract of PID rats, as well as the levels of pro-inflammatory cytokines in serum (Zheng et al., 2012; Zou et al., 2015). On the other hand, the water extract and methanol extract of PS and the total flavonoids of Herba Patriniae exhibited obvious anti-inflammatory effects in animal models of acute pancreatitis, ulcerative colitis, and focal cerebral ischemia-reperfusion, respectively. All of these extracts inhibited the secretion of pro-inflammatory cytokines, such as IL-1β, IL-6, and TNF-α (Cho et al., 2011; Seo et al., 2006; Wei et al., 2019). Although these nonclinical pharmacological studies on Herba Patriniae extracts have indicated the good pharmacological effects of Herba Patriniae in the anti-inflammatory field, further clinical studies are more needed to extend its clinical use.

5.3. Antioxidant effect

Recently, the antioxidant effect of Herba Patriniae has been evaluated in vivo and in vitro, providing information on the pharmacological activity of both mixtures and single compounds. The phenylethyl flavones isolated from PV (25 μM) showed a significant antioxidant effect, and this effect was achieved through the modulation of the mir-144-3p/Nrf2 pathway, thereby eliminating intracellular ROS in vitro (Feng et al., 2018). The water, ethanol, and volatiles extract from PV and PS possessed strong antioxidant effect by DPPH assays, and especially the chlorogenic acid and total flavonoids in the water extracts of PS exhibited stronger free radical scavenging ability (Lin et al., 2018; Sun et al., 2018; Xie et al., 2008). Chlorogenic acid and flavonoids of Herba Patriniae are regarded as bioactive constituents for antioxidant activity. In vivo, it’s worth noting that the 60% ethanol extract of PV had a remarkable antioxidant effect on mice with acute liver injury, which is reflected by the reductions of ALT and AST activities in the serum, MDA content and LDH activity in the liver, and the enhanced liver T-SOD, T-AOC and GSH activities (Huang et al., 2019b). These results provide ideas for further research on its traditional medicine.

5.4. Anti-microbial, anti-viral, and anti-fungi effects

Herba Patriniae is widely used in traditional medicine to treat respiratory diseases caused by viruses. At present, the researches on the antiviral effect of Herba Patriniae were mainly focused on the respiratory syncytial virus (RSV) and severe acute respiratory syndrome (SARS) virus. Li et al. (2006) investigated the antiviral effects of water extract of PS or PV against the SARS virus in vitro. The extract possessed a strong inhibition rate of 45.0% at a concentration of 750.0 mg/mL, and could effectively quench the free radicals that occurred in the process of UV irradiation on λ-lysogenic cells. Li et al. (2004) reported that poly-saccharide mixture of PS or PV has an effective inhibitory effect on RSV in HeLa cells, with a therapeutic index of 116.12 and an EC\textsubscript{50} = 0.0986 mg/mL. These results provide a potential for using animal models to further explore the anti-virus infection mechanism of Herba Patriniae.

In vitro, the antibacterial effect of water extract and ethanol extract from PS were tested on Staphylococcus aureus, Streptococcus, Pasteurella, Salmonella, and Escherichia coli. Among them, the water extract showed a strong inhibitory effect against Staphylococcus aureus, Streptococcus, and Escherichia coli at a concentration of 0.5 g/mL (Tan et al., 2003). However, this paper have not showed the reason for the different antibacterial effects between water extract and ethanol extract, and further study should be carried out to illustrate this issue. In the past researches, saponins, volatile oils, organic acids and flavonoids were considered as the main chemical components within PS. These compounds may have played a key role in the antibacterial process. Among them, the content of total flavonoids and organic acids in the water extract of PS is higher than that of ethanol extract (Sun et al., 2018), and this may be the reason for the results of Tan et al. (2003). The 70% ethanol extract of PV showed dose dependent growth inhibition in Staphylococcus aureus, Escherichia coli, Proteus spp and Bacillus subtilis at 12.5–100 mg/mL, and has high UV radiation stability and thermostability (Dai and Lin, 2011). The tannin extract of PV not only had a significant inhibitory effect on Escherichia coli, Bacillus subtilis and Staphylococcus aureus, but also on Shigella dysenteriae and Salmonella typhimurium, with an inhibition rate of 23.45%–50.78% (Fan, 2014). Besides, Fu et al. (2017) discovered that the water extract of Herba Patriniae showed an obvious inhibitory effect on key genes related to biofilm, and could decrease biofilm formation and change the structure of the biofilms of Pseudomonas aeruginosa. Nevertheless, this study is lack of dose-dependent results, and a test on the drug exposure time to kill bacteria may also be meaningful for
the antibacterial study. Besides, its further study is necessary to associate the antibacterial activity with the corresponding diseases. Taken together, as a natural antimicrobial plant, Herba Patriniae is worthwhile to further study the active components, and besides, it also could be put into the industrial production of food and feed.

Diseases caused by fungal infection include superficial, subcutaneous and deep mycoses, which have a high incidence and easily cause systemic infectious diseases (Liu and He, 2014; Ran et al., 2017). Wu (2017a) studied the anti-fungal effect of Herba Patriniae on Cryptococcus neoformans, Candida albicans, Trichophyton rubrum and Aspergillus fumigatus, but it showed no inhibitory effect on these four fungi. Fan (2014) investigated the inhibitory effect of tannin extract of PV on Aspergillus niger, Aspergillus flavus, and Saccharomyces cerevisiae, and found that its inhibitory effect on these three fungi was poor, and the inhibition rate was less than 28.03%. At present, there are few studies on the anti-fungal effect of Herba Patriniae, and the anti-fungal effect of Herba Patriniae is worthy of further study.

5.5. Sedative and hypnotic effects

At present, neurological diseases have become a major problem affecting people’s quality of life. In traditional medicine, Herba Patriniae has a good curative effect on insomnia and neurasthenia (Qiu, 2005; Yang, 2002). A study conducted by Luo et al. (1986) demonstrated that 60% ethanol, and volatile oil extract from PS have sedative and hypnotic effects. In addition, the ethanol extract of PS at a dose of 1 g/mL showed an observable sedative effect on mice. Its sedative effect was stronger than that of the water extract and its intensity was similar to that of pentobarbital. The 95% ethanol extract of PS was further extracted with petroleum ether, chloroform, ethyl acetate, and n-butanol respectively for sedation and hypnosis experiment. The sedative effect of the n-butanol extract was the most significant among the four different polarity extracts (Tan et al., 2003; Xu et al., 2007). Therefore, the n-butanol extraction part of PS is considered to be an effective sedative extract. Moreover, the water extract of PV also has obvious sedative and central nervous system inhibitory effect, which can shorten the falling asleep time and prolong the sleep time induced by pentobarbital sodium, and the effect was enhanced with the increase of dose (20–60 mg/kg) (Chen et al., 2005; Zhong et al., 2004). Although these studies support the traditional medication experience of Herba Patriniae, systematic studies are needed to determine the bioactive compounds of this effect.

5.6. Others

The proangiogenic effect of PV has been tested on HUVECs, in an ex vivo mouse aortic ring assay, and in an in vivo murine hindlimb ischemia model. In vitro and in vivo pharmacological studies have indicated that the water extract of PV significantly promoted cell proliferation and migration, and induced angiogenesis via activating the FAK signaling pathway (Jeon et al., 2010). In traditional medicine, Herba Patriniae is widely used in the treatment of various skin diseases, such as psoriasis vulgaris, itching (Wang and Wang, 2002; Yan et al., 2015; Zhu and Jiang, 2015). Tohda et al. (2000) reported that the methanol extracts of PV exhibited a significant inhibitory on substance P-induced itch-scratch response. Although the mechanism of antipruritic action is not clear, these results demonstrated that PV could be developed as an antipruritic for the treatment of cutaneous diseases. In addition, decoction containing Herba Patriniae is reported to be used for diarrhea (Qiu, 2005). A study conducted by Zhang et al. (2019a) demonstrated that the 60% ethanol, dichloromethane layer, ethyl acetate layer, N-butanol layer, and water layer extracts of PV exhibited anti-diarrheal effects in a dose-dependent manner (100–400 mg/kg), and the dichloromethane layer showed the strongest anti-diarrheal effect in vivo and in vitro. Furthermore, Patrinoside and patrinoside A isolated from PS were shown to exert a significant effect on improving insulin resistance in

| Table 5 | Toxicity of herba patriniae. |
|---|---|---|---|---|
| Extract | Dosage | Subject | Adverse reaction | Reference |
| PS, root, methanol extract | – | mice | increased the serum aminotransferase and caused histopathological changes | Wang (2009) |
| PS | 200 mg/kg | patient | polyuria | Wang (2009) |
| PS | 200 mg/kg | mice | polyuria | Wang (2009) |
| PS, ethanol extract | 30 g crude drug/kg | mice | mild diarrhea and mild respiratory depression | Wang and Sun (1997) |
| PS, rhizome and root, 60% ethanol extract | 2-4 tablets (1 g crude drug/tablet), 2-3 times daily, for 10 days | patient | dryness in the mouth and stomach discomfort | Wang et al. (1983) |
| PS, root, ethanol extract | 5-10 mL (1 g crude drug/mL), 2-3 times daily, for 10-14 days | patient | temporary stomach discomfort or blushing in the face | Luo et al. (1986) |
| PS, root, 60% ethanol extract | 2-4 tablets (1 g crude drug/tablet), 2-3 times daily, for 10-14 days | patient | dryness in the mouth and stomach discomfort | Luo et al. (1986) |
| PS, root, volatile oil extract | 20 mg/ capsule, 1–2 capsules daily, for 10–14 days | patient | Nauseous or sleepy the next day | Luo et al. (1986) |

*Patrinia scabiosafolia* Fisch. (PV).

3T3-L1 adipocytes via activation PI3K/Akt signaling pathway, which plays an important role in type 2 diabetes (Liu et al., 2019c). Although both PV and PS contain iridoids, there is no report on the insulin resistance of PV. Moreover, there is no research on the proangiogenic, anti-pruritic, and anti-diarrheal effects of PS. Therefore, there are some differences in pharmacological effects between these two species of Herba Patriniae. It is suggested that further study should be conducted to determine the difference of pharmacological activities between the two plants, so as to provide scientific reference for safe and effective medication.

6. Toxicity

In traditional use, Herba Patriniae is almost non-toxic. However, mild side effects can be produced when large dosage is used. Excessive use of PV water extract can cause temporary leukopenia, dizziness, nausea and other symptoms (Deng, 2001). According to the reported toxicity of PS, the methanol extract from the root of PS increased the serum aminotransferase and caused histopathological changes in mice (Wang, 2009). In addition, when the oral dose of PS up to 200 mg/kg, it will lead to polyuria (Wang, 2009). Gavage of 30 g/kg of PS alcohol extract in mice can cause mild diarrhea and mild respiratory depression, but there is no adverse reaction at the dose of 24 g/kg (Wang and Sun, 1997). The volatile oil of PS was given 400, 750 and 1500 times as much as that of human (0.8 mg/kg) to mice for 7 days, that showed no abnormal performance (Luo et al., 1986). In clinical application, individual patients suffered from dry mouth and stomach discomfort after taking PS, and it will disappear after stopping the medicine. Its volatile oil products have no side effects on liver and kidney function and leukocyte count (Wang and Sun, 1997). Above all, Herba Patriniae is quite safe for animals and people at a reasonable dosage (see Table 5).
Table 6
Quantitative analysis for the quality control of Herba Patriniae.

| Analytes                      | Extraction method details                                                                 | Determination method | Results                                                                 | Species | Reference     |
|-------------------------------|------------------------------------------------------------------------------------------|----------------------|------------------------------------------------------------------------|---------|---------------|
| Flavonoids                    | The water boiled extraction method: 2.5 g PV powder was boiled in 50 mL water for three times, 2 h, 1.5 h, 1 h, respectively, the extract was filtered and water was added to 250 mL for constant volume. The ethanol reflux extraction method: 2.5 g PV powder was refluxed and extracted with 50 mL methanol for three times, 2 h, 1.5 h, 1 h, respectively, the extract was filtered and water was added to 250 mL for constant volume. The suoshi extraction method: 2.5 g PV powder was subjected to ultrasonic extracted with 30 mL methanol for 45 min, three times, the extract was filtered and water was added to 250 mL for constant volume. The supernuscent extraction method: 2.5 g PV powder was subjected to ultrasonic extracted with 50 mL methanol for 45 min, three times, the extract was filtered and water was added to 250 mL for constant volume. | UV       | The contents of flavonoids have a close relationship with the extraction method and the parts of PV. To extract flavonoids in roots, stems, leaves and whole grains of PV by the water boiled extraction method, the contents of flavonoids were 24.9, 18.1, 47.9, 34.2 mg/g, respectively; by the ethanol reflux extraction method, the contents of flavonoids were 30.3, 24.1, 51.6, 39.8 mg/g, respectively; by the suoshi extraction method, the contents of flavonoids were 34.9, 29.2, 97.4, 43.3 mg/g, respectively; by the supersonic extraction method, the contents of flavonoids were 32.8, 27.5, 54.1, 41.2 mg/g, respectively. | PV       | Xu and Zhou (2004) |
| Total flavonoids              | The ethanol extract: 100 g PS or PV was immersed in 1.5 L 70% ethanol for 30 min, refluxed and extracted for 2 h, filtered, repeated 3 times, combined filtrate, concentrated and freeze-dried. The water extract: 100 g PS or PV was immersed in 1.5 L distilled water for 0.5 h, refluxed and extracted for 2 h, filtered, repeated 3 times, combined filtrate, concentrated and freeze-dried. | HPLC and UV | In the water extract of PV, the contents of total flavonoids, chlorogenic acid and caffeic acid were 334.00 ± 5.20, 94.18 ± 1.94 and 19.05 ± 0.75 mg/g, respectively. In the ethanol extract of PV, the contents of them were 293.00 ± 2.65, 64.37 ± 2.43 and 21.19 ± 1.24 mg/g, respectively. Moreover, in the water extract of PS, the contents of them were 383.00 ± 3.61, 117.29 ± 0.85 and 1.52 ± 0.09 mg/g, respectively. In the ethanol extract of PS, the contents of them were 318.00 ± 2.65, 83.80 ± 1.15 and 1.12 ± 0.09 mg/g, respectively. | PV       | Sun et al. (2018) |
| Chlorogenic acid              |                                                                                          |                      |                                                                        | PS, PV  |               |
| Caffeic acid                  |                                                                                          |                      |                                                                        | PS, PV  |               |
| Inositol                     | 100 g of Herba patriniae was immersed in 300 mL 90% ethanol for 12 h, filtered, the drug residue was extracted with 200 mL of 90% ethanol, refluxed and extracted for 2 h, then filtered and volatilized residual ethanol on a water bath. | UV       | The contents of inositol of 3 batches were from 28.9-30.1 mg/kg.       | Herba Patriniae | Wang et al. (2002) |
| Oleanolic acid               | 100 g of PV was immersed in 1.5 L water for 0.5 h, then boiled for 0.5 h, filtered, the drug residue was repeatedly boiled with 1 L of water, the two extracted filtrates were combined, the 50 mL extract was concentrated in a water bath to a thick paste. | UV       | The contents of oleenolic acid from 3 batches of PV were from 2.29% to 2.41%. | PV       | Wang et al. (2012) |
| Quercetin                     | 1 g PS or PV powder was extracted with 20 mL of hydrochloric acid-methanol (1:20, v/v) mixed solution under reflux for 1 h, filtered and methanol was added to 25 mL for constant volume. | HPLC     | In PV, twelve batches have been determined with the contents of 0.061-1.046 mg/g for quercetin and 0.082-0.701 mg/g for kaempferol. In PS, fourteen batches have been determined with the contents of 0.062-0.938 mg/g for quercetin and 0.045-0.542 mg/g for kaempferol, indicating that the quercetin and kaempferol content in the samples from different sources were significantly different. | PS, PV  | Liu et al. (2015) |
| Kaempferol                    |                                                                                          |                      |                                                                        |         |               |
| Ursolic acid                  | 1 g Herba Patriniae powder was subjected to ultrasonic extracted with 30 mL methanol for 45 min, after the weight loss is made up, filtered and the extract of 1 mL was extracted and fixed volume to 10 mL with methanol. | HPLC     | The contents of ursolic acid and oleanolic acid for 6 batches were 0.218%-0.498% and 0.158%-0.473%, respectively. | Herba Patriniae | Zhou (2014) |
| Oleanolic acid               |                                                                                          |                      |                                                                        |         |               |
| Isosentixin                   | 1 g PV powder was subjected to ultrasonic extracted with 20 mL methanol for 30 min, extracted twice, the two extracted filtrates were combined. | HPLC     | Four batches have been determined with the contents of 0.78-1.68 mg/g for isosentixin and 1.87-2.42 mg/g for isoorientin, indicating that the isosentixin and isoorientin content in the samples from different sources were significantly different. | PV       | Chen (2008)    |
| Isoorientin                   |                                                                                          |                      |                                                                        | PV       |               |
| Hederagenin                  | 2 g Herba Patriniae powder was subjected to ultrasonic extracted with 50 mL methanol for 60 min, filtered, the drug residue was washed with proper amount of methanol, combined the filtrate and the washing solution, evaporated, and dissolved in 10 mL water, then extracted with 20 mL water-saturated n-butanol, extracted three times, combined the extracts and evaporated to dryness. The residue was heated and hydrolyzed with 20 mL methanol and 4 mL hydrochloric acid for 4 h, then added with 10 mL water and shaken and extracted with 20 mL chloroform, extracted twice, combined the extracts and evaporated to | HPLC     | The contents of hederagenin, oleanolic acid and ursolic acid have been determined in ten batches. The result was that the contents of the compounds were significantly different among the different samples. The concentration ranges were 0.002%-0.556%, 0.019%-0.592% and 0.022%-0.630% for hederagenin, oleanolic acid and ursolic acid. | Herba Patriniae | Mao et al. (2012) |

(continued on next page)
chlorogenic acid, caffeic acid, scutellarin, isoorientin, isovitexin, rats by UPLC-Q-TOF-MS method. As result, 7 prototypical components after intragastric administration of total flavonoids extract from Patriniae. Han et al. (2020) determind the serum pharmacochemistry fortunately, there are few investigations on the pharmacokinetics of Herba that was 0.045 compounds showed significant different content in two species. For et al., 2013a; Liu and Lei, 2019; Mao et al., 2012). In addition, the same fixed in Herba Patriniae. The content of compouds showed significantly anethol, camphogen, β-ionone, and β-damascenone, have been quanti- β-ionone, and β-damascenone were detected in Herba Patriniae, indicating that the contents for these compounds were quite different from different regions. In PS, the contents of palmitic acid, hexanoic acid and cis-anethol were 9.54–12.14%, 8.27–10.23%, respectively, respectively. In PV, the contents of in the last year and PS, PV, Liu et al. (2016a).

7. Quality control

An effective quality control method plays a key role in drug safety and effectiveness. With development of technology, UV, HPLC, and GC-MS have been used for monitor the variety of components in Herba Patriniae (Table 6). The content of total flavonoids has been quantified by UV method. It is worth concerning that the contents of total flavonoids were great difference in different parts, for example, 47.9–57.4 mg/g in leaves, while 18.1–29.2 mg/g in stems (Xu and Zhou, 2004). The extraction solvent also has great influence on the content of total flavonoids. Sun et al. found that the content of total flavonoids in PV extract by water was higher than that by 70% ethanol (334.00 ± 5.20 mg/g v.s. 293.00 ± 2.65 mg/g) (Sun et al., 2018). This phenomenon also occurs in the extraction of organic acids, such as chlorogenic acid and caffeic acid (Sun et al., 2018). These results indicate that flavonoids and organic acids are more easily extracted by aqueous solution.

Up to now, nineteen compounds, including quercetin, kaempferol, isovitexin, isoorientin, ursolic acid, oleanolic acid, hederagenin, β-ionone, and β-damascenone, have been quantified with contents of 0.108–0.805, 0.054–0.384, 0.026–0.114 and 0.056–0.203 mg/g for chlorogenic acid, iso-chlorogenic acid A, protocatechuic acid, caffeic acid and iso-chlorogenic acid C, respectively. In PS, the contents of palmitic acid, hexanoic acid and cis-anethol were 9.54–12.14%, 8.27–10.23%, 6.68–8.34%, respectively. In PV, the contents of palmitic acid, hexanoic acid and cis-anethol were 5.94–7.56%, 7.26 and 7.26%, respectively.

8. Pharmacokinetics

Pharmacokinetics is conducive to understanding the process of drug absorption, distribution, metabolism and excretion in the body. Unfortunately, there are few investigations on the pharmacokinetics of Herba Patriniae. Han et al. (2020) determined the serum pharmacochemistry after intragastric administration of total flavonoids extract from PV in rats by UPLC-Q-TOF-MS method. As result, 7 prototypical components (chlorogenic acid, caffeic acid, scutellarin, isoorientin, isovitexin, luteolin, and apigenin) and 7 metabolic components (Hydrocaffeate, scutellarein, Sulfated apigenin, sulfated luteolin, sulfated kaempferol, methylated kaempferol and one unknown compound) were detected in plasma, which might be the pharmacodynamic basis of its antitumor effect (Han et al., 2020).

9. Patents containing Herba Patriniae in China

To date, researchers have already filed more than 3000 patents related to the compositions containing Herba Patriniae in China. The patents for compositions containing both PS and PV in the last year and those containing either of them in the last decade are listed in Table 7. Most of the patents are human health products (88), 13 patents for animal husbandry, 6 patents for agriculture and 1 patent for fisheries.

Comprehensive consideration of the pharmacological activities, the prescription containing Herba Patriniae in Chinese patent is mainly used to treat gynecological diseases, such as chronic PID (Dai et al., 2019; Deng, 2019; He et al., 2019a; Hou, 2019; Li, 2019a; Lv et al., 2019; Zou et al., 2019), vaginitis (Jiang, 2019b; Li and Li, 2019a; Long, 2019; Luo, 2019b; Nong et al., 2019), cervicitis (Li, 2019c; Long and Yin, 2019), and orchitis (Yuan, 2019), respiratory diseases, such as chronic laryngitis (Gao, 2019d), rhinitis (Gong, 2019), and bronchitis (Zhao, 2019); digestive diseases, such as gastritis (Li, 2019d; Xiong, 2020), hepatitis (Feng, 2019; Jiang et al, 2019; Liu, 2019b; Ru, 2019; Zhao, 2019b), pancreatitis (Dang et al., 2019; Li, 2019e), appendicitis (Zeng, 2019; Zhang, 2019c), colitis and proctitis (Chen et al., 2019d); skin diseases, such as shingles (Dong, 2019), wound infection (Jiang, 2019c; Tan, 2019; Yu, 2019), and tinea pedis (Gao, 2019d); and animal inflammatory diseases, such as infectious bronchitis and fallopian tube injury in chickens (Zhang et al., 2019b), and animal mastitis (Zhou et al., 2019). Besides, in hygiene, it can be used to prepare oral care liquid (Peng et al., 2019b; Ye et al., 2019), laundry liquid (Xie, 2019), and toilet paper (Zhang, 2019). Other patented products containing Herba Patriniae include an anti-cancer decoction for lung cancer (Wang, 2019a; Wang et al., 2019b) and nasopharyngeal carcinoma (Xie and Xie, 2019b), a cosmetic for anti-oxidation (Wu, 2017b), anti-aging (Chen et al., 2018), acne (Ou, 2018), whitens (Geng et al., 2012; Li, 2018a, 2018b), and dark circles (Wang et al., 2018).

### Table 6 (continued)

| Analytes                  | Extraction method | Determination method | Results                                                                 | Species     | Reference     |
|---------------------------|-------------------|---------------------|------------------------------------------------------------------------|-------------|---------------|
| Protocatechuic acid       | 0.5 g Herba Patriniae powder was subjected to ultrasonic extracted with 20 mL 60% methanol with 5% formic acid for 30 min, and methanol was added to 25 mL for constant volume. | HPLC        | Twenty batches have been determined with the contents of 0.176–0.547, 0.950–7.26 and 0.046–0.340 mg/g for protocatechuic acid, chlorogenic acid and caffeic acid, indicating that the contents for these compounds in the samples from different sources were significantly different. | Herba Patriniae | (2019a)       |
| Chlorogenic acid          | 1 g Herba Patrinia powder was extracted with 25 ml of 80% methanol under reflux for 0.5 h, filtered and methanol was added to 25 mL for constant volume. | HPLC        | Five compounds from 10 batches of Herba Patriniae have been quantified with contents of 0.108–1.198, 0.143–0.805, 0.054–0.384, 0.026–0.114 and 0.056–0.203 mg/g for chlorogenic acid, iso-chlorogenic acid A, protocatechuic acid, caffeic acid and iso-chlorogenic acid C, respectively, indicating that the contents for these compounds were quite different from different regions. | Herba Patriniae | (2019)        |
| Caffeic acid              |                   |                     |                                                                        |             |               |
| Protocatechuic acid       |                   |                     |                                                                        |             |               |
| Chlorogenic acid          |                   |                     |                                                                        |             |               |
| Caffeic acid              |                   |                     |                                                                        |             |               |
| Iso-chlorogenic acid A    |                   |                     |                                                                        |             |               |
| Iso-chlorogenic acid C    |                   |                     |                                                                        |             |               |
| Palmic acid               | 30 g PS or PV powder was immersed in 300 mL water for 0.5 h, then extracted under reflux for 3 h and collected volatile oil. | GC-MS       | In PS, the contents of palmic acid, hexanoic acid and cis-anethol were 9.54–12.14%, 8.27–10.23%, 6.68–8.34%, respectively. In PV, the contents of palmic acid, hexanoic acid, and cis-anethol were 5.94–7.56%, 5.94–7.56%, respectively. | PS, PV       | Liu et al. (2016a) |
| Hexanoic acid             |                   |                     |                                                                        |             |               |
| cis-Anethol               |                   |                     |                                                                        |             |               |
| Camphogen                |                   |                     |                                                                        |             |               |
| β-Ionone                  |                   |                     |                                                                        |             |               |
| β-Damascenone            |                   |                     |                                                                        |             |               |

Patrinia villosa Juss. (PV); Patrinia scabiosifolia Fisch. (PS). * Not indicate species.
Table 7

Patients containing Herba Patrniae in the last year, patents contain PS or PV in the past decade.

| Category                              | Formulations          | Application                                    | Reference |
|---------------------------------------|-----------------------|------------------------------------------------|-----------|
| Gynecological diseases                | Syrup/wine            | Endometriosis (regulates qi, activates blood circulation, removes blood stasis, relieves pain) | (Chen et al., n. d., 2019) |
|                                       | Decoction/lotion/tablet | Vaginitis (kills bacteria, relieves itching, improves abnormal symptoms of leucorrea) | (Jiang, 2019b; Li and Li, 2019a; Long, 2019c; Luo, 2019b; Nong et al., 2019) |
|                                       | Tabletteielotion/decocion | Cervicitis and cervical erosion (clears heat, promotes diuresis, removes decaying tissue, promotes new tissue formation) | (Li, 2019a; Zhang and Jiang, 2019) |
|                                        | Capsule               | Endometritis                                  | (Gao, 2019a; 2019e) |
|                                       | Pille/tablet/capsule/granule/decocion | Dysmenorrhea (warms channels, dispels cold, improves blood circulation, regulates menstrual cycle) | (Yang, 2019a; Xie and Xie, 2019a) |
|                                        | Decoction/capsule/wine | Breast disease (increases immunity, removes inflammation, promotes blood circulation, removes blood stasis, regulates qi, detumescence, alleviates pain) | (Gao, 2019c; Wu, 2019c; Yan, 2019c; Zhang, 2019a) |
|                                        | Granule               | Uterine fibroids                              | He and Hong (2019) |
|                                        | Granule               | Tubal blockage                                | Li (2019b) |
|                                        | Decoction/patch       | Prostatitis and prostate hyperplasia (clears heat, detoxifies, diuresis, detumescence, removes blood stasis, relieves pain) | (Li, 2019b; Long and Yin, 2019) |
|                                        | Decoction             | Orchitis (improves immunity)                  | Yuan (2019) |
|                                        | Decoction             | Chronic obstructive pulmonary disease         | Fei et al. (2019) |
|                                        | Decoction             | Chronic laryngitis (improves immunity)        | Gao (2019d) |
|                                        | Spray                 | Rhinitis (antibacterial)                      | Gong (2019) |
|                                        | Oral liquid/granule   | Cough caused by tuberculosis, pneumonia, chronic pharyngitis and lung heat (clears lung heat, relieves cough, eliminates phlegm) | (Peng et al., 2019c; Yang, 2019c, 2019d) |
|                                        | Decoction             | Lung cancer (promotes blood circulation, removes blood stasis, moistens lung, removes phlegm) | (Wang, 2019a; Wang et al., 2019b) |
|                                        | Decoction             | Nasopharyngeal carcinoma (improves immunity)  | Xie and Xie (2019b) |

| Category                              | Formulations          | Application                                    | Reference |
|---------------------------------------|-----------------------|------------------------------------------------|-----------|
| Digestive system disease              | Capsule/powder        | Gastritis (promotes blood circulation, relieves pain, hemostasis) | (Li, 2019b; Xiong, 2020) |
|                                       | Tabletteielotion/decocion | Appendicitis (clears heat, detoxifies, benefits qi, promotes blood circulation, relieves pain, reduces inflammation) | (Zeng, 2019c; Zhang, 2019c) |
|                                       | Granule               | Endometritis                                  | (Gao, 2019a; 2019e) |
|                                        | Capsule               | Uterine fibroids                              | He and Hong (2019) |
|                                        | Granule               | Tubal blockage                                | Li (2019b) |
|                                        | Decoction/patch       | Prostatitis and prostate hyperplasia (clears heat, detoxifies, diuresis, detumescence, removes blood stasis, relieves pain) | (Li, 2019b; Long and Yin, 2019) |
|                                        | Decoction             | Orchitis (improves immunity)                  | Yuan (2019) |
|                                        | Decoction             | Chronic obstructive pulmonary disease         | Fei et al. (2019) |
|                                        | Decoction             | Chronic laryngitis (improves immunity)        | Gao (2019d) |
|                                        | Spray                 | Rhinitis (antibacterial)                      | Gong (2019) |
|                                        | Oral liquid/granule   | Cough caused by tuberculosis, pneumonia, chronic pharyngitis and lung heat (clears lung heat, relieves cough, eliminates phlegm) | (Peng et al., 2019c; Yang, 2019c, 2019d) |
|                                        | Decoction             | Lung cancer (promotes blood circulation, removes blood stasis, moistens lung, removes phlegm) | (Wang, 2019a; Wang et al., 2019b) |
|                                        | Decoction             | Nasopharyngeal carcinoma (improves immunity)  | Xie and Xie (2019b) |

Table 7 (continued)

| Category                              | Formulations          | Application                                    | Reference |
|---------------------------------------|-----------------------|------------------------------------------------|-----------|
| Tabletteielotion/decocion | Capsule/powder        | Gastritis (promotes blood circulation, relieves pain, hemostasis) | (Li, 2019b; Xiong, 2020) |
|                                       | Tabletteielotion/decocion | Appendicitis (clears heat, detoxifies, benefits qi, promotes blood circulation, relieves pain, reduces inflammation) | (Zeng, 2019c; Zhang, 2019c) |
|                                       | Capsule               | Uterine fibroids                              | He and Hong (2019) |
|                                       | Granule               | Tubal blockage                                | Li (2019b) |
|                                       | Decoction/patch       | Prostatitis and prostate hyperplasia (clears heat, detoxifies, diuresis, detumescence, removes blood stasis, relieves pain) | (Li, 2019b; Long and Yin, 2019) |
|                                       | Decoction             | Orchitis (improves immunity)                  | Yuan (2019) |
|                                       | Decoction             | Chronic obstructive pulmonary disease         | Fei et al. (2019) |
|                                       | Decoction             | Chronic laryngitis (improves immunity)        | Gao (2019d) |
|                                       | Spray                 | Rhinitis (antibacterial)                      | Gong (2019) |
|                                       | Oral liquid/granule   | Cough caused by tuberculosis, pneumonia, chronic pharyngitis and lung heat (clears lung heat, relieves cough, eliminates phlegm) | (Peng et al., 2019c; Yang, 2019c, 2019d) |
|                                       | Decoction             | Lung cancer (promotes blood circulation, removes blood stasis, moistens lung, removes phlegm) | (Wang, 2019a; Wang et al., 2019b) |
|                                       | Decoction             | Nasopharyngeal carcinoma (improves immunity)  | Xie and Xie (2019b) |

| Category                              | Formulations          | Application                                    | Reference |
|---------------------------------------|-----------------------|------------------------------------------------|-----------|
| Digestive system disease              | Capsule/powder        | Gastritis (promotes blood circulation, relieves pain, hemostasis) | (Li, 2019b; Xiong, 2020) |
|                                       | Tabletteielotion/decocion | Appendicitis (clears heat, detoxifies, benefits qi, promotes blood circulation, relieves pain, reduces inflammation) | (Zeng, 2019c; Zhang, 2019c) |
|                                       | Capsule               | Uterine fibroids                              | He and Hong (2019) |
|                                       | Granule               | Tubal blockage                                | Li (2019b) |
|                                       | Decoction/patch       | Prostatitis and prostate hyperplasia (clears heat, detoxifies, diuresis, detumescence, removes blood stasis, relieves pain) | (Li, 2019b; Long and Yin, 2019) |
|                                       | Decoction             | Orchitis (improves immunity)                  | Yuan (2019) |
|                                       | Decoction             | Chronic obstructive pulmonary disease         | Fei et al. (2019) |
|                                       | Decoction             | Chronic laryngitis (improves immunity)        | Gao (2019d) |
|                                       | Spray                 | Rhinitis (antibacterial)                      | Gong (2019) |
|                                       | Oral liquid/granule   | Cough caused by tuberculosis, pneumonia, chronic pharyngitis and lung heat (clears lung heat, relieves cough, eliminates phlegm) | (Peng et al., 2019c; Yang, 2019c, 2019d) |
|                                       | Decoction             | Lung cancer (promotes blood circulation, removes blood stasis, moistens lung, removes phlegm) | (Wang, 2019a; Wang et al., 2019b) |
|                                       | Decoction             | Nasopharyngeal carcinoma (improves immunity)  | Xie and Xie (2019b) |
Table 7 (continued)

| Category | Formulations | Application | Reference |
|----------|--------------|-------------|-----------|
| Health care | Health food | Anti-inflammatory, antiviral, antitumor | (Liu et al., 2011, 2012) |
| Hygiene | Mask | Antioxidation | Wu (2017b) |
| Metabolic disease | Pill/tablet/capsule/oral liquid | Postmenopausal osteoporosis | Zhang et al. (2012) |
| Skin diseases | Patch/decocion | Eczema (clears heat, detoxifies, anti-inflammation, antibacterial, reduces swelling and pain, relieves itching) | Mo (2017) |
| Health care | Tea | Improves human immunity, relieves constipation, anti-hypertension, delays ageing, promotes blood circulation, anti-cancer, anti-tumor, detoxifies | Qiu (2019) |
| Health food | Antioxidation | Gao et al. (2013) |
| Hygiene | Cream | Anti-aging (reduces melanin deposition) | (Chen et al., 2018) |
| Essence | Acne (promotes blood circulation, enhances metabolism, antibacterial) | Ou (2018) |
| Lotion/toner/mask | Whitens (preserves moisture, reduces skin pigmentation) and inhibiting melanin production | (Geng et al., 2012; Li, 2018a, 2018b) |

Patrinia villosa Juss. (PV); Patrinia scabiosafolia Fisch. (PS). * Not indicate species.

10. Conclusion and perspectives

Herba Patriniae can be used in clinical treatment in the form of a single herb or compound formulae of TCM to treat diseases for more than 2000 years in China. So far, a total of 233 compounds have been identified from the two species of Herba Patriniae, including triterpenoid saponins, flavonoids, organic acids, iridoids, and volatile oils. However, the two species applied as Herba Patriniae gave obviously different effects in vitro and in vivo. This difference in pharmacological activities possibly related to the differences in phytochemistry. So the interrelationship between compounds and pharmacological activities should be further studied. As the dose increases up to 20 mg/kg in mice, mild side effects were found. While the dose that causes the side effects in human was up to 4–12 g/day, and there are individual differences. Pharmacokinetics can provide scientific explanations for pharmacological and toxicological findings. Unfortunately, the pharmacokinetics of Herba Patriniae was lack, thus a range of pharmacokinetic studies on its active compounds are needed to provide comprehensive data for clinical application. Based on this review, the research on the dosage form of Herba Patriniae is not in-depth, so strengthening the work in this area will help to promote the development and utilization of Herba Patriniae. Altogether, this review extensively summarized the traditional uses, botanical description, phytochemistry, pharmacology, and quality control of Herba Patriniae, and provided information on the similarities and differences between the two plants for their further research and clinical applications.

Author contribution

Keyang Zheng and Birui Shi collected and analyzed documentations. Linna Gong drafted the manuscript. Menghua Liu and Wei Zou designed this review and critically revised the manuscript.

Declaration of competing interest

The authors declare no conflict of interest.
Acknowledgements

This work was supported by the NHC Key Laboratory of Birth Defects Research and Prevention (grant number KF2019002), the Hunan Provincial Science and Technology Department (grant number 2019JJ30013), the Hunan Administration of Traditional Chinese Medicine (grant number 202020D), and the College Students’ Innovation and Entrepreneurship Training Program (grant number 20191212034) of Southern Medical University.

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