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Review

Pinelliae Rhizoma: a systematic review on botany, ethnopharmacology, phytochemistry, preclinical and clinical evidence

Zuanji Liang[Δ], Jinchao Wei[Δ], Sioi Chan, Siyuan Zhang, Li Xu, Chenxiao Shen, Zhangfeng Zhong[*], Yitao Wang[*]

Macao Centre for Research and Development in Chinese Medicine, State Key Laboratory of Quality Research in Chinese Medicine, Institute of Chinese Medical Sciences, University of Macau, Macao SAR 999078, China

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ABSTRACT

Pinelliae Rhizoma (PR), known as Banxia in Chinese, Hange in Japanese, and Banha in Korean, is a renowned herbal medicine in East Asia derived from the dry tuber of *Pinellia ternata* (Thunb.) Breit. (PT). It is extensively utilized in dispensing granules, classical prescriptions, and herbal formulas to treat various conditions, including cough, infection, phlegm, nausea, asthma, and inflammation. Despite numerous studies on PR and its classical prescriptions over recent decades, a comprehensive synthesis of available evidence regarding its multifunctional roles and therapeutic potential is lacking. This review aims to address this gap by examining emerging evidence from metabonomics, preclinical studies, and clinical trials, while exploring potential trends and prospects for future research. A systematic literature search was conducted across six electronic databases, including PubMed, Web of Science, Scopus, ScienceDirect, Wanfang, and China National Knowledge Infrastructure, to identify relevant articles on PR published until March 2023. PR contains 107 compounds with diverse pharmacological activities, including anti-inflammatory, immune regulatory, anti-viral, anti-cancer, anti-asthma, antitussive and expectorant, antioxidant, anti-obesity, anti-atherosclerosis, antimicrobial, emetic and anti-emetic, anti-convulsant and anti-epileptic, sedative and hypnotic, learning and memory enhancement, and anti-depressant effects. Metabonomic studies suggest that raw PR may exhibit cardiotoxicity and pregnancy toxicity while showing no apparent hepatorenal toxicity. However, limited pharmacokinetic investigations on PR constrain its clinical translation. Furthermore, clinical safety data on PR is scarce, with only four clinical trials assessing its positive effects in pediatric epilepsy, nausea and vomiting, soft tissue injury, and chronic sinus tract. This review aims to enhance understanding of PR and provide valuable information and recommendations for further research and development of herbal medicine.

1. Introduction

Throughout history and across cultures, plants have been utilized for medicinal purposes [1, 2] serving as natural products [3, 4] and herbal medicines [5] with unique roles in disease prevention and treatment. Over 80% of the global population primarily relies on herbal medicinal products for primary care, positioning plants as a crucial source for new drug discovery [6]. A notable example is the discovery of artemisinin and dihydroartemisinin, currently used to treat malaria and credited with saving millions of lives worldwide, from the Chinese medicine Artemisiae Annuae Herba by Nobel laureate Youyou Tu [7]. In recent years, amidst the rapid global spread of the Coronavirus disease 2019 (COVID-19) pandemic, Chinese medicine has emerged as a vital component in treating COVID-19 and managing severe acute respiratory syndrome Coronavirus 2 (SARS-CoV-2) infection [8-12]. Mounting evidence indicates that Chinese medicine can alleviate symptoms such as cough and fever, reduce mortality and the incidence of severe or critical events, and promote clinical recovery [10-13].

Pinelliae Rhizoma (PR, Banxia in Chinese, Hange in Japanese, and Banha in Korean), the principal herb in Chinese medicine prescriptions such as Qingfei Paidu Decoction and Huashi Baidu Decoction, plays a vital role in the treatment of COVID-19 [14-17]. Pinelliae Rhizoma (PR) is the dry tuber of *Pinellia ternate* (Thunb.) Breit. (PT), which belongs to the genus *Pinellia* of the Araceae family. PR was characterized as pungent, warm in nature, and poisonous in the ancient and renowned Chinese medicinal text *Shennong Bencao Jing* (Dong Han Dynasty, A.D. 25–220) [18, 19]. PR is commonly utilized for treating cough, inflammation, infection, phlegm, vomiting, and asthma [19, 20], and has been included in the national pharmacopeias of China, Japan, and Korea. Over the past decade (2011–2020) [21], PR has been exported from mainland China to 33 countries and regions across six continents according to China customs statistics, including Asia, Europe, North America, South America, Africa, and Oceania. Asia emerged as the primary export destination, constituting 99.43% of the total export volume and 99.42% of the total export value,

* Corresponding author.
E-mail addresses: zfzhong@um.edu.mo (Z. Zhong); ytwang@um.edu.mo (Y. Wang)
Δ These authors contributed equally to this work.

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more, high-throughput analysis and high-resolution mass spectrometry enable the re-examination of previously reported PR extracts whose constituents were not fully identified. Advanced isolation technology, particularly with bioactivity-guided properties, could expedite the analytical processes.

PR demonstrates significant therapeutic potential; however, its inherent toxicity presents a challenge to its utilization. The narrow margin between medicinal efficacy and adverse effects hinders PR applications. Traditional practitioners have employed processed preparation of decoction pieces and formula compatibility methods to mitigate PR toxicity and enhance therapeutic outcomes. The *Pharmacopoeia of China* recognizes three types of processed PR; however, other drug regulatory systems do not accept processed PR due to significant alterations in PR components after processing, potentially compromising quality control systems and original clinical efficacies. Consequently, tracking the mobilization and alteration of PR components, particularly those associated with potential toxicity resulting from pharmaceutical and formula changes, is crucial for modernizing and globalizing PR applications.

Although our systematic review of PR concluded that traditional and model clinical regimes of PR are effective, further scientific research is necessary to elucidate the pharmacokinetic parameters of PR. The absorption, distribution, metabolism, and excretion phases of PR in humans are crucial factors that require consideration before assessing its safety and developing modern drugs. The combined usage of PR with other herbal medicines represents a canonical model with a long history of clinical application, which has contributed to the sophistication of molecular mechanisms of action and relative pharmacokinetic alterations. To the best of our knowledge, clinical trials providing reliable evidence are a key stage in drug development. However, only four clinical trials have reported on the therapeutic potential of PR, leaving a gap between scientific evidence and clinical practice. To address this gap, clinical trials investigating the various therapeutic effects of PR should be conducted in a more rigorous and standardized manner to mitigate risks. Subsequently, real-world data can be collected and analyzed to generate real-world evidence, which will be valuable for the continued evaluation of PR's clinical safety and efficacy. This evidence can also provide insightful information and beneficial suggestions for other Chinese medicine research.

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Supporting information

Supporting information for this study is available upon request *via* email to the corresponding author.

Declaration of competing interest

These authors have no conflict of interest to declare.

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Dr. Zhangfeng Zhong received his doctoral degree in Biomedical Sciences from the University of Macau in 2016. He continued his research as a Visiting Scholar or Postdoctoral Fellow at Northwestern University, University of Hong Kong, and University of Macau. Currently, he works as an Assistant Professor at University of Macau, Macao, China. His research interests are focused on Chinese medicine R&D, drug screening, and lead compound discovery. Dr. Zhong is also listed among the World's Top 2% Scientists.

Prof Yitao Wang is the chair professor and founding director of the Macao Centre for Research and Development in Chinese Medicine, State Key Laboratory of Quality Research in Chinese Medicine, and Institute of Chinese Medical Sciences at the University of Macau. He currently serves as the Editor-in-Chief of the SCI-indexed journal *Chinese Medicine*. He is focusing on research and development of Chinese medicine. Prof. Wang is also listed among the Clarivate Highly Cited Researchers and World's Top 2% Scientists.