Chemistry, pharmacology and analysis of *Pseudostellaria heterophylla*: a mini-review

De-jun Hu¹†, Farid Shakerian¹†, Jing Zhao¹,²* and Shao-Ping Li¹*  

**Abstract**  
*Pseudostellaria heterophylla* is one of the well-known traditional Chinese medicines and has been used in clinics for 100 years in China. The chemistry and pharmacology of *P. heterophylla* were reviewed to understand its active compounds. Then analysis of these compounds related to quality control of this herb was discussed. For the analysis of chemicals, three aspects have been discussed in this review. The first two aspects focused on the methodologies for analysis of cyclic peptides and carbohydrates in *P. heterophylla*, respectively. The last one dealt with the other methods used for identification of *P. heterophylla*. Some rich chemicals such as oligosaccharides in this plant were rarely evaluated. Many analyses were performed on this plant, however, few of them were accepted as quality control method.  

**Keywords:** *Pseudostellaria heterophylla*, Chemistry, Pharmacology, Analysis

**Introduction**  
*Pseudostellaria heterophylla, tai-zi-shen* (太子参) or *hai-er-shen* (孩儿参) in Chinese, is a well-known traditional Chinese medicines (TCMs) first officially recorded in *Ben Cao Cong Xin*, which contains 721 kinds of herbs, by Wu Yiluo in 1757 [1]. *P. heterophylla* was considered as one of the precious medical material from ancient China and now is one of the most commonly used TCMs in clinic, which invigorating spleen, replenishing qi, moistening lung and benefitting blood. It has been used for treatment of fatigue, spleen asthenia, anorexia, asthenia after severe illness and cough due to lung dryness [2–5]. This medicine is often used for children as a substitute of ginseng because of its mild effects [6].  

*Pseudostellaria heterophylla* mainly distributed in Liaoning, Hebei, Shandong, Anhui and Sichuan provinces. Ningde (Fujian Province) and Shibing (Guizhou Province) in China offer the most suitable environment for *P. heterophylla* cultivation [7]. However, consecutive monoculture of this plant will lead to a serious decline of biomass and quality of its underground tubers. Farms used for cultivation of *P. heterophylla* can only be replanted once every 4 years [8, 9]. As the sources of wild *P. heterophylla* with high quality in geo-authentic production zone are limited and the demand for this medicinal material is rising annually, the government has established a large-scale cultivation areas for it in Jurong (Jiangsu Province), Zherong (Fujian Province), Shibing (Guizhou Province) and Xuancheng (Anhui Province) of China [10]. However, due to differences of ecological environments, accumulation of active components in wild and cultivated *P. heterophylla* and their quality have shown significant differences [11, 12]. Therefore, it is necessary to understand chemical components and pharmacological activities of *P. heterophylla* before establishing an effective quality control method to ensure its safety and efficacy [13].  

**Chemical constituents in *P. heterophylla***  
Various components were found in *P. heterophylla*, including cyclic peptides (pseudostellarin), polysaccharides, amino acids, saponins, and sapogenins based on chemical studies [14]. In recent years, cyclic peptides with special structures (Fig. 1) isolated from *P. heterophylla* have attracted many researchers’ interest. And high-speed counter-current chromatography (HSCCC) was demonstrated to be an efficient separation method for cyclic peptides [15–17]. Up to date, pseudostellarin...
Fig. 1 Structures of main chemicals in Pseudostellaria heterophylla
Fig. 1 (continued)
A-G have been separated from *P. heterophylla* [18–21], which was summarized in Table 1. In addition, polysaccharides (Fig. 1), as one of main bioactive components in *P. heterophylla*, have been reported to exhibit multiple pharmacological activities [22]. Lectins with high hemagglutination activity were also found in *P. heterophylla* [23, 24]. They also have minor inhibitory effect on glycohydrolases, such as α-glucosidase, β-glucosidase and β-glucuronidase which are involved in HIV infection [24]. However, these lectins were devoid of antifungal activity, labile to acid and alkali and also exhibited poor thermostability [23].

**Pharmaceutical activities of *P. heterophylla***

Based on the abundant chemical constituents, *P. heterophylla* has multiple pharmaceutical activities including immunomodulatory [3, 25], antidiabetic [26–29], antitussive [5], antioxidant [30] activities, as well as protective effects on retinal injury and exercise-induced oxidative stress etc. [31–33].

Plant cyclopeptides comprise a large group of small molecules from natural medicines, which exhibit various pharmacological activities, such as immunomodulatory, anti-inflammatory, antioxidant, anti-aging and antitumor effects [34, 35]. Previous studies showed that heterophyllin B, one of main cyclopeptides in *P. heterophylla*, effectively suppressed the adhesion and invasion of human esophageal carcinoma cells by mediating PI3 K/ AKT/β-catenin pathways and regulated the expression levels of adhesion- and invasion-associated genes [36]. Furthermore, cyclopeptides have been demonstrated as the major active components correlated to the cytotoxic activities against three human tumor cell lines (MGC80-3, HepG2 and RKO) [37].

In recent years, increasing studies have been focused on the bioactivities of polysaccharides from *P. heterophylla*. The fraction riched with polysaccharides of *P. heterophylla* has protective effects against cobalt chloride-induced hypoxic injury in H9c2 cell [14]. Crude polysaccharides from *P. heterophylla* also can improve exercise endurance and have protective effects against oxidative stress [31–33]. Polysaccharides with molecular weight of 50 kDa - 210 kDa are not only significantly lowering blood sugar but also reducing total triglyceride level in serum [28]. Polysaccharides of *P. heterophylla* have been proved their benefits to chronic fatigue syndrome. That may be why *P. heterophylla* is usually used as a tonic herb [38]. However, crude polysaccharides from *P. heterophylla* are commonly used. A water-soluble, pectic polysaccharide with molecular weight of 48 kDa, composed of rhamnose, galactose, arabinose and galacturonic acid and 1,4-linked galacturonic acid as main chain with small amount of 1,2-linked rhamnose, could obviously stimulated insulin secretion [26]. A novel homogeneous polysaccharide, named as H-1-2, was also isolated from *P. heterophylla* polysaccharide. The mean molecular weight of H-1-2 was 14 kDa and it was only composed of d-glucose monosaccharide. In vitro, HepG2, 3T3-L1, and L6 cells were used to assess cellular glucose consumption and cellular glucose uptake. The results showed that H-1-2 could clearly increase glucose uptake and utilization in muscle and adipose cells, which is beneficial for screening leading compounds of anti-diabetes [27]. The saponins extract from *P. heterophylla* has also been demonstrated to have protective effects on retinal laser injuries [4]. In addition, ethyl acetate fraction extracted from *P. heterophylla* exhibited a dose-dependent antitussive effect [5].

**Chemical analysis of *P. heterophylla***

Various methods have been developed to analyze the components in *P. heterophylla*. High performance liquid chromatography (HPLC), thin layer chromatography (TLC), gas chromatography (GC), matrix-assisted laser desorption/ionization mass spectrometry (MALDI-MS), near infrared (NIR) spectroscopy and nuclear magnetic

| Table 1  | Main chemical constitutes in *P. heterophylla* |
|----------|----------------------------------------------|
| **Type of components** | Components purified | References |
| Peptides |  |  |
| Heterophyllin A, B, D, J |  | [15, 17, 19, 61–64] |
| Pseudostellarin A–C |  | [20, 63] |
| Pseudostellarin D–F |  | [21, 65] |
| Pseudostellarin G |  | [18] |
| Pseudostellarin H |  | [66] |
| Polysaccharides |  |  |
| Rhamnogalacturonan I |  | [26] |
| H-1-2 (MW 1.4 × 104 Da, a type of glucan, main chain with 1 → 4 linked glucose, and a small amount of branched chain with 1,6-linked glucose) |  | [27] |
| PH-I A, PH-I B and PH-I C |  | [22] |
| Lectin |  |  |
| 36 kDa lectin |  | [23, 24] |
resonance (NMR) etc. have been applied for characterization of components in *P. heterophylla*, which were summarized in Table 2. Peng et al. evaluated the concentration of heavy metals in cultivation soils and *P. heterophylla*, and their bioconcentration factors (BFs) of investigated heavy metals are not higher than 0.5 except for Cd, where Pb and As were especially low. Only Cd could be enriched slightly in *P. heterophylla* while others could not [39].

### Analysis of cyclic peptides in *P. heterophylla*

Cyclic peptides are the characteristic components in *P. heterophylla*, and heterophyllin B (Fig. 1) is the most typical one. Its structure was elucidated as a cyclic octapeptide (cyclo-(Gly–Gly–Leu–Pro–Pro–Pro–Ile–Phe)) based on TLC, HPLC, MS and NMR analysis [40]. HSCCC (high speed counter current chromatography) was successfully applied for the separation of heterophyllin B from *P. heterophylla* [17]. Heterophyllin B was also used as quality control marker of *P. heterophylla* in Chinese Pharmacopoeia 2010 [41], but not in Chinese Pharmacopoeia 2015 [42]. This status indicated that heterophyllin B is not a reasonable marker for quality of *P. heterophylla*. Therefore, further research to find efficient markers for authenticity and quality evaluation of *P. heterophylla* is urgently needed.

Two cyclic peptides (heterophyllin A, B), 12 nucleosides, and 16 amino acids were simultaneously quantified by ultra-performance liquid chromatography tandem triple quadrupole mass spectrometry (UPLC-QQQ-MS/MS) [43]. The other studies focused on cyclic peptides were for simultaneous analysis of pseudostellarin A, C, D, and G using HPLC coupled with electrospray ionization tandem mass spectrometry (ESI–MS) [25], and UPLC-quadrupole time of flight (QTOF)-MS/MS methods for analysis of pseudostellarin A, B, D, F, and heterophyllin A in *P. heterophylla* [44–46]. 1H-NMR-based metabolomics coupled with HPLC was also employed to investigate the metabolites in *P. heterophylla* [47], which has the unique advantages in the accurate identification of components.

### Analysis of carbohydrates in *P. heterophylla*

Polysaccharides are the main bioactive macromolecule components in *P. heterophylla*. Their pharmaceutical activities have been discussed in “Pharmaceutical activities of *P. heterophylla*” section. Polysaccharides in *P. heterophylla* were not well investigated to date, even if some of their beneficial effects such as antioxidant, immunostimulant and antitumor activities have been demonstrated. In fact, few types of polysaccharides have been identified in structure. However, the biological activities of polysaccharides are closely correlated to their molecular size, types and ratios of constituent monosaccharides, and features of glycosidic linkages (e.g., configuration and position of glycosidic linkages, and sequence of monosaccharides) [48, 49]. Recently, HPSEC, HPLC after 1-phenyl-3-methyl-5-pyrazolone (PMP) derivatization, NMR, Fourier transform infrared analysis (FT-IR) and chemical

### Table 2 Chemical analysis of *P. heterophylla*

| Analytes                                                                 | Methods                                                                 | References |
|-------------------------------------------------------------------------|-------------------------------------------------------------------------|------------|
| Pseudostellarin A, C, D, and G                                          | HPLC–ESI–MSn                                                            | [25]       |
| Pseudostellarin A, B, C, D, E, G                                        | HPLC–APCI (atmospheric pressure chemical ionization)-MS                  | [67]       |
| Pseudostellarin A, B, E, F, G, Heterophyllin A, B, D                    | UPLC–triple TOF–MS/MS, UPLC–ESI–TOF MS/MS                              | [64, 68, 69]|
| Maltotriose, sucrose, thymine, inosine triphosphate, pseudostellarin A, B, D, F, heterophyllin A and sphinganine etc. | UPLC–triple TOF–MS/MS                                                  | [44–46]    |
| 21 compounds                                                            | Ultra-performance liquid chromatography-triple time-of-flight mass/mass spectrometry (UPLC–triple TOF–MS/MS) | [70]       |
| 34 compounds (heterophyllin A and B, alanine, lactate, lysine, threonine, sucrose, tyrosine, linolenic acid, γ-aminobutyrate, glutamine, raffinose, xylose etc.) | 1H-NMR-based metabolomics coupled with HPLC                             | [47]       |
| Free amino acid                                                         | NIR                                                                     | [71]       |
| Nucleosides and nucleobases                                              | QTRAP LC–MS/MS                                                          | [55–57, 72]|
| Volatile components: palmitic acid (21.37%), 9,12-octadecadienoic acid ethylester (16.98%), trans-oleic acid (5.94%), chondrillasterol (3.99%), stigmast-7-en-3-ol (3.92%), 5,6-dihydroergosterol (2.48%), 1-monolinolein (2.35%) | GC–MS                                                                 | [73]       |
| Polysaccharide                                                          | High-performance size-exclusion chromatograph (HPSEC)                  | [74]       |
| Water-soluble sugar                                                     | Phenol–sulfuric acid                                                   | [75]       |
| Fingerprint                                                             | HPLC                                                                    | [16, 37, 58–60, 76–78] |
| Fingerprint                                                             | GC–MS                                                                   | [79]       |
Characterization of P. heterophylla

The isobaric tags for relative and absolute quantification (iTRAQ) MS/MS have been applied for discrimination of different habitats of P. heterophylla [51, 52]. Furthermore, Wu et al. developed a method based on Raman spectroscopy coupled with chemometric to discriminate the geographic regions of cultivation [12]. Near infrared (NIR) spectroscopy combined with support vector data description (SVDD) was attempted to identify the geographical origins of P. heterophylla [6]. NMR has also been developed for identification of wild P. heterophylla from different cultivated fields [47, 53]. In addition, high-throughput RNA sequencing (RNA-seq) was employed as de novo assembly for studying the transcriptome in P. heterophylla, and significantly differentially expressed genes in P. heterophylla from different fields were found [54].

Besides, nucleosides and nucleobases in P. heterophylla were quantified by QTRAP LC–MS/MS for evaluating the processing methods and discriminating different idioplasm resources of P. heterophylla [55–57]. HPLC and GC–MS fingerprints were also developed for identification of P. heterophylla [58–60].

Conclusion

Pseudostellaria heterophylla is one of the well-known TCMs with multiple pharmacological activities in last decades. Even researchers evaluated the chemicals especially cyclic peptides in this plant, the methods for quality control of P. heterophylla are still not reasonable. Some chemicals such as oligosaccharides, which are rich in this plant based on our research (data will be published in others), were rarely evaluated. The investigation of oligosaccharides, with high amount in aqueous extract of P. heterophylla, may lead to develop a rational and scientific quality control methods for this herb.

References

1. Liu D, Han BX, Yao HJ, Dai J, Chen NF. Advances on chemical constituents in Radix Pseudostellariae. Chin J Ethnomed Ethnopharm. 2014;16:18–20.
2. Sheng R, Xu X, Tang Q, Bian D, Li Y, Qian C, He X, Gao X, Pan R, Wang C, Luo Y, Xia Y, Dai Y. Polysaccharide of radix pseudostellariae improves chronic fatigue syndrome induced by poly I:C in mice. Evid Based Compl Altern. 2011;1:9.
3. Choi YY, Kim MH, Ahn KS, Lim JY, Lee SG, Yang WM. Immunomodulatory effects of Pseudostellaria heterophylla (Miquel) Pax on regulation of Th1/Th2 levels in mice with atopic dermatitis. Mol Med Rep. 2017;15:649–56.
4. Rui G, Wei W, Yuliang W, Kai L, Xiaobing C, Changle Z, Longshu S. Protective effects of Radix Pseudostellariae extract against retinal laser injury. Cell Physiol Biochem. 2014;33:1643–53.
5. Pang W, Lin S, Dai Q, Zhang H, Hu J. Antitussive activity of Pseudostellaria heterophylla (Miquel) Pax extracts and improvement in lung function via adjustment of multi-cytokine levels. Molecules. 2011;16:3360–70.
6. Lin H, Zhao J, Chen Q, Zhou F, Sun L. Discrimination of Radix Pseudostellariae according to geographical origins using NIR spectroscopy and support vector data description. Spectrochim Acta A. 2011;79:1381–5.
7. Wu L, Chen J, Wu H, Qin X, Wang J, Wu Y, Khan MU, Lin S, Xiao Z, Luo X, Zhang Z, Lin W. Insights into the regulation of rhizosphere bacterial communities by application of bio-organic fertilizer in Pseudostellaria heterophylla monoculture regime. Front Microbiol. 2016;7:1788.
8. Wu H, Wu L, Wang J, Zhu Q, Lin S, Xu J, Zheng C, Chen J, Qin X, Fang C, Zhang Z, Azeem S, Lin W. Mixed phenolic acids mediated proliferation of pathogens Talaporomyces helicus and Kosakonia sacchari in continuously monocultured Radix pseudostellariae Rhizosphere Soil. Front Microbiol. 2016;7:335.

Acknowledgements

Not applicable.

Authors’ contributions

DH and FS draft the manuscript. JZ and S-PL initiated the topic, revised and finally confirmed the manuscript. All authors read and approved the final manuscript.

Funding

The research was partially supported by grants from the National Natural Science Foundation of China (Nos. 81673389 and 81603069), the Science and Technology Development Fund of Macau (074/2016/A2, 075/2018/A2, 034/2017/A1 and 040/2016/A) and the University of Macau (MYRG2018-00083 and CPG2019-00027).

Availability of data and materials

All reported or analyzed data in this review is extracted from published articles.

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

Author details

1 State Key Laboratory of Quality Research in Chinese Medicine, Institute of Chinese Medical Sciences, University of Macau, Macau, China. 2 College of Pharmacy, Chengdu University of Chinese Medicine, Chengdu, China.

Received: 6 March 2019 Accepted: 15 May 2019

Published online: 23 May 2019

Abbreviations

P. heterophylla: Pseudostellaria heterophylla; TCMs: traditional Chinese medicines; HSCCC: high-speed counter-current chromatography; HPLC: high performance liquid chromatography; TLC: thin layer chromatography; GC: gas chromatography; MALDI–MS: matrix-assisted laser desorption/ionization mass spectrometry; NMR: near infrared; NMR: nuclear magnetic resonance; BFs: bioconcentration factors; UPLC–QQQ–MS/MS: ultra-performance liquid chromatography tandem triple quadrupole mass spectrometry; ESI–MS: electrospray ionization tandem mass spectrometry; TOF: time of flight; PMP: 1-phenyl-3-methyl-5-pyrazolone; FT-IR: Fourier transform infrared analysis; iTRAQ: isobaric tags for relative and absolute quantification; SVDD: support vector data description; RNA-seq: RNA sequencing.
9. Wu L, Chen J, Wu H, Wang J, Wu Y, Lin S, Khan MU, Zhang Z, Lin W. Effects of consecutive monoculture of *Pseudostellaria heterophylla* on soil fungal community as determined by pyrosequencing. Sci Rep. 2016;6:26601.

10. Zhao WD, Pang L, Dong N, Yang S. LC-ESI-MS/MS analysis and pharmacokinetics of heterophyllin B, a cyclic octapeptide from *Pseudostellaria heterophylla* in rat plasma. Biomed Chromatogr. 2015;29:1693–9.

11. Wu L, Li Z, Li J, Khan MA, Huang W, Zhang Z, Lin W. Assessment of shifts in microbial community structure and catabolic diversity in response to *Rheummannia glutinosum* microbiota. Appl Soil Ecol. 2013;67:1–9.

12. Wu M, Chen L, Huang X, Zheng Z, Qiu B, Guo L, Lin Z, Chen G, Cai Z. Rapid authentication of *Pseudostellaria heterophylla* (Taizishen) from different regions by Raman spectroscopy coupled with chemometric methods. J Lumin. 2018;202:239–45.

13. Deng Y, Bangxing H, Dejun H, Jing Z, Shaoping L. Qualitation and quantification of water soluble non-starch polysaccharides from *Pseudostellaria heterophylla* in China using saccharide mapping and multiple chromatographic methods. Carbohydr Polym. 2018;199:619–27.

14. Wang Z, Liao SG, He Y, Li J, Zhong RF, He X, Liu X, Xiao TT, Lan YY, Long QD, Wang YL. Protective effects of fractions from *Pseudostellaria heterophylla* against coalb chloride-induced hypoxic injury in H9c2 cell. J Ethnopharmacol. 2013;147:540–5.

15. Han C, Chen J, Liu J, Lee FSC, Wang X. Isolation and purification of *Pseudostellaria* B (cyclic peptide) from *Pseudostellaria heterophylla* (Miq.) Pax by high-speed counter-current chromatography. Talanta. 2007;71:801–8.

16. Han C, Shen Y, Chen J, Lee FSC, Wang X. HPLC fingerprinting and TLC-TOF-MS analysis of the extract of *Pseudostellaria heterophylla* (Miq.) Pax root. J Chromatogr B. 2008;862:125–31.

17. Yuan LM, Fu RN, Zuo C, Fan JM, Li XJ. A case report of an effective treatment for diabetic foot ulcers with integration of traditional Chinese medicine and Western medicine. J Diabetes Complications. 2009;23:360–4.

18. Morita H, Kobata H, Takeya K, Itokawa H, Pseudostellarin G. a new tyrosinase inhibitory cyclic octapeptide from *Pseudostellaria heterophylla*. Tetrahedron. 1994;50:6797–804.

19. Morita H, Kayashita T, Kobata H, Gonda A, Takeya K, Itokawa H. *Pseudostellaria* A-C, new tyrosinase inhibitory cyclic peptides from *Pseudostellaria heterophylla*. Tetrahedron. 1994;50:6797–804.

20. Morita H, Kayashita T, Kobata H, Gonda A, Takeya K, Itokawa H. *Pseudostellaria* D-F, new tyrosinase inhibitory cyclic peptides from *Pseudostellaria heterophylla*. Tetrahedron. 1994;50:6797–804.

21. Wang HX, Ng TB. Concurrent isolation of a Kunitz-type trypsin inhibitor from *Pseudostellaria heterophylla* roots. Biochem Biophys Res Commun. 2006;342:349–53.

22. Wang HX, Ng TB. A novel lectin from *Pseudostellaria heterophylla* roots with sequence similarity to Kunitz-type soybean trypsin inhibitor. Life Sci. 2001;69:327–33.

23. Wang J, Li J, Li H, Wu X, Gao W, HPLC-ESI-MS/N analysis, fed-batch cultivation enhances bioactive compound biosynthesis and immune-regulative effect of adventitious roots in *Pseudostellaria heterophylla*. Appl Biochem Biotechnol. 2015;177:63–75.

24. Chen J, Pang W, Kan Y, Zhao L, He Z, Shi W, Yan B, Chen H, Hu J. Structure of a pectic polysaccharide from *Pseudostellaria heterophylla* and stimulating insulin secretion of INS-1 cell and distributing in rats by oral. Int J Biol Macromol. 2017;106:456–63.

25. Chen J, Pang W, Shi W, Yang B, Kan Y, He Z, Hu J. Structural elucidation of a novel polysaccharide from *Pseudostellaria heterophylla* and stimulating glucose uptake in cells and distributing in rats by oral. Molecules. 2016;21:1233.

26. Hu J, Pang W, Chen J, Bai S, Zheng Z, Wu X. Hypoglycemic effect of polysaccharides with different molecular weight of *Pseudostellaria heterophylla*. BMC Compl Altern Med. 2013;13:267.

27. Xie XS, Wang YL, Cai Z, Fan JM, Li XJ. A case report of an effective treatment for diabetic foot ulcers with integration of traditional Chinese medicine and Western medicine. J Diabetes Complications. 2009;23:360–4.

30. Ng TB, Liu F, Wang LX. The antioxidant effects of aqueous and organic extracts of *Panax quinquefolium*, *Panax notoginseng*, *Codonopsis pilosula*, *Pseudostellaria heterophylla* and *Glehnia littoralis*. J Ethnopharmacol. 2004;93:285–8.

31. Li S, Chen Z, Wang X, Zhang CL. Crude polysaccharides from Radix pseudostellariae improves exercise endurance and decreases oxidative stress in forced swimming rats. J Food Agric Environ. 2013;11:123–6.

32. Chen Z, Li S, Wang X, Zhang CL. Protective effects of Radix Pseudostellariae polysaccharides against exercise-induced oxidative stress in male rats. Exp Ther Med. 2013;5:1089–92.

33. Chuanlong Z, Xiaoxia Z. Effects of polysaccharides from *Pseudostellaria heterophylla* on exercise endurance capacity and oxidative stress in forced swimming rats. Sci Res Essays. 2011;6:2360–5.

34. Tan NH, Zhou J. Plant cyclopeptides. Chem Rev. 2006;106:840–95.

35. Yang C, You L, Yin X, Liu Y, Leng X, Wang W, Sai N, Ni J. Heterophyll B ameliorates lipopolysaccharide-induced inflammation and oxidative stress in RAW 264.7 macrophages by suppressing the PI3K/Akt pathways. Molecules. 2018;23:717.

36. Tantai JC, Zhang Y, Zhao H. Heterophyll B inhibits the adhesion and invasion of ECA-109 human esophageal carcinoma cells by targeting PI3K/AKT/beta-catenin signaling. Mol Med Rep. 2016;13:1097–104.

37. Lin S, Cai QY, Zeng JW, Zhu XQ, Wu JZ. Correlation between cytotoxic activity and HFLC fingerprint chromatogram of the effect of Radix pseudostellariae. Nat Prod Res Dev. 2012;24:349–52.

38. Sheng R, Xu X, Tang Q, Bian D, Li Y, Qian C, He X, Gao X, Pan R, Wang C, Luo Y, Xia Y, Dai Y. Polysaccharide of Radix Pseudostellariae improves chronic fatigue syndrome induced by poly I: C in mice. Evid Based Complement Alternat Med. 2011;2011:840516.

39. Peng Y, Chen Y, Yang R. Analysis of heavy metals in *Pseudostellaria heterophylla* in Baiyi Country of Wudang District. J Geochem Explor. 2017;176:57–63.

40. Jia A, Li X, Tan N, Liu X, Shen Y, Zhou J. Enzymatic cyclization of linear peptide to plant cyclopeptide heterophyllin B. Sci China Ser B. 2006;49:63–6.

41. Commission CP. Pharmacopoeia of the People’s Republic of China. Beijing: China Medical Science Press, 2010.

42. Commission CP. Pharmacopoeia of the People’s Republic of China. Beijing: China Medical Science Press, 2015.

43. Hua Y, Wang S, Chai C, Liu Z, Liu X, Zou L, Wu Q, Zhao H, Ying Y. Quality evaluation of *Pseudostellariae Radix* based on simultaneous determination of multiple bioactive components combined with grey relational analysis. Molecules. 2017;22(1):13.

44. Hou Y, Ma Y, Zou LS, Liu X, Liu XH, Luo YY, Liu JX, Lan CW, Yuan JD. Difference of chemical compositions in *Pseudostellariae Radix* from different origins by UPLC-Triple TOF-MS/MS. J Chin Mass Spectrom Soc. 2015;5:36–59.

45. Hou Y, Ma Y, Zou LS, Liu X, Liu XH, Luo YY, Liu JX, Lan CW, Yuan JD. Difference of chemical compositions in *Pseudostellariae Radix* from different origins by UPLC-Triple TOF-MS/MS. Chin Pharm J. 2015;50:1104–10.

46. Hou Y, Ma Y, Zou LS, Liu X, Liu XH, Luo YY, Liu JX, Lan CW, Yuan JD. Dynamic accumulation of metabolites in *Pseudostellariae Radix* from Fujian province based on UPLC-Triple TOF-MS/MS determination. Chin J New Drugs. 2015;24:90–6.

47. Hou Y, Hou Y, Wang S, Ma Y, Liu Z, Liu X, Luo Y, Liu J, Liu J. Comparison of chemical compositions in *Pseudostellariae Radix* from different cultivated fields and germlays by NMR-based metabolomics. Molecules. 2016;21:1538.

48. Lv GP, Hu DJ, Cheong KL, Li ZY, Qing XM, Zhao J, Li SP. Decoding glycome and its application as a new stationary phase for capillary gas chromatography. Anal Lett. 2002;35:203–12.

49. Li SP, Wu DT, Lv GP, Zhao J. Carbohydrates analysis in herbal glycomics. Macromol. 2017;106:456–63.

50. Chen YY, Wang W, Ding Y, Xing DM, Du LJ. Determination of polysaccharides in *Pseudostellaria heterophylla* by high-speed countercurrent chromatography. Chin Pharm J (China). 2005;40:540–2.
52. Hua Y, Wang S, Liu Z, Liu X, Zou L, Gu W, Hou Y, Ma Y, Luo Y, Liu J. iTRAQ-based quantitative proteomic analysis of cultivated Pseudostellaria heterophylla and its wild-type. J Proteomics. 2016;139:13–25.

53. Hua Y, Hou Y, Wang SN, Zou LS, Liu XH, Gu W, Luo YY, Liu JX. 1H-NMR based metabolomic analysis of chemical compositions in cultivated and wild Pseudostellariae radix. Chin Pharm J (China). 2017;52:272–6.

54. Hua Y, Wang S, Liu Z, Liu X, Zou L, Gu W, Luo Y, Liu J. Transcripthonic analysis of Pseudostellariae Radix from different fields using RNA-seq. Gene. 2016;588:7–18.

55. Ma Y, Hou Y, Zou LS, Liu XH, Lan CW, Yuan JD. Dynamic changes of nucleosides and nucleobases in Pseudostellariae radix in different harvest periods by QTRAP LC–MS/MS. Chin Pharm J (China). 2015;1:75–9.

56. Ma Y, Hou Y, Zou LS, Liu XH, Lan CW, Q-TRAP-LC-MS/MS analysis on nucleosides in Pseudostellariae Radix with different processing methods. Chin Trad Herbal Drugs. 2015;4:46–47.

57. Ma Y, Hou Y, Zou LS, Liu XH, Lan CW, Yuan JD. Q-TRAP LC-MS/MS analytical study on nucleosides and nucleobases of Pseudostellariae Radix cultivated in different idioplasm resources. Zhong Yao Cai. 2015;38:711–4.

58. Wang T, Xia L, He X, Zhao J, Xue X. HPLC fingerprint of the ethyl acetate extracts from Zherong Radix Pseudostellariae. Adv Mater Res. 2014;955–959:834–7.

59. Wang T, Gong D, Xia L, He X. Study on fingerprint of Zherong Radix Pseudostellariae by HPLC. Adv Mater Res. 2014;1010–1012:160–3.

60. Pang YP, Yang J, Xia L, Yu S, Hong S. The analysis basing on identification of Zherong Radix Pseudostellariae of HPLC fingerprint. Adv Mater Res. 2014;955–959:843–7.

61. Tan NH, Zhou J, Zhao SX, Zhang HJ, Wang DZ, Chen CX, Liu JX. Heterophyllin A and B, two cyclopeptides, from the roots of Pseudostellaria heterophylla. Phytochemistry. 1993;32:629–32.

62. Tan NH, Zhou J, Chen CX, Zhao SX. Cyclopeptides from the roots of Pseudostellaria heterophylla. Phytochemistry. 1993;32:1327–30.

63. Yang YB, Tan NH, Zhang F, Lu YQ, He M, Zhou J. Cyclopeptides and Amides from Pseudostellaria heterophylla (Caryophyllaceae). Helv Chim Acta. 2003;86:3376–9.

64. Hou Y, Ma Y, Zou LS, Liu X, Liu XH, Luo YY, Liu JX, Lan CW, Yuan JD. Changes of chemical composition of Pseudostellariae Radix using different processing methods by UPLC-Triple TOF-MS/MS. Chin Trad Herbal Drugs. 2014;45:2850–4.

65. Morita H, Kayashita T, Takeya K, Itoikawa H. Conformational analysis of a cyclic heptapeptide, pseudostellarin D by molecular dynamics and Monte Carlo simulations. Chem Pharm Bull. 1996;44:2177–80.

66. Morita H, Kayashita T, Takeya K, Itoikawa H. Cyclic peptides from higher plants, part 15 Pseudostellarin H, a new cyclic octapeptide from Pseudostellaria heterophylla. J Nat Prod. 1995;58:943–7.

67. Shen Y, Han C, Chen J, Wang X. Analysis of cyclic peptides in Pseudostellaria heterophylla (Miq.) Pax by HPLC-APCI-MS. Chromatographia. 2007;66:319–23.

68. Fu XS, Zou LS, Liu XH, Ju WZ, Ma Y, Hou Y, Li YR. Analysis of cyclic peptides in Pseudostellariae Radix by UPLC-ESI-TOF MS/MS. J Chin Mass Spectrom Soc. 2013;34:179–84.

69. Han C, Chen J, Liu J, Wang X, Frank SCL. Analysis of cyclic peptides in Pseudostellaria Heterophylla (Miq.) Pax by high performance liquid chromatographic/electrospray ionization time of flight mass spectrometry. Chin J Anal Chem. 2006;34:1719–22.

70. Hua Y, Hou Y, Wang SN, Ma Y, Zou LS, Liu XH, Luo YY, Liu JX. Chemical differentiation of Pseudostellariae Radix from different cultivated fields and germplasms by UPLC-triple TOF-MS/MS coupled with multivariate statistical analysis. Nat Prod Commun. 2016;11:1827–31.

71. Lin H, Chen Q, Zhao J, Zhou P. Determination of free amino acid content in Radix Pseudostellariae using near infrared (NIR) spectroscopy and different multivariate calibrations. J Pharm Biomed Anal. 2009;50:893–8.

72. Ma Y, Hou Y, Zou LS, Liu XH, Xu L, Yuan JD. Dynamic changes of nucleosides and nucleobases in Pseudostellariae Radix from Fujian province analyzed by QTRAP LC–MS/MS. Chin J New Drugs. 2014;23:2325–30.

73. Shen Y, Han C, Liu J, Liu A, Ji X, Liu C. Analysis of volatile components of Pseudostellaria heterophylla (Miq.) Pax by microwave-assisted solvent extraction and GC-MS. Chromatographia. 2008;68:679–82.

74. Chen Y, Ding Y, Wang W, Wang R, Su H, Du L. Determination of polysaccharides in Radix pseudostellariae extract by size-exclusion high-performance liquid chromatography. Tsinghua Sci Technol. 2007;12:389–93.

75. Chen FF, Zhang G, Wang YY. Analysis of active constituents in autotetraploid of Pseudostellaria heterophylla(Miq.) Pharm Biotechnol. 2010;17:523–6.

76. Liu WK, Hu HY, Liu XC, Duan Q. Fingerprint of Radix Pseudostellariae by HPLC. Chin Trad Herbal Drugs. 2007;38:761–4.

77. Li SN, Gao SL, Jiang T. HPLC fingerprints of crude drug of Pseudostellaria heterophylla and root tuber of its autotetraploid plant. J Plant Resour Environ. 2007;16:36–9.

78. Han C, Chen J, Chen B, Lee FSC, Wang X. Fingerprint chromatogram analysis of Pseudostellaria heterophylla (Miq.) Pax root by high performance liquid chromatography. J Sep Sci. 2006;29:2197–202.

79. Liu XH, Wang M, Cai BC, Wang YX, Lin XY. GC-MS fingerprint of root tuber of Pseudostellaria heterophylla. Chin Trad Herbal Drugs. 2007;38:113–6.