

· 综述 ·

中药天葵子的化学成分研究进展

张海彬^{1,2},程海波¹,沈卫星¹,闫秋莹¹,谭佳妮¹,徐长亮¹,范汇森^{1,2},苗筠杰^{1*},孙东东^{1*}

(1.南京中医药大学转化医学研究中心,国家中医药管理局名医验方评价与转化重点研究室,江苏省中医药防治肿瘤协同创新中心,江苏省抗肿瘤验方研究与产业化工程实验室,江苏南京 210023;2.南京中医药大学药学院,江苏南京 210023)

摘要: 中药天葵子是毛茛科植物天葵 *Semiaquilegia adoxoides* (DC.) Makino 的干燥块根,为我国常用中药品种。具有清热解毒,消肿散结之功效,其主要成分有生物碱、氰基和硝基类、酚酸类等。该文对天葵子化学成分的研究进行整理和总结,为进一步研究提供参考。

关键词: 天葵子;植物化学;化学成分

中图号:R284.1 文献标志码:A 文章编号:1672-0482(2018)02-0205-05

DOI:10.14148/j.issn.1672-0482.2018.0205

Research Progress on Chemical Constituents from *Radix Semiaquilegiae*

ZHANG Hai-bin^{1,2}, CHENG Hai-bo¹, SHEN Wei-xing¹, YAN Qiu-ying¹, TAN Jia-ni¹, XU Chang-liang¹, FAN Hui-sen^{1,2}, MIAO Yun-jie^{1*}, SUN Dong-dong^{1*}

(1. Translational Medicine Center of Nanjing University of Chinese Medicine, Key Laboratory of Famous Doctors' Proved Recipe Evaluation and Transformation of State Administration of Traditional Chinese Medicine, Jiangsu Collaborative Innovation Center of Traditional Chinese Medicine (TCM) Prevention and Treatment of Tumor, Jiangsu Province Laboratory of Anti-Cancer Empirical Formulae Research and Industrialization, Nanjing, 210023, China; 2. College of Pharmacy, Nanjing University of Chinese Medicine, Nanjing, 210023, China)

ABSTRACT: *Radix Semiaquilegiae* (Tiankuizi in Chinese), the root of *Semiaquilegia adoxoides*, has been widely used in China, according to the traditional Chinese medicine (TCM) principle, it has effect of heat clearing and detoxicating, detumescence, lump dissipation. The main components of *Radix Semiaquilegiae* are alkaloids, cyano compounds and nitro compounds, phenolic acids. This review summarizes the achievements of the investigations in phytochemistry on *Radix Semiaquilegiae* in order to provide reference for further study.

KEY WORDS: *Radix Semiaquilegiae*; phytochemistry; Chemical constituents

1 Introduction

Radix Semiaquilegiae (Tiankuizi in Chinese), the root of *Semiaquilegia adoxoides* belongs to the genus Ranunculaceae plant.^[1]

This plant is distributed in the subtropical area of the Yangtze River in China, according to the investigations in phytochemistry on *Radix Semiaquilegiae*, various biologically active compounds have been founded. In addition, in TCM, the plant is mainly applied for the treatment of tumor and mastitis in clinical practice. This review aims to systematically summarise the published literatures related to the chemical constituents of *S. Radix* and to provide information

as a basis of further development and utilization of this herbal resource.

Clinically used to treat acute mastitis with honey sometimes^[2-8], *Radix Semiaquilegiae* contains a variety of chemical compositions and cyanoglycosides as the main components shows significant medicinal activity.^[9].

Monomeric compounds from *Radix Semiaquilegiae* can inhibit the activity of cholinesterase^[10], and have the anti-inflammatory^[11] and anti-tumor activity in vitro^[12-15]. Alkaloid fractions of *Radix Semiaquilegiae* have inhibitory effect on mouse sarcoma S₁₈₀^[16], while the water layer and the n-butanol layerer of *Radix Semiaquilegiae* have antioxidative

收稿日期:2017-10-09

基金项目:国家自然科学基金(81673559, 81403079, 81503535, 81373511, 81573910);江苏省自然科学基金(BK20141467, BK20131416);江苏省高校优势学科项目

作者简介:张海彬(1993-),男,硕士研究生。*通信作者:孙东东,男,副研究员,主要从事抗肿瘤中药品种基础研究,E-mail:sundd@njucm.edu.cn;苗筠杰,男,助理研究员,主要从事中药化学与分析研究,E-mail:yj.miao@njucm.edu.cn

activity^[17].

2 Phytochemistry

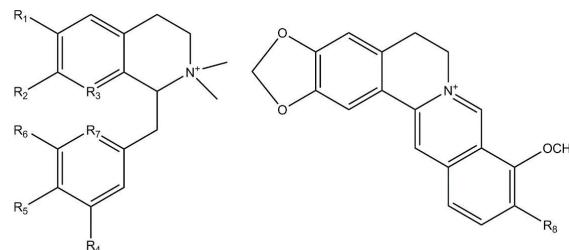
The advancement of analysis technologies has allowed many studies on *Semiaquilegia adoxoides* to reveal numbers of phytochemicals, including alkaloids, diterpenes, cyano compounds and nitro compounds, lactones, coumarins, lignins, glycosides, sterols and others.

2.1 Alkaloids

To date, four alkaloids have been isolated and identified from *Radix Semiaquilegiae* (Table 1, Figure 1), namely thalifendine (1), semiaquilegine A (2), magnoflorine (3), and berberine (4), respectively. The structures of Thalifendine and Semiaquilegine A have been elucidated by NMR spectroscopic analysis.

Table 1 Alkaloids

No.	Name	Molecular Formula	Physical state
1	Thalifendine	C ₁₉ H ₁₆ NO ₄	Yellow needle ^[18]
2	Semiaquilegine A	C ₁₉ H ₂₁ NO ₄	White powder ^[19]
3	Magnoflorine	C ₂₀ H ₂₄ NO ₄	Yellow amorphous powder ^[20]
4	Berberine	C ₂₀ H ₁₈ NO ₄	Yellow needle ^[21]



Semiaquilegine A	R1 OH	R2 OMe	R3 CH	R4 OH	R5 OH	R6 H	R7 CH
Magnoflorine	OMe	OH	C	H	OMe	OH	C
Thalifendine						R8 OH	
Berberine						OCH ₃	

Figure 1 Structures of compounds from *Radix Semiaquilegiae* (Alkaloids)

2.2 Diterpenes

Two diterpenes have been isolated from EtOH extraction fraction of the root of *Semiaquilegia adoxoides*, namely *E*-sequialegin and *Z*-sequialegin, respectively (Table 2, Figure 2).

Table 2 Diterpenes

No.	Name	Molecular Formula	Physical state
4	<i>E</i> -sequialegin	C ₃₈ H ₄₆ O ₉	White amorphous powder ^[22]
5	<i>Z</i> -sequialegin	C ₃₈ H ₄₆ O ₉	White amorphous powder ^[23]
6	Semiaquilegoside A	C ₂₆ H ₃₈ O ₉	Colorless needle crystal ^[24]

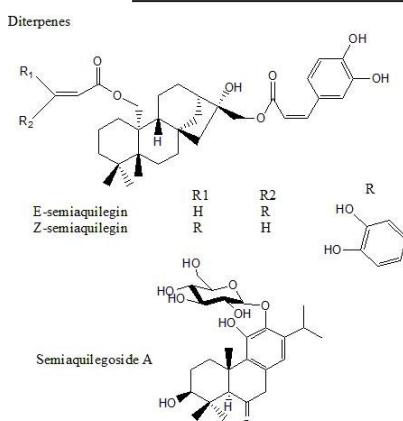


Figure 2 Structures of compounds from *Radix Semiaquilegiae* (diterpenes)

2.3 Cyano compounds and nitro compounds

Cyano compounds and nitro compounds are the main characteristic components of *Radix Semiaquilegiae*. Up to now, 11 compounds with cyano and nitro have been obtained and identified from this herb. These compounds have the similar molecular configuration (Table 3). Their chemical structures are shown in Figure 3.

2.4 Lactones and coumarins

Lactones and a coumarins compounds were found in *Radix Semiaquilegiae* (Table 4). Their structures are shown in Figure 4.

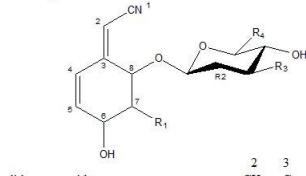
Table 3 Cyano compounds and nitro compounds

No.	Name	Molecular Formula	Physical state
7	lithospermaside	C ₁₄ H ₁₉ NO ₈	White amorphous powder ^[25]
8	(<i>Z</i>)-6 α -(β -D-glucosyloxy)-4 α ,5 α -dihydroxy-2-cyclohexene-1, α -acetonitrile	C ₁₄ H ₁₉ NO ₈	White amorphous powder ^[20]
9	Menisdauri	C ₁₄ H ₁₉ NO ₇	White amorphous powder ^[20]

(续表)

No.	Name	Molecular Formula	Physical state
10	ehretioside	C ₁₄ H ₁₇ NO ₇	Colorless needle crystal ^[26]
11	thalictroside	C ₁₉ H ₂₇ NO ₁₂	Colorless needle crystal ^[26]
12	4-[β -D-apiofuranosyl-(1 \rightarrow 6)-O- β -D-glicopyranosyloxy]-phenylacetonitrile (1E, 4 α , 5 β , 6 α)-4,5,6-trihydroxy-2-cyclohexen-1-ylideneacetonitrile	C ₁₉ H ₂₅ NO ₁₀ ^[26]	
13	(1E, 4 α , 5 β , 6 α)-4,5,6-trihydroxy-2-cyclohexen-1-ylideneacetonitrile	C ₈ H ₉ NO ₃	White amorphous powder ^[26]
14	2-(β -D-glucopyranosyloxy)-4-hydroxybenzeneacetonitrile	C ₁₄ H ₁₇ NO ₇	white needles ^[27]
15	-4-Hydroxy-1-(2-nitroethyl)benzene-4-O-(6'-O- β -D-xylopyranosyl- β -D-sitosterol	C ₁₉ H ₂₇ NO ₁₂	White powdered crystal ^[23]
16	4-hydroxy-2- β -D-glucopyranosyl oxyphenylacetonitrile	C ₁₄ H ₁₇ NO ₇	Ehretioside B ^[26]
17	4-[β -D-xylopyranosyl-(1 \rightarrow 6)-O- β -D-glucopyranosyloxy]-1-(2-nitroethyl)benzene		White amorphous powder ^[28]

With cyano and nitro



2	CH	3	C	R1	R2	R3	R4
				S-OH	OH	OH	CH ₂ OH

(Z)-6 α -(β -D-glucosyloxy)-4 α ,5 α -dihydroxy-2-cyclohexen-1 α -acetonitrile

Menisdaurin
ehretioside B

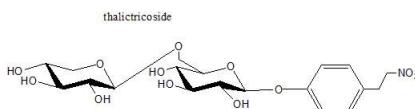
4-hydroxy-2- β -D-glucopyranosyl oxyphenylacetonitrile

2-(β -D-glucopyranosyloxy)-4-hydroxybenzene acetonitrile

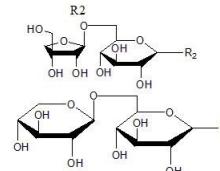
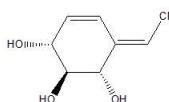
4-[β -D-apiofuranosyl-(1 \rightarrow 6)-O- β -D-glucopyranosyloxy]-phenylacetonitrile

4-Hydroxy-1-(2-nitroethyl)benzene -4-O-(6'-O- β -D-xylopyranosyl)- β -D-sitosterol

4-[β -D-xylopyranosyl-(1 \rightarrow 6)-O- β -D-glucopyranosyloxy]-1-(2-nitroethyl)benzene



4,5,6-trihydroxy-2-cyclohexen-1-ylideneacetonitrile



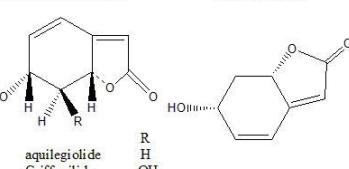
R₂-O- \bigcirc -R₁

Figure 3 Structures of compounds from *Radix Semiaquilegiae* (cyanos and nitros)

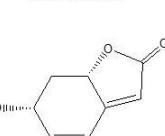
Table 4 Lactones and coumarins

No.	Name	Molecular Formula	Physical state
18	Griffonilide	C ₈ H ₈ O ₄	Colorless prismatic crystals ^[25]
19	Aquilegiolide	C ₈ H ₈ O ₃	white needles ^[22]
20	Menisdaurilide	C ₈ H ₈ O ₃	white needles ^[22]
21	4,6-dimethoxy-5-methyl-2H-Pyran-2-one	C ₈ H ₁₀ O ₄	white needles ^[11]

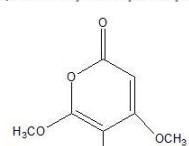
lactones and coumarins



menisdaurilide



4,6-dimethoxy-5-methyl-2H-Pyran-2-one

Figure 4 Structures of compounds from *Radix Semiaquilegiae* (lactones and coumarins)

2.5 Others chemical constituents

Radix Semiaquilegiae contains organic acids, including octanedioic acid, fumaric acid and palmitic acid. The root of this plant contains a lot of phenolic acids, such as hexanoic acid, octanoic acid, nonanoic acid, myristic acid, pentadecanoic acid and heptadecanoic acid (Table 5). Their structures are shown in following Figure 5.

Table 5 Phenolic acids

No.	Name	Molecular Formula	Physical state
24	4-hydroxybenzaldehyde	C ₇ H ₆ O ₂	Colorless crystal ^[24]
25	4-hydroxybenzoic acid	C ₇ H ₆ O ₃	Colorless crystal ^[24]
26	3-hydroxy-4-methoxybenzoic acid	C ₈ H ₈ O ₄	Colorless crystal ^[28]
27	2,4-dihydroxybenzoic acid	C ₇ H ₆ O ₄	Colorless crystal ^[22]
28	Bis(2-ethylhexyl) phthalate	C ₂₄ H ₃₈ O ₄	Yellow syrup ^[28]
29	Dibutyl terephthalate	C ₁₆ H ₂₂ O ₄	Yellowishneedles ^[28]
30	Methyl 2-(2,4-dihydroxyphenyl) acetate	C ₉ H ₁₀ O ₄	Colorless crystal ^[22]
31	Ferulic acid	C ₁₀ H ₁₀ O ₄	Light yellow crystalline powder ^[29]
32	2-propenoic acid, 3-(4'-hydroxyphenyl)-(4'-carboxyl)-phenyl ester	C ₁₆ H ₁₂ O ₅	Colorless needles ^[24]
33	4-(bromomethyl)-2-hydroxybenzoic acid	C ₈ H ₇ BrO ₃	Brown red needle crystal ^[24]
34	5-(2-hydroxyethyl)-2-O-β-glucosylohenol	C ₁₄ H ₂₀ O ₈	Colorless needles ^[29]
35	Salidroside	C ₁₄ H ₂₀ O ₇	Colorless needles ^[24]
36	p-Hydroxyphenethylalcohol	C ₈ H ₁₀ O ₂	Whtie crystal ^[22]
37	3,4-dihydroxybenzoic acid	C ₇ H ₆ O ₄	White to micro-brown needle ^[11]
38	p-β-D-glucosyloxybenzoic acid	C ₁₃ H ₁₆ O ₈	Whtie needle ^[11]
39	Monordicophenoide A	C ₁₈ H ₂₄ O ₁₂	Brown gum-like substance ^[26]

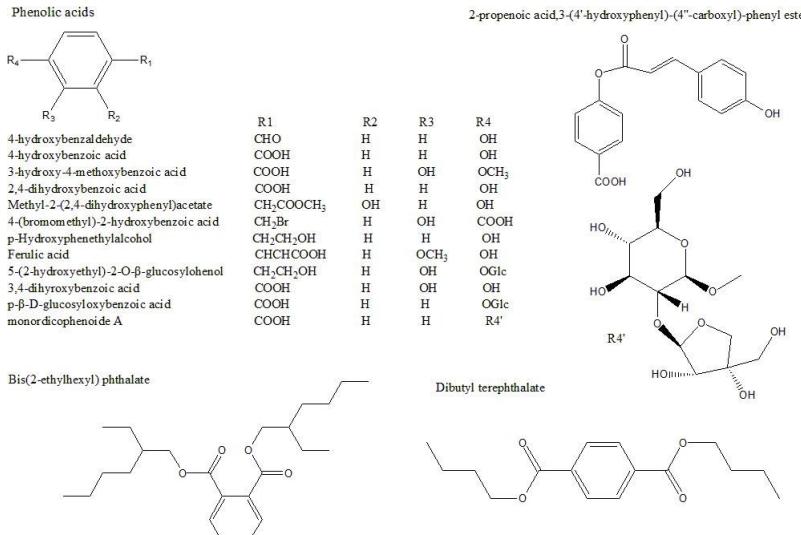


Figure 5 Chemical Compositions of Phenolic Acids from *Radix Semiaquilegiae*

3 Conclusion

Modern pharmacological studies have shown that *Radix Semiaquilegiae* has anti-inflammatory, cytotoxic and other activities, with the great potential in the pharmaceutical field. The results of phytochemistry indicated that the major components of *Radix Semiaquilegiae* are phenolic acids, cyan compounds and nitro compounds which exhibit multiple

pharmacological effects. In addition, the bioactive components and their corresponding pharmacological activities should be investigated systematically in order to optimize the development and utilization of this herbal resource.

References:

- [1] China Pharmacopoeia Commission. Chinese Pharmacopoeia: Vol I [S]. Beijing: China medical science press, 2015: 59.

- [2] WANG CL. The treatment of acute mastitis with fresh *Semiaquilegia adoxoides* [J]. Primary J Chin Mater Med, 2001, 16(4) : 62.
- [3] CHENG YQ. *Semiaquilegia adoxoides* for lactation mastitis [J]. J Exter Ther Tradit Chin Med, 2002, 11(4) : 52.
- [4] CHENG YQ. The treatment of acute mastitis with *Semiaquilegia adoxoides* [J]. Hubei J Tradit Chin Med, 2002, 24(9):19.
- [5] ZHOU YB. The clinical application of 2 methods of *Semiaquilegia adoxoides* [J]. Huan Guid J TCMP, 1996, 2(4):51.
- [6] DAI DS, LIN F. *Semiaquilegia adoxoides* honey ointment in the treatment of acute mastitis[J]. Chin J Med, 1966, 7: 461.
- [7] SONG JP. Qingrejiedu *Semiaquilegia adoxoides* [N]. China Pharmaceutical News, 2001-07-31(6).
- [8] LI HJ. Gexia zhuyu decoction combined with clinical observation of 73 cases of Miao medicine *semaquilegia adoxoides* treatment of gastric ulcer[J]. Mod Diag Treat, 2013, 24(8) : 1747-1748.
- [9] XU R, XIAO HT, WANG JT, et al. Advance on chemical compositions and pharmacological studies of *Semiaquilegia adoxoides* [J]. Nat Prod Res Dev, 2014, 26:1154-1159, 1092
- [10] ZOU JH. Studies on the chemical constituents of *Semiaquilegia adoxoides* and *Trollies ledebouri* [D]. Beijing: Chinese Academy of Medical Sciences and Peking University Medical College, 2004.
- [11] LEE CL, HWANG TL, PENG CY, et al. Anti-neutrophilic inflammatory secondary metabolites from the traditional Chinese medicine, Tiankuizi[J]. Nat Prod Commun, 2012, 7(12) : 1623-1626.
- [12] LI C, WANG MH. Potential biological activities of magnoflorine:a compound from aristo lochia debilis Sieb. et Zucc [J]. Korean Journal of Plant Resources, 2014, 27(3) : 223-228.
- [13] SUN Y, XUN K, WANG Y, et al. A systematic review of the anticancer properties of berberine, a natural product from Chinese herbs[J]. Anti-Cancer Drugs, 2009, 20: 757-769.
- [14] LIN CC, KAO ST, CHEN GW, et al. Apoptosis of human leukemia HL-60 cells and murine leukemia WEHI-3 cells induced by berberine through the activation of caspase-3[J]. Anticancer Res, 2006, 26:227.
- [15] LAN YH. Studies on chemical constituents of *Semiaquilegia adoxoides* (Ⅱ) [D]. Tianjin: Tianjin University, 2006.
- [16] GUAN P. Study of chemical compositions and antitumor activity of *Semiaquilegia adoxoides* (DC.) Makino [D]. Beijing: China Academy of Chinese Medical Sciences, 2010.
- [17] ZHOU XR, XU R, XIAO W, et al. Antioxidative properties and components of different extraction fractions from *semaquilegiae radix* in vitro[J]. Chin J Exper Tradit Med Formul, 2015, 21(15) : 116-119.
- [18] SU YF, LAN HY, ZHANG ZX, et al. Chemical constituents of *Semiaquilegia adoxoides* [J]. Chin Tradit Herb Drug, 2006, 37(1) : 27-29.
- [19] NIU F, CUI Z, CHANG HT, et al. Constituents from the roots of *semaquilegia adoxoides* [J]. Chin J Chem, 2006, 24 (12):1788-1791.
- [20] HAN QB, JIANG B, MEI SX, et al. Constituents from the roots of *Semiaquilegia adoxoides* [J]. Fitoterapia, 2001, 72 (1) : 86-88.
- [21] YAN QY, CHENG HB, ZHANG HB, et al. Separation and analysis on chemical components from the ethanol extract of *Semiaquilegiae Radix* [J]. CJTCMP, 2016(10) : 4172-4175.
- [22] NIU F, CHANG HT, JIANG Y, et al. New diterpenoids from *Semiaquilegia adoxoides* [J]. J Asian Nat Prod Res, 2006, 8 (1/2) : 87-91.
- [23] SU Y, ZHANG Z, GUO C. A new nitroethylphenolic glycoside from *Semiaquilegia adoxoides* [J]. Fitoterapia, 2004, 75 (3/4) : 420-422.
- [24] NIU F. Studies on the Constituents and Quality Control of *Semiaquilegia adoxoides* (DC.) Makino [D]. Shenyang: Shenyang Pharmaceutical University, 2006.
- [25] ZOU JH, YANG JS. Study on chemical constituents isolated from *Semiaquilegia adoxoides* [J]. Chin Pharm J, 2004, 39 (4) : 256-257.
- [26] ZHANG H, LIAO ZX, YUE JM. Cyano- and nitro-containing compounds from the Roots of *Semiaquilegia adoxoides* [J]. Chine J Chem, 2004, 22(10) : 1200-1203.
- [27] SU YF, ZHANG ZX, GUO CY, et al. Anobel cyanogenic glycoside from *Semiaquilegia adoxoides* [J]. J Asian Nat Prod Res, 2005, 7(2) : 171-174.
- [28] NIU F, XIE GB, CUI Z, et al. Chemical constituents from roots of *semaquilegia adoxoides* [J]. J Chin Pharma Sci, 2006, 15(4) : 251-254.
- [29] WU XP. Studies on essential oil components in earthnut of *semaquilegia adoxoides* DC [J]. J Anhui Agri, 2005, 33 (10) : 1864-1866.
- [30] LIU YZ, WANG JQ, XIE L, et al. Studies on the chemical constituents of muskroot-like semiaquilegia (semaquilegia adoxoides) I . the structure of semiaquilinoside[J]. Chin Tradit Herb, 1999, 30(1) : 5-7.
- [31] ZHANG ZX. Study on chemical constituents from *Semiaquilegia adoxoides* [D]. Tianjin: Tianjin University, 2004.
- [32] BANERJEE S, ZHANG Y, ALI S, et al. Molecular evidence for increased antitumor activity of gemcitabine bygenistein *in vitro* and *in vivo* using an orthotopic model of pancreatic cancer [J]. Cancer Res, 2005, 65(19) : 9064-9072.

(编辑:陈军 董宇)