Journal of Pharmacy and Pharmacology, 2022, **74**, 1718–1742
https://doi.org/10.1093/jpp/rgac068
Advance access publication 15 September 2022
Review

JPP Journal of Pharmacy and Pharmacology

OXFORD

A comprehensive review of traditional uses, phytochemistry and pharmacology of *Reynoutria* genus

Zi-Long Zhang[1,‡], Yu-Ze Li[1,‡], Guo-Qing Wu[1], Dong-Dong Zhang[1], Chong Deng[1], Zhi-Min Wang[2], Xiao-Mei Song[1] and Wei Wang[1,*]

[1]School of Pharmacy, Shaanxi University of Chinese Medicine, Xian Yang, Shaanxi 712046, China
[2]Institute of Chinese Materia Medica, China Academy of Chinese Medical Sciences, BeiJing 100700, China

[‡]These authors contributed equally: Zi-Long Zhang, Yu-Ze Li.
[*]Correspondence: Wei Wang, School of Pharmacy, Shaanxi University of Chinese Medicine, Xian Yang, Shaanxi 712046, China. Tel: +86 029 3818 5165; Fax: +86 029 3818 5168; Email: 2051003@sntcm.edu.cn

Abstract

Objectives The genus *Reynoutria* belonging to the family Polygonaceae is widely distributed in the north temperate zone and used in folk medicine. It is administered as a sedative, tonic and digestive, also as a treatment for canities and alopecia. Herein, we reported a review on traditional uses, phytochemistry and pharmacology reported from 1985 up to early 2022. All the information and studies concerning *Reynoutria* plants were summarized from the library and digital databases (e.g. ScienceDirect, SciFinder, Medline PubMed, Google Scholar, and CNKI).

Key findings A total of 185 articles on the genus *Reynoutria* have been collected. The phytochemical investigations of *Reynoutria* species revealed the presence of more than 277 chemical components, including stilbenoids, quinones, flavonoids, phenylpropanoids, phospholipids, lactones, phenolics and phenolic acids. Moreover, the compounds isolated from the genus *Reynoutria* possess a wide spectrum of pharmacology such as anti-atherosclerosis, anti-inflammatory, antioxidative, anticancer, neuroprotective, anti-virus and heart protection.

Summary In this paper, the traditional uses, phytochemistry and pharmacology of genus *Reynoutria* were reviewed. As a source of traditional folk medicine, the *Reynoutria* genus have high medicinal value and they are widely used in medicine. Therefore, we hope our review can help genus *Reynoutria* get better development and utilization.

Keywords: *Reynoutria*; traditional uses; phytochemistry; pharmacology

Introduction

The genus *Reynoutria*, a genus of the family Polygonaceae, is mainly distributed in the wide temperate areas of the northern hemisphere. This genus comprises about seven species, five of which were discovered in China. As a country that has been using herbal medicine to treat diseases since ancient times, China has abundant natural drug resources and experience in clinical application. The plants of the genus *Reynoutria*, with rich chemical compositions and pharmacological activities, have been used in Traditional Chinese medicines or folk medicines to treat various diseases, which have become a hot spot for phytochemical studies.[1] Currently, more than 277 compounds have been extracted and identified from the genus *Reynoutria*, with stilbenoids,[2] quinones[3] and flavonoids[4] being major compounds. Meanwhile, several studies showed that the compounds and extracts isolated from the genus *Reynoutria* possessed a wide spectrum of pharmacology *in vivo* or *in vitro* such as anti-atherosclerosis,[5] anti-inflammatory,[6] antioxidative,[7] anticancer,[8] neuroprotective,[9] anti-virus,[10] heart protection,[11] hair darkening.[12] So, it is necessary for better research to review the genus *Reynoutria*. In this study, we comprehensively summarized research on the traditional uses, phytochemistry, and pharmacology of the genus *Reynoutria*. The extant information on these species allows us to provide a scientific basis for future research studies and to explore their potential therapeutic use.

Search strategy

Comprehensive research and analysis of previously published literature were conducted for studies on the traditional use, distribution, chemistry and pharmacological properties of the genus *Reynoutria*. The search was conducted using databases such as ScienceDirect, SciFinder, Medline PubMed, Google Scholar, Baidu Scholar and CNKI by using the keywords such as *Reynoutria*, *Reynoutria japonica*, *Reynoutria ciliinervis* and *Reynoutria multiflora*. Meanwhile, since some of the main *Reynoutria* species have long been reported as *Fallopia* species, we also used other keywords such as '*Fallopia japonica*' and '*Fallopia multiflora*' in the search strategy. Furthermore, part of the analyzed studies was got by a manual search of articles in the reference lists of the included studies. The PRISMA template for determining the list of the article is displayed in Figure 1. The chemical structures were drawn using ChemDraw Professional 20.0 software.

Traditional uses

Genus *Reynoutria* has seven species all over the world, which included *Reynoutria* × *bohemica* Chrtek & Chrtková,

Received: April 22, 2022. Editorial Acceptance: August 22, 2022

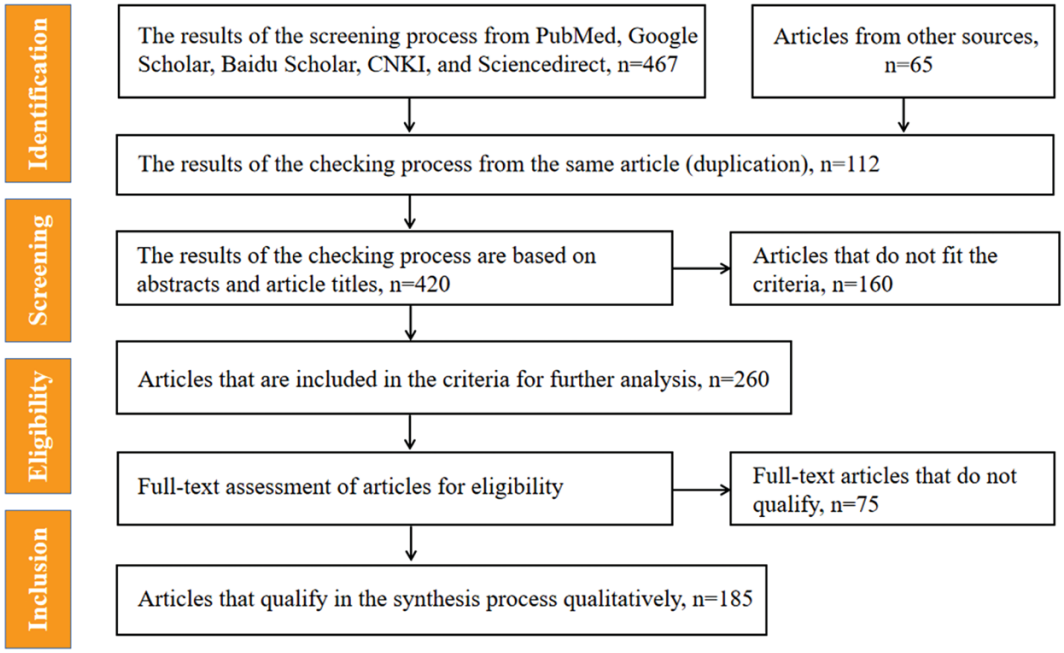


Figure 1 Research data search and selection flow.

Reynoutria ciliinervis (Nakai) Moldenke, *Reynoutria compacta* (Hook.f.) Nakai, *Reynoutria forbesii* (Hance) T.Yamaz., *Reynoutria japonica* Houtt., *Reynoutria multiflora* (Thunb.) Moldenke, *Reynoutria sachalinensis* (F.Schmidt) Nakai.[13] *Reynoutria* plants originated in Asia, and six species of the genus are known. Due to human activities, *Reynoutria* plants were introduced into Europe and North America, and resulted in the hybrid species *Reynoutria* × *bohemica*.[14] Among them, the tuberous root of *R. japonica and R. multiflora* known as "Hu Zhang" and "He Shouwu", respectively, are famous Traditional Chinese medicines in China.[15, 16] Meanwhile, *R. compacta*, *R. ciliinervis* and *R. forbesii* also have been reported as folk herbs.[17–20] A summary of their local names, geographical distribution and traditional uses were presented in Table 1. The distribution of genus *Reynoutria* in the world is shown in Figure 2.

Phytochemistry

Currently, approximately 277 chemical components have been isolated and identified from the genus *Reynoutria*. The fundamental chemical constitutions are stilbenoids, quinones, and chromones. In this article, 277 compounds have been reported, including 58 stilbenoids (**1–58**), 51 quinones (**59–109**), 48 flavonoids (**110–157**), 21 phenylpropanoids (**158–178**), 9 phospholipids (**179–187**), 9 lactones (**188–196**), 23 phenolics and phenolic acids (**197–219**), 19 fatty acids (**220–238**), and 39 other compounds (**239–277**), which are shown in Figures 3–15 and Table 2.

Stilbenoids

The stilbenoids are divided into two groups, one with 2,3,5,4′-tetrahydroxy stilbene (**1–19**) and the other with resveratrol (**20–40**). 2,3,5,4′-Tetrahydroxy stilbene glycosides mostly form glycosides at the 2-hydroxy position and the glucose group's 2-position hydroxy often be replaced by different groups (Figure 3). While resveratrol glycosides mostly form glycosides at the 3-hydroxy or 4′-hydroxy position (Figure 4). It is worth noting that most stilbenoids are *trans*-stilbenoids, which may be related to the stronger photostability of *trans*-stilbenoids. Furthermore, 17 stilbenoid glycoside dimers (**42–58**) have been isolated from *R. multiflora* (**Figure 5**), which often consist of two stilbenes units polymerized.

Quinones

Quinones can be divided into anthraquinones (**59–85**), naphthoquinones (**86–93**), benzoquinones (**94–95**) and dianthrones (**96–109**). Among them, anthraquinones are emodin-type anthraquinones, whose 1,8-hydroxy positions are easy to form ethers and glycosides with methyl and sugar groups. All reported naphthoquinones are α-(1,4) naphthoquinones (**Figure 6**). Meanwhile, the dianthrones (**Figure 7**) mostly exist in the form of intermediate linkage and form glycosides at the 8 position.

Flavonoids

According to structures, 48 flavonoids are divided into chromones (**110–122**), flavones (**123–139**), flavanones (**140–155**), isoflavone (**156**) and flavonone (**157**).

Chromones are a group of natural compounds that are commonly found in plants. The oxygen-containing heterocycles are the core of flavonoid. Mostly chromones (Figure 8) are substituted at the 2, 5, and 7 positions and form glycosides at the 7 position. Flavonoid's basic parent nucleus is 2-phenyl chromone. Notably, flavones (Figure 9) mostly form glycosides with various sugars at the 3 position. Whereas flavanones (Figure 10) rarely form glycosides, they're more often replaced by galloyl at the 3 position. Meanwhile, flavanones can form dimer or trimer.

Phenylpropanoids

Phenylpropanoids, a class of compounds consisting of a benzene ring linked to three carbons (C6–C3), can be divided into simple phenylpropanoids (**158–166**), coumarins (**167–171**) and lignans (**172–178**) (Figure 11). This type of component is

Table 1 Traditional uses of the genus *Reynoutria*

Species	Local name	Parts	Distribution	Dosage forms	Traditioanal uses
R. multiflora (Thunb.) Moldenke	Heshouwu Chishouwu	Tuberous roots	China (Shaanxi, Gansu, Sichuan, Yunnan, and Guizhou), Japan, Korea, Thailand, Vietnam, Europe and North America.	Decoction, vinum, pill, powder (taken orally); ointment, powder, liniment (external application);	Anti-aging, lowering blood lipids, anti-atherosclerosis, enhancing immunity, intelligence-enhancing, anti-bacteria and anti-myocardial ischemial[1]
	Yejiaoteng Shouwuteng	Stems		Decoction (taken orally); liniment (external application)	Sedative, hypnotic, hyperglycemia, lipid-lowering and anti-inflammatory[17]
R. ciliinervis (Nakai) Moldenke	Zhushaqi (Shaanxi), Hongyaozi (Henan)	Tuberous roots	China (Jilin, Liaoning, Henan, Shaanxi, Gansu, Qinghai, Hubei, Sichuan, Guizhou and Yunnan), Korea.	Decoction, vinum, powder (taken orally); powder, ointment, liniment (external application)	Acute stomach pain, enterogastritis, amygdalitis, shigellosis, lumbago, tract infection and traumatic injury[19]
R. japonica Houtt.	Huzhang Zilonggen (Anhui)	Tuberous roots	China (Liaoning, Jilin, Henan, Shaanxi, Gansu and Sichuan), Europe and North America.	Decoction (taken orally); ointment, liniment (external application)	Anti-inflammation, pain relief, high blood pressure, high cholesterol, anti-tumor, hemostasis and enhancing immunity[18]
R. compacta (Hook.f.) Nakai	Huoxuelong Suantongzi	Tuberous roots	China (Sichuan and Yunnan), Japan, Korea and Europe.	Decoction (taken orally)	Rheumatism, relieving cough and expelling phlegm[19]
R. forbesii(Hance) T.Yamaz.	Manshouwu Manhuzhang	Tuberous roots	China (Henan, Shaanxi, Hubei, Sichuan, Guizhou and Yunnan), Japan[20]	-	-

"–"means no reports were found

less distributed in the genus *Reynoutria*. Notably, vanicosides A (**164**) and B (**165**) were reported from *R. sachalinensis*, which could induce an apoptotic death pathway in the melanoma cell lines.

Phospholipids

Phospholipids are an important class of lipid concomitants, which are present in almost all cells of plants and animals. A total of 9 phospholipids (**179–187**) (Figure 12) are obtained from the genus *Reynoutria*.

Lactones

Lactones are formed by the esterification of molecules containing both carboxyl and hydroxyl groups. The characteristic of lactone is that there is only one ester group in the ring. Now 9 lactones (**188–196**) are reported from the genus *Reynoutria*. The structures of the specific compounds are shown in Figure 12.

Phenolics and phenolic acids

Phenolic compounds are important secondary metabolites in plants, which have good antioxidant activity for the existence of phenolic hydroxyl and phenolic compounds. While phenolic acid is a kind of organic acid containing a phenol ring. A total of 20 phenolics (**197–216**) and 3 phenolic acids (**217–219**) have been isolated from the genus *Reynoutria*. The structures of specific compounds are shown in Figure 13.

Fatty acids

Fatty acids are the main components of neutral fat, phospholipids and glycolipids. According to the chain length, fatty acids can be divided into short-chain fatty acids, medium-chain fatty acids, and long-chain fatty acids. A total of 19 fatty acids (**220–238**), mostly long chain saturated fatty acids, were reported in the genus *Reynoutria* (Figure 14).

Other compounds

In addition, 39 other compounds are isolated from the genus *Reynoutria*, including 3 saccharides (**239–241**), 4 polyols (**242–245**), 5 steroids (**246–250**), 6 terpenoids (**251–256**), 6 alkaloids (**257–262**) and 15 miscellaneous compounds (**263–277**). Specific compounds structure are shown in Figure 15.

Pharmacology activities

Anti-atherosclerosis

The compound 2,3,5,4′-tetrahydroxystilbene-2-*O*-β-D-glucoside (TSG) from the genus *Reynoutria* has a protective effect on vascular endothelium. *In vitro*, 50 or 100 μM TSG could block the (transforming growth factor-β/drosophila mothers against decapentaplegic protein) TGFβ/Smad signal pathway and improve the endothelial dysfunction of umbilical veins caused by tumor necrosis factor α (TNF-α).[88] TSG (1 or 10 μmol/l) protected umbilical vein endothelium from LPS damage by inhibiting mitochondria-dependent apoptotic pathway,[90] which also could ameliorate lysophosphatidylcholine (LPC)-induced umbilical vein endothelial cell injury through ROS/p-JNK pathway,[91] and inhibit LPC-induced vascular endothelial growth factor (VEGF) and VEGF165mRNA expression.[92] TSG (1×10^{-5} mol/l) inhibited vascular smooth muscle cell proliferation via the NO/cyclic guanosine monophosphate/cGMP–dependent protein

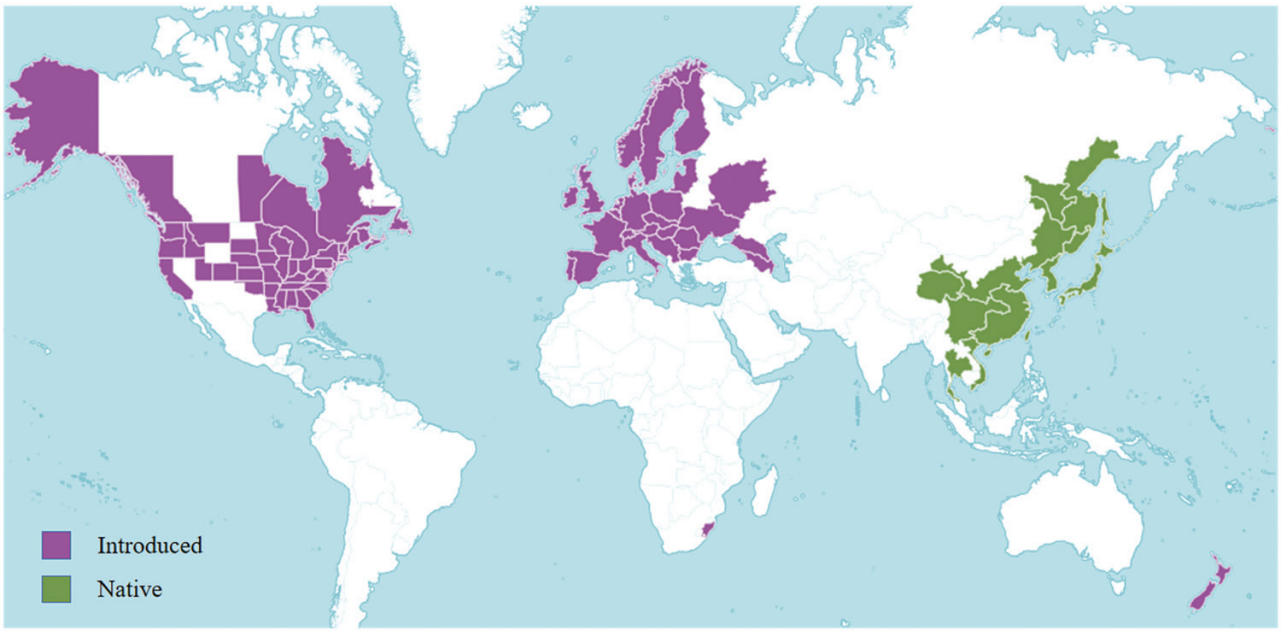


Figure 2 Distribution of genus *Reynoutria* in different regions of the world.

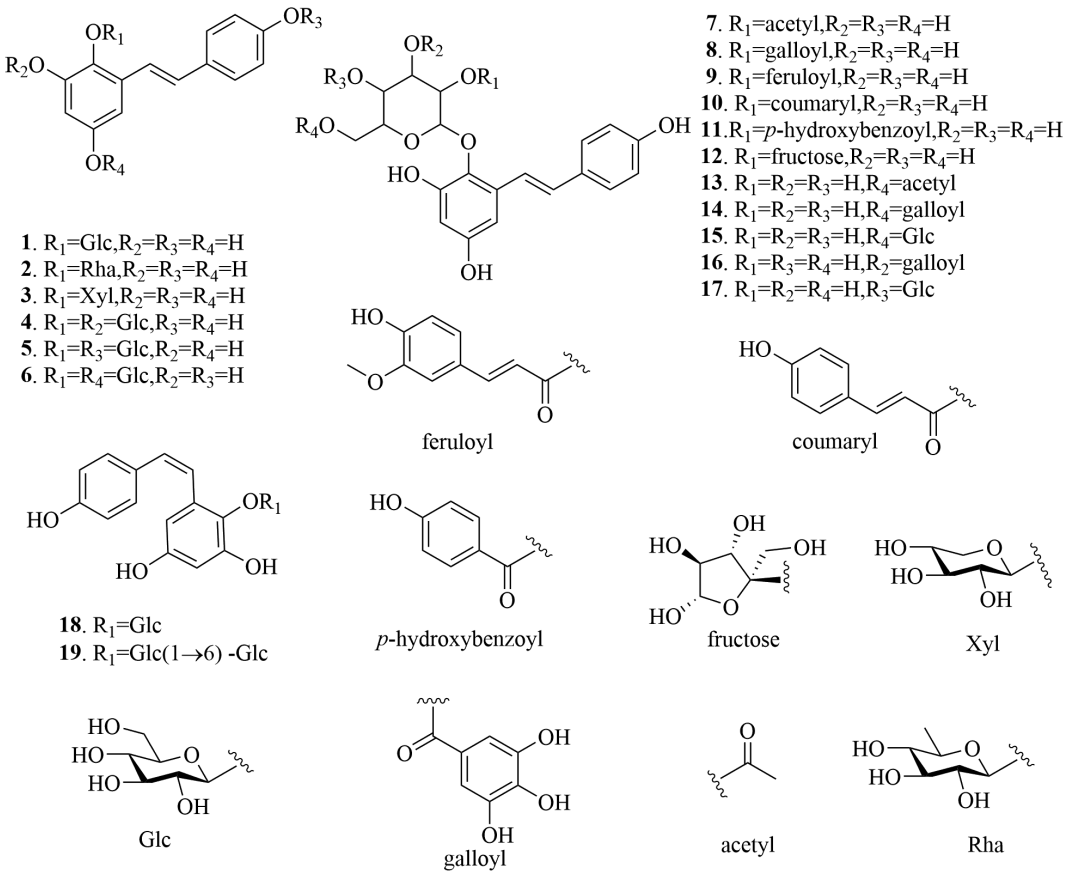


Figure 3 Structure of 2,3,5,4′-tetrahydroxystilbene glucoside in the genus *Reynoutria*.

kinase (NO/cGMP/PKG) pathway.[93] In vivo, TSG (100 mg/kg/day) inhibited excessive autophagy in vascular tissue and improved microvascular endothelial dysfunction by activating the protein kinase B/mammalian target of the rapamycin (Akt/mTOR) pathway.[94] In addition, studies showed that TSG (60 or 120 mg/kg/day) could restore endothelial diastole and remodel the aortic intima.[95] Meanwhile, emodin (20 or 40 mg/kg) could treat atherosclerosis through Janus kinase 2/Signal Transducer and Activator of Transcription 3 (JAK2/STAT3) cell signal pathways.[96] Hyperlipidemia is also

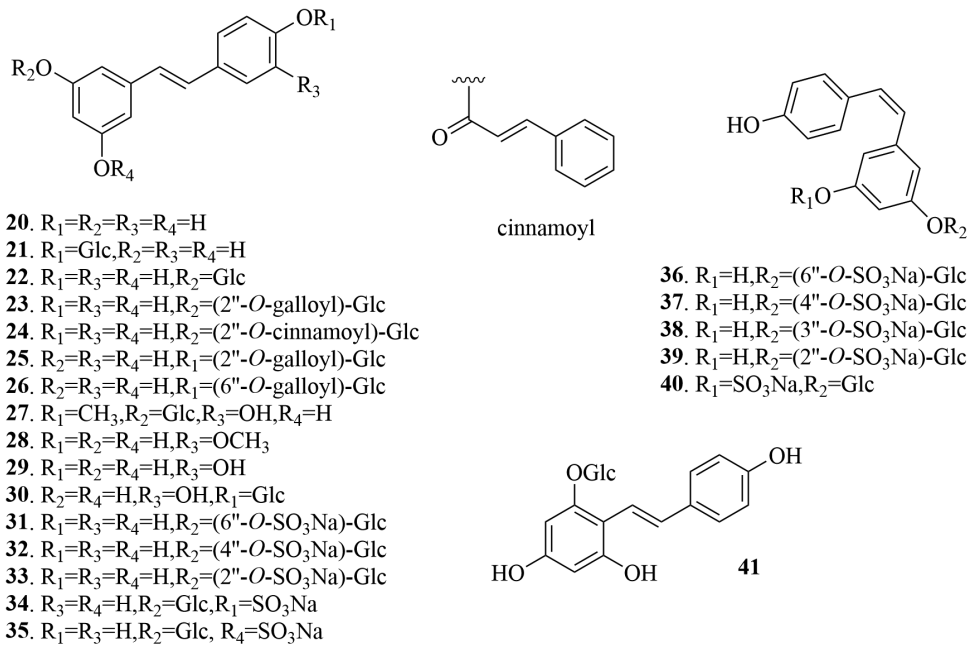


Figure 4 Structure of resveratrol glucoside in the genus *Reynoutria*.

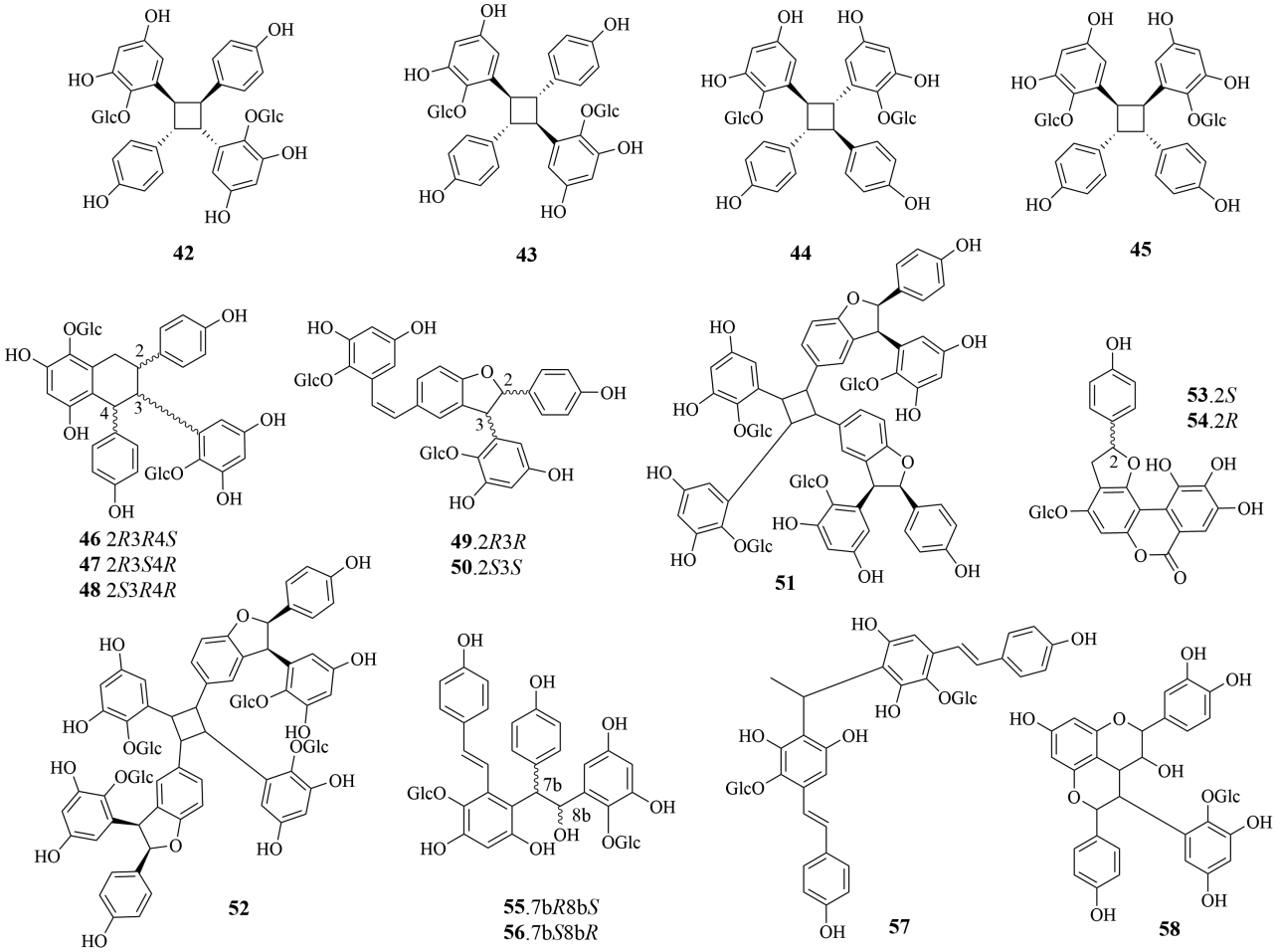


Figure 5 Structure of stilbene glycoside dimers in the genus *Reynoutria*.

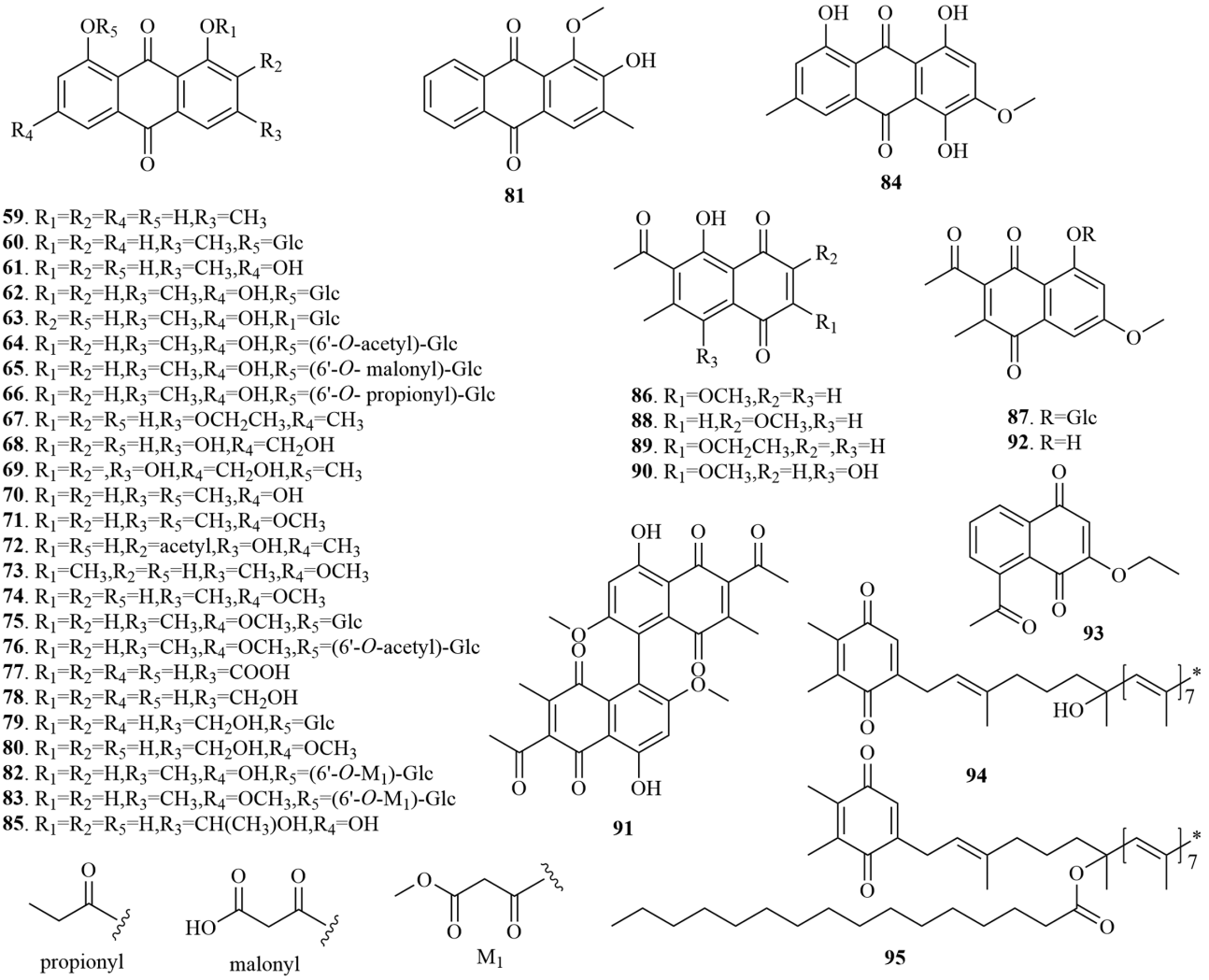


Figure 6 Structure of anthraquinones, naphthoquinones, and benzoquinones in the genus *Reynoutria*.

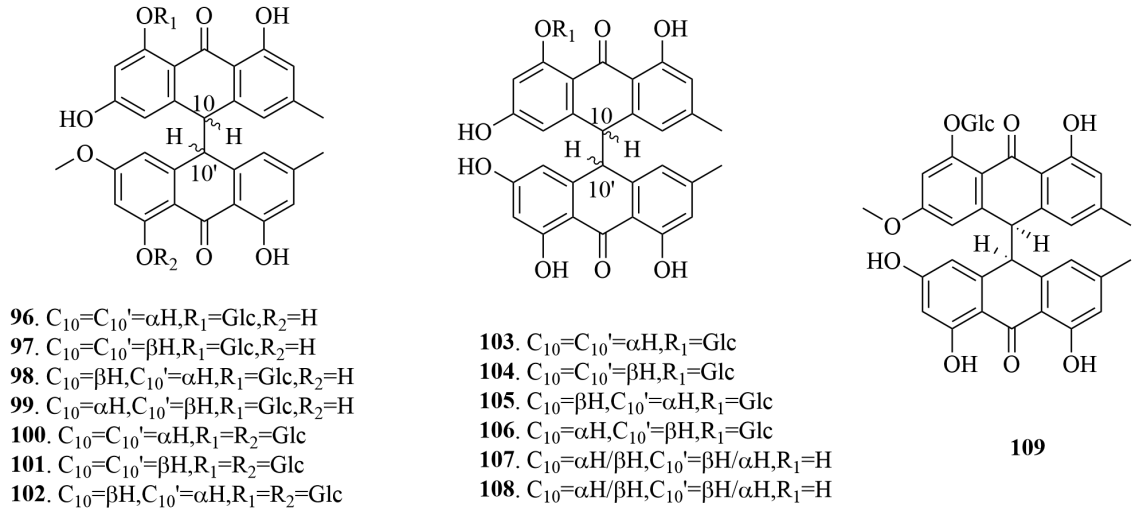
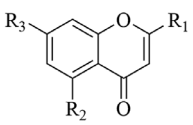
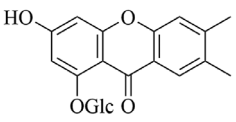


Figure 7 Structure of dianthrones in the genus *Reynoutria*.

thought to be a cause of atherosclerosis. *R. multiflora* 70% ethanol extract (16.2 g/kg) was able to significantly reduce blood lipids.[97] Polydatin (50 or 100 mg/kg/day) could reduce total cholesterol (TC), triglyceride (TG), and low-density lipoprotein cholesterol (LDL-C) in hyperlipidemic rabbits[98] and high-fat/high-cholesterol-fed hamsters.[99]

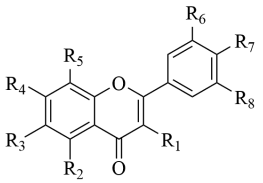




122

110. R_1=CH_3,R_2=R_3=OH
111. R_1=R_2=CH_3,R_3=OH
112. R_1=$CH_2CHOHCH_3$,R_2=CH_3,R_3=OGlc
113. R_1=$CH_2CHOHCH_3$,R_2=CH_3,R_3=O-fucopyranosyl (1→2) -Glc
114. R_1=CH_3,R_2=CH_2COOH,R_3=OH
115. R_1=CH_3,R_2=CH_2COOCH_3,R_3=OH
116. R_1=CH_3,R_2=CH_2OH,R_3=OH
117. R_1=CH_3,R_2=COOH,R_3=OH
118. R_1=$CH_2CHOHCH_3$,R_2=CH_2COOH,R_3=OH
119. R_1=R_2=CH_3,R_3=OGlc
120. R_1=CH_3,R_2=OH,R_3=OGlc
121. R_2=CH_3,R_3=OH,R_1=CH=C(CH_3)OGlc

Figure 8 Structure of chromones in the genus *Reynoutria*.



123. R_1=R_3=R_5=H,R_2=R_4=R_7=OH,R_6=R_8=OCH_3
124. R_1=R_3=R_5=R_6=R_8=H,R_2=R_4=R_7=OH
125. R_1=R_3=R_5=H,R_2=R_7=OH,R_6=R_8=OCH_3,R_4=OGlc
126. R_1=R_3=R_6=R_8=H,R_2=R_4=R_7=OH,R_5=OGlc
127. R_1=R_5=R_6=H,R_2=R_4=R_7=R_8=OH,R_3=OGlc
128. R_1=R_2=R_4=R_7=OH,R_3=R_5=R_6=R_8=H
129. R_1=R_2=R_4=R_6=R_7=OH,R_3=R_5=R_8=H
130. R_2=R_4=R_6=R_7=OH,R_3=R_5=R_8=H,R_1=OGlc
131. R_2=R_4=R_6=R_7=OH,R_3=R_5=R_8=H,R_1=OGal
132. R_2=R_4=R_7=R_8=OH,R_3=R_5=R_6=H,R_1=OGlc(1→6)-Rha
133. R_2=R_4=R_6=R_7=OH,R_3=R_5=R_8=H,R_1=OAra
134. R_2=R_4=R_6=R_7=OH,R_3=R_5=R_8=H,R_1=ORha
135. R_2=R_4=R_6=R_7=OH,R_3=R_5=R_8=H,R_1=OXyl
136. R_1=R_2=R_4=R_7=OH,R_3=R_6=R_8=H,R_5=$CH_2CH_2C(CH_3)_2OH$
137. R_2=R_7=OH,R_3=R_5=R_6=R_8=H,R_1=R_4=ORha
138. R_2=R_4=R_6=R_7=OH,R_3=R_5=H,R_1=OCH_3,R_8=OXyl
139. R_1=R_3=R_5=R_6=H,R_2=R_7=R_8=OH,R_4=OGlc

Figure 9 Structure of flavones in the genus *Reynoutria*.

Anti-inflammatory

In vitro, it was reported that TSG (50 μM) could achieve anti-inflammatory effects by reducing LPS-induced pro-inflammatory cytokine release.[100] Crude extract of *R. japonica* and emodin (40 mg/kg) both inhibited chemotaxis through inhibition of the Mitogen-activated protein kinase/extracellular regulated protein kinases(MEK/ERK) pathway, resulting in anti-inflammatory effects.[101] In addition, emodin (20 μg/mL) can reduce the activation of NF-κB in RAW264.7 cells and achieve a good anti-inflammatory effect.[102] *In vivo*, 10 μM polydatin could inhibit the NLRP3 inflammasome pathway and reactive oxygen species(ROS) production.[103] Meanwhile, TSG (60 mg/kg) significantly up-regulated peroxisome proliferators -activated receptors (PPAR)-γ and inhibited the NF-κB pathway, which could ameliorate acetic acid-induced colitis injury.[104] Chlorogenic acid (120 mg/kg/day) could alleviate DSS-induced mucosal injury and reduce the expression of a series of inflammatory-related proteins, which was related to the MAPK/ERK/JNK signaling pathway.[105]

Anti-oxidative

TSG had good free radical scavenging ability and could attenuate the (1-methyl-4-phenylpyridiniumion) MPP^+-induced rise in ROS levels in PC12 cells to achieve antioxidant effects.[106] It produced antioxidant effects by modulating superoxide dismutase (SOD)-3 and GST-4, which could improve the survival time of *Caenorhabditis elegans*.[7] Moreover, 50 μM TSG could increase SOD and Glutathione peroxidase (GSH-Px) activities in serum and organs of galactose-aging rats; reduced 2-thiobarbituric acid content to achieve antioxidant effects.[7] Both polydatin and resveratrol (200 mg/kg) showed significant antioxidant activity.[107] *R. multiflora* acidic polysaccharides had good 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical scavenging activity and anti-proliferative activity.[108] Likewise, *R. multiflora* polysaccharides also had high hydroxyl radical scavenging activity.[109]

Anti-cancer

It was shown that 50 μM emodin significantly inhibited the proliferation of RAW 264.7 cells through the Ca^{2+}-STAT pathway.[110] Meanwhile, emodin and emodin-8-methyl ether inhibited the growth of human colon cancer cells by inhibiting Recombinant Cell Division Cycle Protein 25B (Cdc25B) phosphatase (IC_{50} = 62.5, 30, 34 μg/ml, respectively).[111] Whereas emodin-8-*O*-glucoside and physcion-8-*O*- glucoside possessed farnesyl protein transferase (FPTase)[60] (IC_{50} = 46.3 and 28.2 μg/ml, respectively). What is noteworthy is that rhein could reverse the drug resistance in doxorubicin-resistant SMMC-7721 cells, IC_{50} = 26.81 μM,[112] polydatin (6 μM) inhibited AMC-HN-8 and HeLa cells proliferation and induced apoptosis by inhibiting platelet-derived growth factor (PDGF)/AKT signal pathway,[113] and 80 or 120 μM chrysophanol suppressed the proliferation of SNU-C5 cells by inhibiting the overexpression of epidermal growth factor receptor(EGFR).[114] The extract of *R. multiflora* roots (100 or 200 μg/ml) was able to inhibit MCF-7 cells and promote apoptosis.[115]

Neuroprotective

It has been shown that TSG (6.25–50 μM) could inhibit MPP^+ cytotoxicity in SH-SY5Y cells by protecting mitochondrial function, and preventing caspase-3 activation.[116] And TSG (200 μM) could protect rat hippocampus neuron cells through phosphatidylinositol 3 kinase (PI3K)/Akt signal pathway and mitochondrial apoptotic pathways,[117] which also could prevent 6-OHDA-induced apoptosis in PC12 cells by regulating the ROS-NO signal pathway (10–50 μM)[118] and protect HT22 cells by suppressing glutamate-induced disruption of MMP and anion channel-1 (30–200 μg/ml).[119] The hexane extract of *R. multiflora* (0.1–10 μg/ml) may inhibit glutamate-induced apoptosis cortical neurons by inhibiting death receptor 4 (DR4) and caspase activation.[120] The water extract of *R. multiflora* (0.1–10 μg/ml) exerted a protective effect on hippocampal neurons by inhibiting brain-derived neurotrophic factor (BDNF) expression and cyclic adenosine monophosphate (cAMP)-response element binding protein (CREB) phosphorylation.[121] Notably, emodin (10–40 μM) could induce Neuro2a cell regeneration by activating

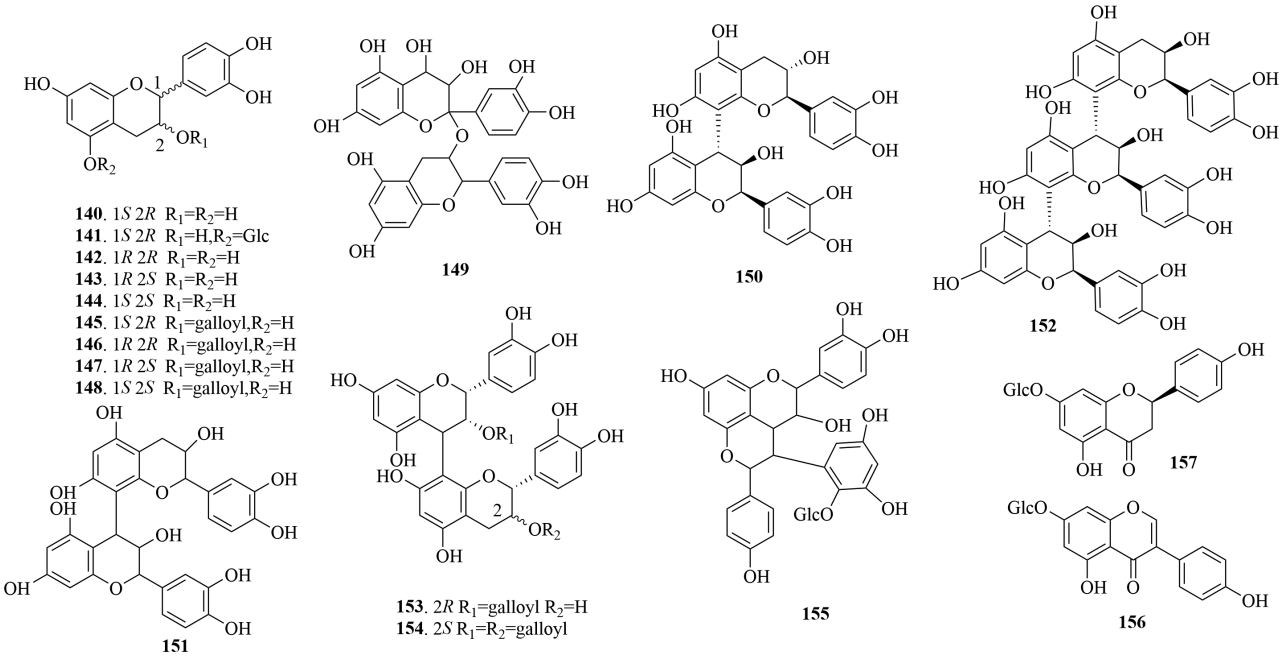


Figure 10 Structure of flavanones and isoflavone in the genus *Reynoutria*.

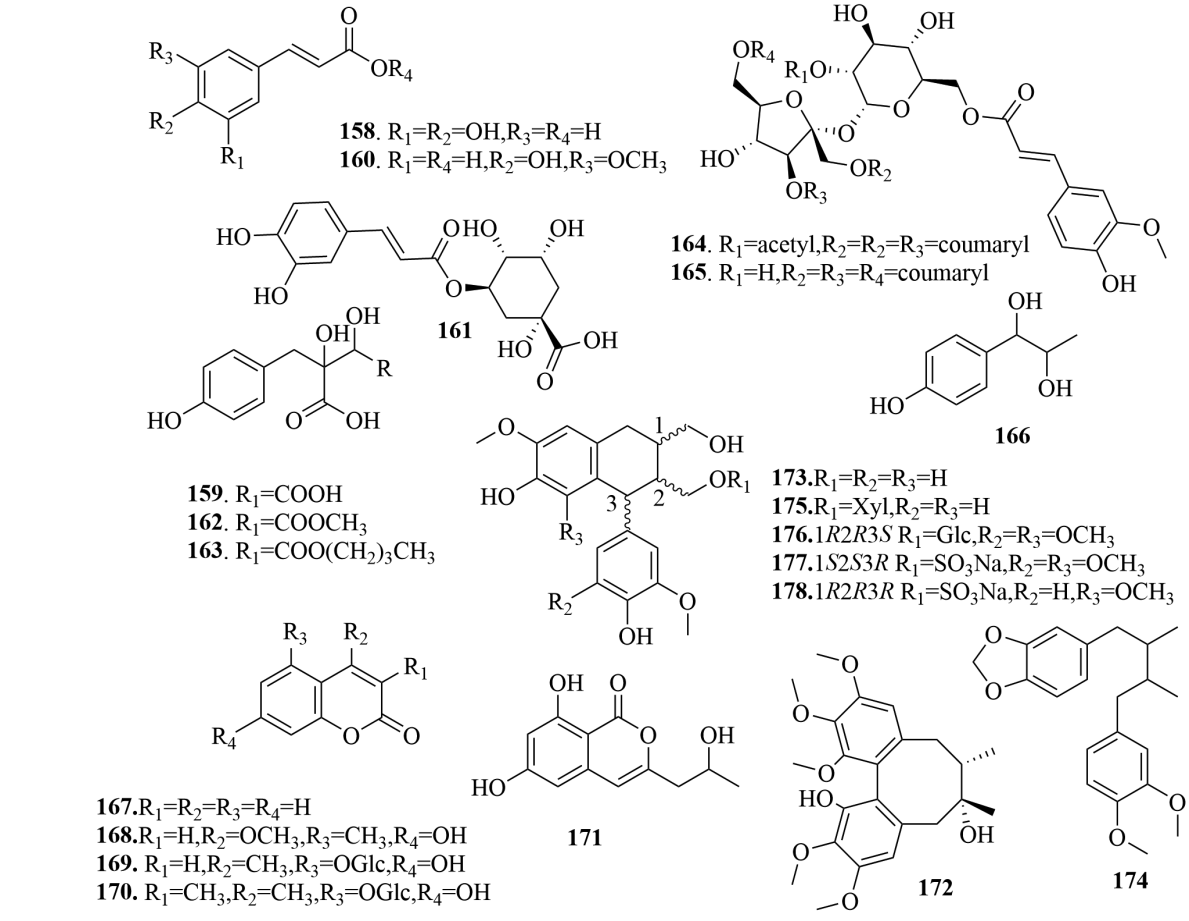


Figure 11 Structure of phenylpropanoids in the genus *Reynoutria*.

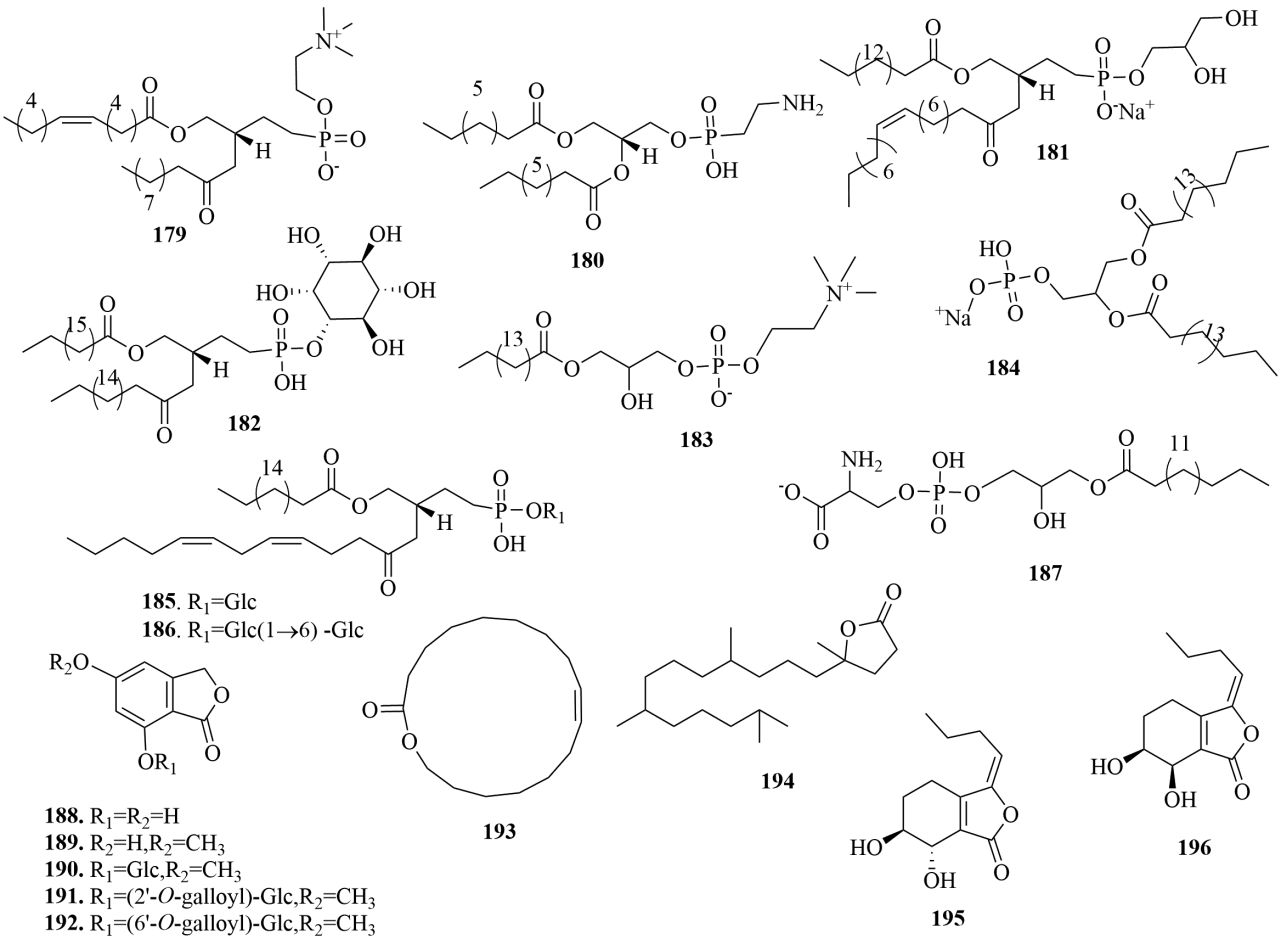


Figure 12 Structure of phospholipids and lactones in the genus *Reynoutria*.

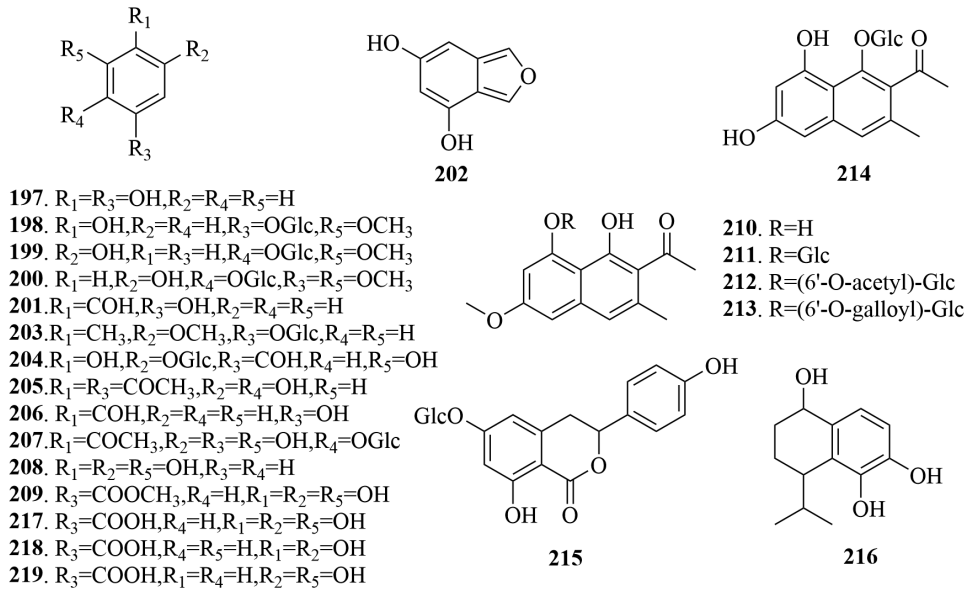
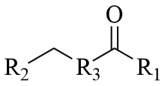


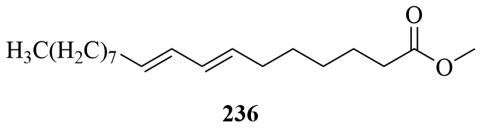
Figure 13 Structure of phenolics and phenolic acids in the genus *Reynoutria*.

the PI3K/Akt/GSK-3β-mediated signal pathway.[122] *In vivo*, ethanolic extract of *R. multiflora* (2 g/kg/day) improved cognitive dysfunction in diabetic rats by downregulating myosinlightchainkinase (MLCK) signaling expression.[123]

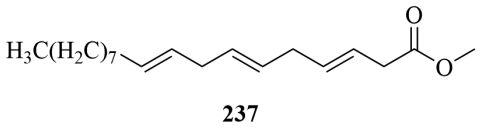
Alzheimer's disease (AD) is the most common neurodegenerative disorder, characterized by progressive neuronal loss with amyloid β-peptide (Aβ) plaques. *In vivo*, TSG (120 and 240 μmol/kg/d) not only prevented learning memory impairment



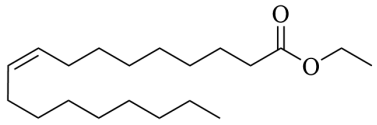
220. R_1=OH,R_2=COOH,R_3=CH_2
221. R_1=OH,R_2=$(CH_2)_2CH_3$,R_3=CH_2
222. R_1=OH,R_2=$(CH_2)_{13}CH_3$,R_3=CH_2
223. R_1=OH,R_2=$(CH_2)_{15}CH_3$,R_3=CH_2
224. R_1=OH,R_2=$CHCH(CH_2)_7CH_3$,R_3=$(CH_2)_9$
225. R_1=OCH_3,R_2=$(CH_2)_5CHO$,R_3=CH_2
226. R_1=OCH_3,R_2=$(CH_2)_{12}CH_3$,R_3=CH_2
227. R_1=OCH_3,R_2=$(CH_2)_{13}CH_3$,R_3=CH_2
228. R_1=OCH_3,R_2=$(CH_2)_{14}CH_3$,R_3=CH_2
229. R_1=OCH_3,R_2=$(CH_2)_{18}CH_3$,R_3=CH_2
230. R_1=OCH_3,R_2=$(CH_2)_6CH_3$,R_3=$(CH_2)_8CH_3$
231. R_1=OCH_2CH_3,R_2=$(CH_2)_{11}CH_3$,R_3=CH_2
232. R_1=OCH_2CH_3,R_2=$(CH_2)_{12}CH_3$,R_3=CH_2
233. R_1=OCH_2CH_3,R_2=$(CH_2)_{13}CH_3$,R_3=CH_2
234. R_1=OCH_2CH_3,R_2=$(CH_2)_{14}CH_3$,R_3=CH_2
235. R_1=CH_3,R_2=$(CH_2)_{16}CH_3$,R_3=O



236



237



238

Figure 14 Structure of fatty acids in the genus *Reynoutria*.

by preventing the elevation of Aβ levels and amyloid plaque formation but also treated learning memory impairment by breaking down amyloid plaques.[124] In particular, physcion-8-*O*-β-glucoside (5–40 mg/kg/day) significantly enhanced learning memory in $Aβ_{1-40}$-induced dementia rats.[125]

Parkinson's disease (PD) is a progressive, age-related and neurodegenerative disorder characterized by tremors, rigidity and cognitive impairment. *In vitro*, TSG (0.1 to 10 μM) had a therapeutic effect on Parkinson's via the PI3K/Akt signal pathway against MPP^+-induced PC12 cell damage and apoptosis.[126] *In vivo*, TSG (20 mg/kg/day) was able to reduce MPTP-induced neurotoxicity in animal brains and treat Parkinson's disease through BDNF-Tyrosine Kinase receptor B (TrkB) and Fibroblast growth factor 2 (FGF2)-Akt signal pathways.[127] Ethanolic extract of *R. multiflora* (400 or 800 mg/kg/day) had significant therapeutic effects on Parkinson's syndrome induced by a combination of paraquat and daidzein manganese.[128]

Ischemic brain injury

In vitro, hexane extract from *R. multiflora* (0.1–10 μg/ml) was found could prevent cerebral ischemic injury and significantly reduce infarct volume and neurological deficits.[129] Emodin (10–40 mM) reduced infarct size after focal ischemia by activating the PI3K/Akt survival pathway.[130] *In vivo*, TSG (120 mg/kg) was found to promote angiogenesis and recovery from ischemic brain injury by increasing microvessel density and upregulating the expression of CD31 in the brain,[131] which also inhibited c-Jun N-terminal kinase (JNK) and B-cell lymphoma-2(Bcl-2)-related apoptotic signal pathways while suppressing NF-κB activation and reducing inducible nitric oxide synthase (iNOS) gene expression to protect neuronal cells and reduce brain infarct volume (25 μM).[132] Notably, it also had a significant protective effect on brain injury in ischemia-reperfused mice (6 or 12 mg/kg), which ameliorated neuronal injury in the ischemic cortex and hippocampus by inhibiting NADPH oxidase 4 (NOX4), caspase-3(9), and Beclin 1 expression.[133] Moreover, polydatin (25, 50 mg/kg/day) was effective in reducing oxygen and glucose deprivation (OGD) damage to cultured neurons and significantly reduced cognitive impairment.[134]

Memory improvement

TSG (42, 84 and 168 mg/kg) reduced serum levels of ROS, 2-thiobarbituric acid, NO and insulin-like growth factors-1 (IGF-1) and increased SOD and GSH-Px activity in D-galactose-induced senescent mice to improve memory capacity.[135] Subsequent studies indicated that it improved memory capacity in mice by regulating the ERK signal pathway[136] and the amyloid precursor protein (APP) signal pathway.[137] Otherwise, resveratrol (25, 50 and 100 mg/kg) significantly increased the activity and expression of antioxidant enzymes and SOD to improve memory ability in mice.[138]

Anti-virus

Emodin (1–10μg/ml) inhibited the infectivity of S protein-pseudotyped retroviruses on VeroE6 cells, which was a potential drug to treat coronavirus SARS.[10] Meanwhile, it inhibited transcription and expression of EBV lysis protein (1.1, 2.1 and 4.2 μg/ml),[139] and inhibited Coxsackievirus B4 (CVB4)-induced apoptosis both *in vitro* and *in vivo* (EC_{50} =12.06 μM). Hereby, it could be used as a potential antiviral agent for CVB4 infection.[140] Both resveratrol and emodin were found could inhibit the growth of H3N2 and H1N1 strains and A/WSN/33 (H1N1) influenza virus through the TLR9-MYD88-IRF7 pathway (IC_{50} = 37.3 μM and 24.7 μM).[141] Resveratrol, (+)- catechin and emodin-8-*O*-β-D-glucoside showed an inhibitory effect on HIV-1-induced syncytium formation (EC_{50} = 4.37, 14.4, 11.29 μg/ml, respectively).[142] In addition, resveratrol inhibited varicella-zoster virus (VZV) replication by limiting the synthesis of IE62 protein in a dose-dependent and reversible manner (EC_{50} =19 μM).[143] Of particular note is that resveratrol (50 μg/mL) could inhibit the replication of herpes simplex virus-1(HSV-1) and HSV-2 by reducing viral adherent cells and inhibiting virus reactivation.[144] It has been found experimentally that resveratrol inhibited duck enteritis virus replication by reducing several early viral proteins essential for virus replication (IC_{50} = 3.85 μg/mL).[145]

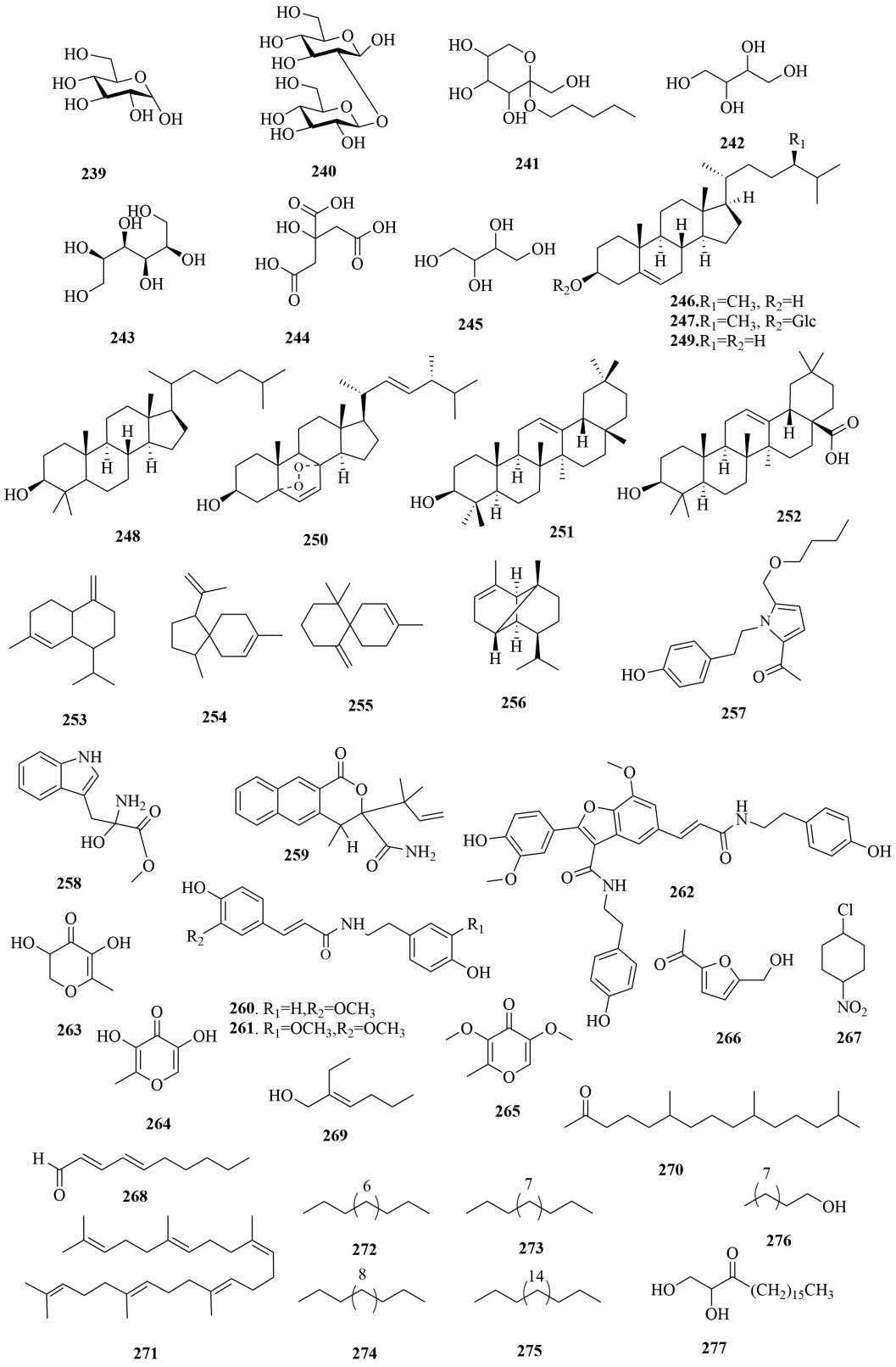


Figure 15 Structure of other compounds in the genus *Reynoutria*.

Heart protection

TSG (0.4 mM) protected against PA-induced cardiomyocyte apoptosis by stimulating miR-129-3p-targeted inhibition of Smad3 signaling,[146] which also prevented overload stress-induced cardiac remodeling by reducing angiotensin II, decreasing TGF-β1 expression, inhibiting ERK 1/2 and p38 MAPK (30, 60 and 120 mg/kg/day).[11] It is noteworthy that resveratrol (5 or 50 mg/kg/day) remodeled the heart by enhancing the activity of AMPK and silencing information regulator 1(SIRT1) in the heart and cellular

Table 2 Chemical compounds isolated and identified from the genus *Reynoutria*

No	Compounds	From	Part	Ref.
2.1 Stilbenoids				
2.1.1 2,3,5,4′-Tetrahydroxystilbene and their glycosides				
1.	2,3,5,4′-Tetrahydroxystilbene-2-*O*-β-D-glucoside	*R1*	P1	[21]
2.	2,3,5,4′-Tetrahydroxystilbene-2-*O*-rhamnoside	*R1*	P1	[22]
3.	2,3,5,4′-Tetrahydroxystilbene-2-*O*-xyloside	*R1*	P1	[23]
4.	2,3,5,4′-Tetrahydroxidene-2,3-di-*O*-glucoside	*R1*	P1	[24]
5.	2,3,5,4′-Tetrahydroxystilbene-2,4′-*O*-glucoside	*R1*	P1	[25]
6.	2,3,5,4′-Tetrahydroxystilbene-2-*O*-β-D-glucopyransoyl-5-*O*-*α*-D-glucoside	*R1*	P1	[25]
7.	2,3,5,4′-Tetrahydroxystilbene-2-*O*-(2″-*O*-acetyl)-β-D-glucoside	*R1*	P4	[26]
8.	2,3,5,4′-Tetrahydroxystilbene-2-*O*-(2″-*O*-galloyl)-β-D-glucoside	*R1*	P1	[27]
9.	2,3,5,4′-Tetrahydroxystilbene-2-*O*-(2″-*O*-feruloyl)-*β*-D-glucoside	*R1*	P4	[28]
10.	2,3,5,4′-Tetrahydroxystilbene-2-*O*-(2″-*O*-coumaryl)-*β*-D-glucoside	*R1*	P4	[28]
11.	2,3,5,4′-Tetrahydroxystilbene-2-*O*-(2″-*O*-*p*-hydroxybenzoyl)-*β*-D-glucoside	*R1*	P1	[29]
12.	2,3,5,4′-Tetrahydroxysterene-2-*O*-(2″-*O*-*β*-D-fructose)-*β*-D-glucoside	*R1*	P1	[25]
13.	2,3,5,4′-Tetrahydroxystilbene-2-*O*-(6″-*O*-acetyl)-*β*-D-glucoside	*R1*	P1	[29]
14.	2,3,5,4′-Tetrahydroxystilbene-2-*O*-(6″-*O*-galloyl)-*β*-D-glucoside	*R1*	P1	[27]
15.	2,3,5,4′-Tetrahydroxystilbene-2-glucosyl-(1→6)-*β*-D-glucoside	*R1*	P4	[26]
16.	2,3,5,4′-Tetrahydroxystilbene-2-*O*-(3“-*O*-galloyl)-*β*-D-glucoside	*R1*	P1	[27]
17.	2,3,5,4′-Tetrahydroxystilbene-2-glucosyl-(1→4)-*β*-D-glucoside	*R1*	P1	[25]
18.	*cis*-2,3,5,4′-tetrahydroxysterene-2-*O*-glucoside	*R1*	P1	[22]
19.	*cis*-2,3,5,4′-Tetrahydroxystilbene-2-glucosyl-(1 → 6)-β-D-glucoside	*R1*	P1	[30]
2.1.2 resveratrol and their glycosides				
20.	Resveratrol	*R1*	P1	[31]
		R2	P1	[32]
		R3	P1	[33]
21.	Resveratrol-4′-*O*-β-D-glucoside (resveratroloside)	*R1*	P1	[34]
		R3	P1	[16]
22.	Resveratrol-3-*O*-β-D-glucoside (polydatin)	*R1*	P1	[31]
		R2	P1	[32]
		R3	P1	[33]
23.	Resveratrol-3-*O*-β-D-(2″-*O*-galloyl)-glucoside	*R1*	P1	[31]
		R2	P1	[32]
24.	Resveratrol-3-*O*-β-D-3-(2″-*O*-cinnamoyl)-glucoside	*R2*	P1	[32]
25.	Resveratrol-4′-*O*-β-D-(2″-*O*-galloyl)-glucopyranoside	*R3*	P1	[35]
26.	resveratrol-4′-*O*-β-D-(6″-*O*-galloyl)-glucopyranoside	*R3*	P1	[35]
27.	Rhapontin	*R1*	P3	[36]
28.	Isorhapontigenin	*R1*	P1	[37]
29.	Piceatannol	*R1*	P1	[37]
30.	Piceatannol glucoside	*R3*	P1	[38]
31.	*trans*-Stilbene glycoside sulfate 1	*R3*	P1	[39]
32.	*trans*-Stilbene glycoside sulfate 2	*R3*	P1	[39]
33.	*trans*-Stilbene glycoside sulfate 3	*R3*	P1	[39]
34.	*trans*-Stilbene glycoside sulfate 4	*R3*	P1	[39]
35.	*trans*-Stilbene glycoside sulfate 5	*R3*	P1	[39]
36.	*cis*-Stilbene glycoside sulfate 1	*R3*	P1	[39]
37.	*cis*-Stilbene glycoside sulfate 2	*R3*	P1	[39]
38.	*cis*-Stilbene glycoside sulfate 3	*R3*	P1	[39]
39.	*cis*-Stilbene glycoside sulfate 4	*R3*	P1	[39]
40.	*cis*-Stilbene glycoside sulfate 5	*R3*	P1	[39]
2.1.3 2,4,6,4′-Tetrahydroxystilbene glucoside				
41.	2,4,6,4′-Tetrahydroxystilbene-2-*O*-β-glucoside	*R1*	P1	[40]

Table 2. Continued

No	Compounds	From	Part	Ref.
2.1.4 Stilbene glycoside dimers				
42.	Multifloraiside A	*R1*	P1	[41]
43.	Multifloraiside B	*R1*	P1	[41]
44.	Multifloraiside C	*R1*	P1	[41]
45.	Multifloraiside D	*R1*	P1	[41]
46.	Multifloraiside E	*R1*	P1	[41]
47.	Multifloraiside F	*R1*	P1	[41]
48.	Multifloraiside G	*R1*	P1	[41]
49.	M ultifloraiside H	*R1*	P1	[42]
50.	Multifloraiside I	*R1*	P1	[42]
51.	Multifloraiside J	*R1*	P1	[42]
52.	Multifloraiside K	*R1*	P1	[42]
53.	Polygonumoside A	*R1*	P4	[43]
54.	Polygonumoside B	*R1*	P4	[43]
55.	Polygonumoside C	*R1*	P4	[43]
56.	Polygonumoside D	*R1*	P4	[43]
57.	Polygonumnolide D	*R1*	P1	[44]
58.	Polygonflavanol A	*R1*	P1	[45]
2.2 Quinones				
2.2.1 Anthraquinones				
59.	Chrysophanol	*R1*	P1	[29]
		R2	P1	[46]
		R3	P1	[47]
60.	Chrysophanol-8-*O*-glucoside	*R1*	P1	[48]
		R3	P1	[49]
61.	Emodin	*R1*	P1	[50]
		R2	P1	[32]
		R3	P1	[33]
62.	Emodin-8-*O*-β-D-glucoside (anthraglycoside B)	*R1*	P1	[27]
		R2	P1	[46]
		R3	P1	[33]
		R4	P5	[51]
63.	Emodin-1-*O*-β-D-glucoside	*R1*	P1	[6]
64.	Emodin-8-*O*-(6′-*O*-acetyl)-glucoside	*R1*	P1	[52]
65.	Emodin-8-*O*-(6′-*O*-malonyl)-glucoside(emoghrelin)	*R1*	P1	[53]
66.	Emodin-8-*O*-(6′-propionyl)-glucoside	*R1*	P1	[54]
67.	Emodin-3-ether	*R1*	P1	[55]
68.	*ω*-Hydroxy emodin (citreorosein)	*R1*	P1	[29]
		R2	P1	[32]
		R3	P1	[56]
69.	*ω*-Hydroxy emodin-8 methyl ether (questinol)	*R1*	P1	[57]
		R3	P1	[58]
70.	Emodin-1-methyl ether	*R1*	P1	[57]
71.	Emodin-6,8-dimethyl ether	*R1*	P1	[52]
72.	2-Acetyl emodin	*R1*	P1	[29]
73.	Emodin-1,6-dimethyl ether	*R1*	P1	[29]
74.	Physcion	*R1*	P1	[27]
		R2	P1	[59]
		R3	P1	[33]
75.	Physcion-8-*O*-β-D-glucoside (anthraglycoside A)	*R1*	P1	[60]
		R2	P1	[46]
		R3	P1	[56]

Table 2. Continued

No	Compounds	From	Part	Ref.
76.	Physcion-8-O-(6′-O-acetyl)-glucoside	*R1*	P1	[61]
77.	Rhein	*R1*	P1	[62]
		R2	P1	[46]
		R3	P5	[63]
78.	Aloe-emodin	*R1*	P1	[29]
		R3	P5	[63]
79.	Aloe-emodin-8-O-glucoside	*R1*	P1	[31]
80.	Fallacinol	*R1*	P1	[52]
		R3	P1	[33]
81.	Digitolutein	*R1*	P1	[64]
82.	Polyganin A	*R3*	P1	[65]
83.	Polyganin B	*R3*	P1	[65]
84.	Xanthorin	*R3*	P1	[66]
85.	Isorhodoptilometrin	*R3*	P1	[66]
2.2.2 Naphthoquinones				
86.	2-Methoxy-6-acety1-7-methy1-juglone	*R1*	P1	[67]
		R3	P1	[58]
87.	6-Methoxyl-2-acetyl-3methyl-1,4-naphthoquinone-8-O-β-D-glucoside	*R1*	P1	[28]
88.	7-Acetyl-2-methoxy-6-methyl- 8-hydroxyl-1, 4-naphthoquinone	*R3*	P1	[68]
89.	6-Acetyl-2-methoxy-5-hydroxy-7-methyl-1,4-naphthoquinone	*R3*	P1	[66]
90.	6-Acetyl-5,8-dihydroxy-2-methoxy-7-methyl-1,4-naphthoquinone	*R3*	P1	[66]
91.	Cuspidatumin C	*R3*	P1	[66]
92.	3-Acetyl-5-hydroxy-7-methoxy-2-methyl-1,4-naphthoquinone	*R3*	P1	[66]
93.	cuspidatumin A	*R3*	P1	[68]
2.2.3 Benzoquinones				
94.	Phylloquinone B	*R3*	P1	[69]
95.	Phylloquinone C	*R3*	P1	[69]
2.2.4 Di-anthraquinones				
96.	Polygonumnolide A1	*R1*	P1	[70]
97.	Polygonumnolide A2	*R1*	P1	[70]
98.	Polygonumnolide A3	*R1*	P1	[70]
99.	Polygonumnolide A4	*R1*	P1	[70]
100.	Polygonumnolide B1	*R1*	P1	[70]
101.	Polygonumnolide B2	*R1*	P1	[70]
102.	Polygonumnolide B3	*R1*	P1	[70]
103.	Polygonumnolide C1	*R1*	P1	[71]
104.	Polygonumnolide C2	*R1*	P1	[71]
105.	Polygonumnolide C3	*R1*	P1	[71]
106.	Polygonumnolide C4	*R1*	P1	[71]
107.	Polygonumnolide E	*R1*	P4	[44]
108.	*trans*-Emodin dianthrones	*R1*	P1	[71]
109.	*cis*-Emodin dianthrones	*R1*	P1	[71]
2.3 Flavonoids				
2.3.1 Chromones				
110.	Noreugenin	*R1*	P3	[36]
111.	2,5-Dimethyl-7-hydroxychromone	*R1*	P1	[67]
		R2	P1	[46]
		R3	P1	[58]
112.	2-(2′-Hydroxypropyl)-5-methylchromogenketone-7-O-β-D-glucopyranoside	*R1*	P1	[67]
113.	(*s*)-2-(2-hydroxypropyl)-5-methyl-7-hydroxychromogenketone-7-O-α-L-fucosyl (1→2)-β-D-glucoside	*R1*	P1	[4]
114.	5-Carboxymethyl -7-hydroxy-2-methyl chromone	*R1*	P1	[48]
		R2	P1	[46]

Table 2. Continued

No	Compounds	From	Part	Ref.
115.	2-Methyl-5-hydroxymethyl-7-hydroxychromone	*R2*	P1	[46]
116.	2-Methyl-5-methylcarboxymethyl-7-hydroxychromone	*R2*	P1	[46]
117.	2-Methyl-5-carboxylicacid-7-hydroxy-chromone	*R2*	P1	[46]
118.	2-(2′-Hydroxypropyl)-5-methyl-7-hydroxychromone	*R1*	P2	[72]
119.	2,5-Dimethyl-7-hydroxy-chromone-7-*O*-β-D-glucopyranoside	*R1*	P2	[72]
		R2	P1	[46]
120.	Noreugenin-7-*O*-β-D-glucopyranoside	*R1*	P2	[72]
121.	Polygonumoside E	*R1*	P1	[67]
122.	Polygonimitin B	*R1*	P1	[24]
2.3.2 Flavones				
123.	Tricin	*R1*	P1	[67]
124.	Apigenin	*R3*	P5	[63]
125.	Tricin-7-*O*-β-D-glucoside	*R1*	P4	[5]
126.	Vitexin	*R1*	P3	[36]
127.	Isoorientin	*R1*	P1	[73]
128.	Kaempferol	*R1*	P1	[29]
		R3	P1	[47]
129.	Quercetin	*R1*	P1	[31]
		R3	P5	[63]
		R4	P5	[51]
130.	Isoquercetin (querctin-3-*O*-β-D-glucopyranoside)	*R3*	P1	[66]
		R4	P5	[51]
131.	Hyperoside	*R1*	P3	[36]
			P1	[74]
		R3	P1	[66]
132.	Rutin	*R1*	P3	[36]
		R3	P5	[63]
133.	Quercetin-3-*O*-β-D-arabinosidey	*R1*	P1	[74]
		R3	P1	[68]
134.	Querctin-3-*O*-β-D-rhamnoside	*R3*	P1	[66]
135.	Querctin-3-*O*-β-D-xyloside (reynoutrin)	*R3*	P1	[66]
136.	Icaritin	*R1*	P1	[6]
137.	Kaempferitrin	*R2*	P1	[6]
138.	Annulatin-3′-*O*-β-D-xyloside	*R2*	P1	[6]
139.	Luteolin-7-*O*-glucoside	*R3*	P1	[66]
2.3.3 Flavanones				
140.	(+)-Catechin (C)	*R1*	P1	[75]
		R3	P1	[69]
		R4	P3	[76]
		R5	P3	[76]
141.	(+)-Catechin-5-*O*-β-D-glucopyranoside	*R3*	P1	[77]
142.	Epicatechin (EC)	*R1*	P1	[75]
		R3	P1	[47]
		R4	P3	[76]
		R5	P3	[76]
143.	Gallocatechin(GC)	*R1*	P1	[75]
144.	Epigallocatechin (EGC)	*R1*	P1	[75]
145.	Catechin gallic acid (CG)	*R1*	P1	[75]
146.	Epicatechin gallate (ECG)	*R1*	P1	[75]
		R4	P3	[76]
		R5	P3	[76]
147.	Gallocatechin gallate (GCG)	*R1*	P1	[75]
148.	Epigallocatechin gallate (EGCG)	*R1*	P1	[75]

Table 2. Continued

No	Compounds	From	Part	Ref.
149.	Proanthocyanidin	*R1*	P1	[78]
150.	Proanthocyanidin B1	*R1*	P1	[78]
		R4	P3	[76]
151.	Proanthocyanidin B2	*R1*	P1	[78]
		R4	P3	[76]
		R5	P3	[76]
152.	Proanthocyanidin C1	*R4*	P3	[76]
153.	3-*O*-galloyl-procyanidin B-2	*R1*	P1	[79]
154.	3,3′-di-*O*-galloyl-procyanidin B-2	*R1*	P1	[79]
155.	Polygonflavanol A	*R1*	P1	[45]
2.3.4 Isoflavone				
156.	Genistin	*R1*	P2	[72]
		R3	P5	[63]
2.3.5 Flavonone				
157.	Hesperetin	*R3*	P5	[63]
2.4 Phenylpropanoids				
2.4.1 Simple phenylpropanoids				
158.	Caffeic acid	*R1*	P2	[72]
		R3	P1	[69]
159.	Piscidic acid	*R2*	P1	[6]
160.	Ferulic acid	*R3*	P1	[69]
161.	Chlorogenic acid	*R3*	P1	[69]
162.	2-Methyl-(4-hydroxybenzyl)-tartrate	*R2*	P1	[6]
163.	2-Monobutyl-(4-hydroxybenzyl)-tartrate	*R2*	P1	[6]
164.	Vanicosides A	*R4*	P6	[80]
165.	Vanicosides B	*R4*	P6	[80]
166.	1,2-Propanediol-1-(4-hydroxy-phenyl)	*R1*	P1	[30]
2.4.2 Coumarins				
167.	Coumarin	*R3*	P1	[68]
168.	7-Hydroxy- 4-methoxy-5-methylcoumarin	*R3*	P1	[58]
169.	7-Hydroxy-4-methylcoumarin-5-*O*-glucoside	*R1*	P1	[28]
170.	7-Hydroxy-3,4-dim-methyl-coumarin-5-*O*-glucososide	*R1*	P1	[28]
171.	Polyisocoumarin	*R3*	P1	[81]
2.4.3 Lignans				
172.	Schizandrin	*R1*	P4	[82]
173.	Isolariciresinol	*R2*	P1	[46]
174.	5-[4-(3, 4-dimethoxyphenyl)-2,3-dimethylbutyl]-1,3-benzodioxole	*R2*	P1	[46]
175.	Isolariciresinol-9-*O*-β-D-xylopyranoside	*R2*	P1	[46]
176.	(+)-Lyoniresinol-3-*α*-*O*-β-D-glucopyranoside	*R1*	P1	[30]
177.	Sodium(−)-lyoniresinol-2a-sulfate	*R3*	P1	[77]
178.	Sodium(+)-isolaricireinol-2a-sulfate	*R3*	P1	[77]
2.5 Phospholipids				
179.	Phosphatidylcholine (PC)	*R1*	P4	[82]
180.	Phosphatidylethanolamine (PE)	*R1*	P1	[83]
181.	Phosphatidylglycerol (PG)	*R1*	P1	[83]
182.	Phosphatidylinositol (PI)	*R1*	P1	[83]
183.	Iysophosphatidylcholine (LPC)	*R1*	P1	[84]
184.	Phosphatidylserine	*R1*	P1	[84]
185.	1-*O*-Stearoyl-2-*O*-$\Delta^{4',7'}$-dodecenoyl-3-*O*-phosphatidicacid-*O*-β-D-glucoside	*R1*	P4	[28]
186.	1-*O*-stearoyl-2-*O*-$\Delta^{4',7'}$-dodecenoyl-3-*O*-phosphatidicacid-*O*-(6″-*O*-*α*-D-2-glucose)-β-D-glucoside	*R1*	P4	[28]
187.	Phosphatidic acid	*R1*	P1	[83]

Table 2. Continued

No	Compounds	From	Part	Ref.
2.6 Lactones				
188.	5,7-Dihydroxy-isobenzofuran	*R2*	P1	[46]
		R3	P1	[56]
189.	5-Methoxy-7-hydroxy-isobenzofuran	*R2*	P1	[46]
190.	5-Methoxy-isobenzofuran-7-O-β-D-glucoside	*R2*	P1	[46]
191.	Polyphthaliside A	*R3*	P1	[81]
192.	Polyphthaliside B	*R3*	P1	[81]
193.	Ambrettolide	*R3*	P1	[68]
194.	4,8,12,16-Tetramethylheptadecan-4-olide	*R1*	P4	[85]
195.	*cis-E*-3-butylidene-4,5,6,7-tetrahydro-6,7-dihydroxy-l(3H)-isobenzofuranone	*R1*	P1	[40]
196.	*trans-E*-3-butylidene-4,5,6,7-tetrahydro-6,7-dihydroxy-l(3H)-isobenzofuranone	*R1*	P1	[40]
2.7 Phenolics and phenolic acids				
2.7.1 Phenolics				
197.	1,4-Benzenediol	*R1*	P4	[57]
198.	Tachioside	*R3*	P1	[69]
199.	Isotachioside	*R3*	P1	[69]
200.	2,6-Dimethoxy-phydroquinone-1-O-β-D-glucopyranoside	*R3*	P1	[66]
201.	4-Hydroxyacetophenone	*R3*	P5	[63]
202.	5,7-Dihydroxyisobenzofuran	*R3*	P1	[56]
203.	2-(Hydroxymethyl)-6-(3-methoxy-4-methylphenoxy)tetrahydro-2H-pyran-3,4,5-triol	*R1*	P1	[86]
204.	1-(3-O-β-D-glucopyranosyl-4,5-dihydroxy-phenyl)-acetophenone	*R3*	P1	[69]
205.	2,5-Diacethylhy-droquinone	*R2*	P1	[46]
206.	*p*-Hydroxybenzaldehyde	*R1*	P4	[57]
207.	2,3,4,6-Tetrahydroxyacetophenone-3-O-β-D-glucoside	*R1*	P1	[74]
208.	Pyrogallol	*R1*	P1	[67]
209.	Methylgallate	*R1*	P1	[54]
210.	Torachrysone	*R3*	P1	[66]
211.	Torachrysone-8-O-β-D-glucoside	*R2*	P1	[6]
		R3	P1	[69]
212.	Torachrysone-8-O-(6′-galloyl)-β-D-glucoside	*R2*	P1	[6]
213.	Torachrysone-8-O-(6′-O-acetyl)-β-D-glucoside	*R2*	P1	[32]
		R3	P1	[69]
214.	6-Hydroxymusizin-8-O-β-D-glucoside	*R2*	P1	[32]
215.	Thunberginol C-6-O-β-D-glucopyranoside	*R1*	P1	[30]
216.	5,6,7,8-Tetrahydro-2,5-dimethyl-8-(1-methyl-ethyl)-l-naphthalenol	*R1*	P4	[85]
2.7.2 Phenolic acids				
217.	Gallic acid	*R1*	P4	[87]
		R2	P1	[6]
		R3	P1	[69]
218.	Protocatechuic acid	*R3*	P1	[68]
219.	2,6-Dihydroxy-benzoic acid	*R1*	P1	[30]
2.8 Fatty acids				
220.	Succinic acid	*R2*	P1	[6]
221.	Hexanoic acid	*R1*	P4	[85]
222.	Palmitic acid	*R3*	P1	[69]
223.	Stearic acid	*R3*	P1	[69]
224.	Arachidonic acid	*R3*	P1	[69]
225.	Nonanoic acid,9-oxo,methyl ester	*R1*	P4	[85]
226.	Hexadecaroic acid methyl ester	*R1*	P4	[85]
227.	Heptadecanoic acid methyl ester	*R1*	P4	[85]
228.	Octadecanoic acid methyl ester	*R1*	P4	[85]
229.	Docosanoic acid methyl ester	*R1*	P4	[85]

Table 2. Continued

No	Compounds	From	Part	Ref.
230.	10-octadecenoic acid methyl ester	*R1*	P4	[85]
231.	Tetradecanoic acid ethyl ester	*R1*	P4	[85]
232.	Hexadecanoic acid ethyl ester	*R1*	P4	[85]
233.	Heptadecanoic acid ethyl ester	*R1*	P4	[85]
234.	Octadecanoic acid ethyl ester	*R1*	P4	[85]
235.	Acetic acid octadecyl ester	*R1*	P4	[85]
236.	9,11-Octadecadienoic acid methly ester	*R1*	P4	[85]
237.	(*Z*,*Z*,*Z*)-9,12,15-octadecatrienoic acid methyl ester	*R1*	P4	[85]
238.	Ethyl oleate	*R1*	P4	[85]
2.9 Saccharides				
239.	α-D-glucose	*R2*	P1	[6]
240.	Inotodisaccharide	*R2*	P1	[6]
241.	*n*-Butyl-β-D-fructopyranoside	*R2*	P1	[6]
2.10 Polyols				
242.	Erythritol	*R2*	P1	[6]
243.	D-mannitol	*R3*	P1	[47]
244.	Citricn acid	*R3*	P1	[47]
245.	(1*S*,2*R*,3*R*,4*S*)-4-(hydroxymethyl)-4-pentylcyclopentane-1,2,3-triol	*R1*	P1	[27]
2.11 Steroids				
246.	β-Sitosterol	*R2*	P1	[6]
		R3	P5	[63]
247.	Daucosterol	*R2*	P1	[6]
		R3	P5	[63]
		R4	P5	[51]
248.	Dammaran-3*β*-ol	*R4*	P5	[51]
249.	Campesterol	*R4*	P5	[51]
250.	Ergosterol peroxide	*R4*	P5	[51]
2.12 Terpenoids				
251.	β-Amyrin	*R1*	P3	[36]
		R4	P5	[51]
252.	Oleanolic acid	*R3*	P1	[68]
253.	1,2,3,4,4a,5,6,8a-Octahydro-7-methyl-4-methyl naphthalene	*R1*	P4	[85]
254.	1,8-Dimethyl-4-(1-melthylethenyl)-spiroene	*R1*	P4	[85]
255.	3,7,7-Trimethyl-11-methylenespiro[5.5]undec-2-ene	*R1*	P4	[85]
256.	Copaene	*R1*	P4	[85]
2.13 Alkaloids				
257.	Pyrrolezanthine-6-monobutyl-ether	*R2*	P1	[6]
258.	Indole-3-(L-*α*-amino-*a*-hydroxypropionic acid) -methyl ester	*R1*	P1	[30]
259.	Polygonimitin A	*R1*	P1	[30]
260.	*n*-Trans-feruloyl tyramine	*R1*	P1	[67]
261.	*n-Trans*-feruloyl-3'-O-methyldopamine	*R1*	P1	[62]
262.	(*E*)-2-(4-hydroxy-3-methoxyphenyl)-3-[N-2-(4-hydroxyphenyl)ethyl]carbamoyl-5-[N-2-(4-hydroxyphenyl)ethyl]carbamoylethenyl-7-methoxybenzofuran	*R1*	P1	[88][89]
2.14 Miscellaneous compounds				
263.	2,3-Dihydro-3,5-dihydroxy-6-methyl-4-H-pyranone(DDMP)	*R1*	P4	[57]
264.	5-Hydroxymaltol	*R1*	P4	[57]
265.	Zanthopyranone	*R2*	P1	[46]
266.	5-Hydroxymethyl-furfura	*R1*	P4	[57]
267.	l-Chloro-4-mitro-benzene	*R1*	P4	[85]
268.	(*E*,*E*)-2,4-decedienal	*R1*	P4	[85]
269.	2-Ethyl-2-hexenlol	*R1*	P4	[85]
270.	6,10,14-Trimethyl-2-pentadecanone	*R1*	P4	[85]
271.	Squalene	*R1*	P4	[85]

Table 2. Continued

No	Compounds	From	Part	Ref.
272.	dodecane	*R1*	P2	[72]
273.	Tridecane	*R1*	P2	[72]
274.	Tetradecane	*R1*	P2	[72]
275.	Eicoeane	*R1*	P4	[85]
276.	1-Decanol	*R4*	P5	[51]
277.	1,2-Dihydroxy nonadecone -3	*R1*	P4	[85]

R1: *R. multiflora*; R2: *R. ciliinervis*; R3: *R. japonica*; R4: *R. sachalinensis*; R5: *Reynoutria* × *bohemica*
P1: Tuberous roots; P2: stems; P3: leaves; P4: processed roots; P5: flowers; P6: rhizomes

autophagy.[147] Polydatin (100, 200 mg/kg/day) significantly limited the infarct size through activation of protein kinase C-ATP-sensitive potassium channel (PKC-KATP)-dependent signaling and anti-oxidative stress mechanisms,[148] which also had an attenuating effect on ventricular remodeling.[149] *In vivo and vitro*, TSG inhibited the production of reactive oxygen species and elevated Bcl-2 protein levels to protect the heart from doxorubicin (DOX)-induced effects.[150] A study has shown that resveratrol at lower doses still ensured the survival of cardiomyocytes through autophagy of the mTOR-Rictor pathway (0.1 and 1 mM in cells and 2.5 mg/kg/day in rats).[151]

Liver protection

In vitro, emodin (20–160 μM) protected against hepatocyte apoptosis by inhibiting the PI3K/AKT/mTOR signal pathway.[152] *In vivo*, polydatin (50 or 100 mg/kg) inhibited liver tissue inflammation in carbon tetrachloride injured mice by lowering alanine aminotransferase (ALT) and aspartate aminotransferase (AST) and restoring the balance of antioxidants in liver tissue.[153] Meanwhile, polydatin (6.25, 12.5 and 25 μg/ml) reduced the expression of genes related to alcohol and lipid metabolism and inhibited oxidative stress in the liver. Notably, it significantly upregulated the expression of DNA damage-related genes to reduce hepatocyte apoptosis,[154] and attenuate nonalcoholic fatty liver disease (30 or 90 mg/kg) by reducing the expression of SREBP-1c and genes involved in adipogenesis, including fatty acid synthase (FAS) and stearoyl-CoA desaturase 1 (SCD1),.[155] TSG (100 or 300 mg/kg) significantly reduced CCl_4-induced liver injury in rats by inhibiting Smad and ERK signal pathways,[156] which also protected the liver from injury by inducing hepatic autophagic cell death by activating PI3K/Akt and Erk pathways (100 or 200 mg/kg).[157]

Anti-bacterial

Emodin (10 μg/ml) significantly inhibited the growth and infection of Vibrio traumaticus and the combination with other antibiotics may help patients to treat Vibrio traumaticus sepsis.[158] Resveratrol was found to have a minimum inhibitory concentration (MIC) of 50 μg/ml against *Mycobacterium avium* wax,[159] the MIC against *Mycobacterium pubescens* was 64 μg/ml,[160] *H. pylori* was 25 μg/ml,[161] *Vibrio cholerae* was 60 μg/ml,[162] *Campylobacter coli* was 50 μg/ml,[163] and Lactic acid bacteria was 50 μg/ml.[164]

Anti-fungal

Emodin inhibited phosphorylation induced by the protein kinase CK2 and showed resistance to Candida with MIC and minimal fungicidal concentration (MFC) values between 12.5 and 200 μg/ml. Notably, even at low concentrations, it was effective in preventing the formation of mycelium.[165] Resveratrol had a toxic effect on dormant gray mold conidia.[166] The inhibitory activity of resveratrol against *Trichophyton rubrum*, *Trichophyton flocculentum* epidermidis, and *Microsporum gypsum* was about 25–50 μg/ml,[167] against *Candida albicans*, *Saccharomyces cerevisiae* and *Serratia marcescens* was 10–20 μg/ml.[168]

Hyperglycemia

Proanthocyanidins isolated from *R. multiflora* were found to display potent α-amylase and moderate α-glucosidase inhibitory activity with an acarbose equivalence (AE) value of 1,954.7 μmol AE/g and 211.1 μmol AE/g, respectively.[169] *Cis*-TSG was more effective than *trans*-TSG in terms of hypoglycemic effect and improvement of glucose intolerance and insulin resistance. In HepG2 cells, *cis*-THSG also showed stronger Phosphoenolpyruvate carboxykinase (PEPCK) transcriptional repression to reduce blood glucose than *trans*-THSG.[170]

Obesity

R. *multiflora* extract (0.46 mg/ml) had a strong inhibitory effect on fatty acid synthase FAS can be used to prevent obesity.[171] Meanwhile, *R. multiflora* root ethanol extract (5 or 10 μg/ml) prevented obesity by inhibiting adipocyte differentiation in 3T3-L1 cells and stimulating the expression of genes for lipolysis and fatty acid oxidation and brown fat-specific genes in white adipose tissue.[172]

Bone protection

TSG (10^{-3}, $10^{-4}$and 10^{-5} mg/ml) treated osteoporosis by activating the PI3K/Akt pathway, which promotes proliferation and differentiation of MC3T3-E1 cells.[173] Similarly, *trans*-resveratrol (0.7 mg/kg) increased epiphyseal bone density and inhibited the decrease of bone calcium content in bilateral ovariectomies (OVX) rats, which had a protective effect against estrogen deficiency-induced bone loss.[174]

Promotes hair growth

In vitro, *R. multiflora* extract (10 or 100 μg/ml) could promote hair growth by prolonging the initial phase of hair growth and activating follicle stem cells to delay hair degeneration.[175] It was found that *R. multiflora* water extract (0.01 mg/ml) was able to reduce the accumulation of ROS in cells, protect cells from hydrogen peroxide and improve pigmentation of isolated human hair follicles.[176] Studies showed that fermented water extract of *R. multiflora* leaves (4.7 mg/12 cm^2) could

induce hair growth in resting hair follicles by upregulating Shh and β-catenin expression.[177] Meanwhile, TSG (200 μM) had a good hair regrowth effect on hair loss, which may be achieved by inhibiting p53, Fas, and Bcl2-Associated X (Bax)-induced apoptosis.[178]

Toxicity

Chrysophanol-8-*O*-glucoside had strong hepatotoxicity which can increase LDH leakage and ROS, and decrease GSH and MMP in L-02 hepatocytes.[179] In vitro neurotoxicity experiments showed that *R. japonica* water extract (300 and 400 μg/ml) had general toxicity and neurotoxicity on hippocampal neurons and astrocyte cells, respectively.[180] Experimental evidence indicated that in the setting of hepatic immune activation, *cis*-2,3,5,4′-tetrahydroxystilbene-2-*O*-β-D-glucoside was a key factor in the pathogenesis of the idiosyncratic hepatotoxicity of *R. multiflora*.[181] In addition, Aloe-emodin could cause zebrafish liver lesions by increasing the mRNA and protein expression levels of pro-inflammatory and pro-apoptotic targets in NF-κB and P53 pathways and pathological sections.[182] All the pharmacological effects of this genus are summarized in Supplementary Table S1.

Discussion and Further Perceptives

This review summarized current research development regarding the traditional uses, phytochemistry and pharmacology of genus *Reynoutria*. More than 277 compounds have been isolated and identified from this genus. Meanwhile, modern pharmacological research revealed *Reynoutria* plants have significant pharmacological properties including anti-cancer, anti-atherosclerotic, anti-inflammatory and neuroprotective. Regardless, there are still several aspects that need to be concerned about the further development of the genus *Reynoutria*.

First, *Fallopia multiflora* and *Fallopia multiflora* var. *ciliinerve* have been now reclassified as a member of the genus *Reynoutria*, just as *R. japonica* was divided from the genus *Fallopia* to the genus *Reynoutria*. Now, they were formally called *Reynoutria multiflora* (thumb.) Moldenke and *Reynoutria ciliinervis* (Nakai) Moldenke, respectively. However, in Asian countries such as China, they are still regarded as *Fallopia* plants, which is urgent to be corrected.

Second, the current phytochemical studies on the genus *Reynoutria* focus on *R. multiflora* and *R. japonica*. Other *Reynoutria* plants are regarded as invasive plants in Europe and America, and their phytochemical and biological activities have not yet been comprehensively investigated.

Third, 277 compounds have been reported from genus the *Reynoutria*, including 58 stilbenoids, 51 quinones, 48 flavonoids, 21 phenylpropanoids, 9 phospholipids, 9 lactones, 23 phenolics and phenolic acids, 19 fatty acids, and 39 other compounds. Among them, stilbenoids are the main active compounds, which have a variety of pharmacology activities. 2,3,5,4′-tetrahydroxystilbene-2-*O*-β-D-glucoside showed excellent activity in anti-aging, anti-inflammatory, hepatoprotective and free radical scavenging.[183] Resveratrol has significant anti-infective, antiviral, and cardiovascular protective effects.[184] More stilbenoids with various activities need to be found in this genus. Of course, it cannot be ignored that monomeric compounds with outstanding pharmacological activities can be considered the source of new drugs with excellent therapeutic effects.

Finally, *Reynoutria* plants were widely used in the treatment of chronic hepatopathy, but it was noteworthy that they were reported to have hepatotoxicity as well. For instance, pang et al found that the high dosage of *R. multiflora* had either an injuring effect on normal rats or a therapeutic effect on the rats with chronic liver injury.[185] Therefore, it is still necessary to further study the material basis and mechanism of hepatotoxicity to provide a scientific basis for clinical medication.

Conclusion

Reynoutria is a genus in the family Polygonaceae, many species of which have been used in traditional Chinese medicines or folk medicines to treat various diseases. This review summarized all the compounds of genus *Reynoutria*, including stilbenoids, quinones, flavonoids and so on. Stilbenoids and quinones were generally considered major bioactive ingredients in *Reynoutria*, exhibiting various important qualities. In addition, pharmacological studies showed that compounds and extracts isolated from *Reynoutria* plants possess a wide range of pharmacological activities, such as anti-cancer, anti-atherosclerotic, anti-inflammatory and neuroprotective. In short, as a source of traditional folk medicine, *Reynoutria* plants are widely used in medicine. Therefore, we believe it's necessary to review this genus, which will help to gain a greater understanding and appreciation of genus *Reynoutria*.

Supplementary Material

Supplementary data are available at *Journal of Pharmacy and Pharmacology* online.

Author Contributions

All the authors have accepted responsibility for the entire content of this submitted manuscript and approved submission.

Funding

This work is supported by a program project for Shaanxi Province (grant number 2022SF-254; 2019ZDLSF04-03-02); Subject Innovation Team of Shaanxi University of Chinese Medicine (grant number 2019-YL12) and the Natural Science Basic Research Project of Department of science and technology of Shaanxi Province (grant number: 2021JQ-744).

Conflict of Interest

The authors declare that there is no conflict of interest.

Data Availability

The underlying data supporting the study are available within the article.

References

1. Wang H-J, Yang L-Y, Zhou B et al. Advances in chemical constituents and pharmacological effects of *Polygonum multiflora*. *Chin J Exp Med Form* 2019; 25: 192–205.

2. Chen W-S, Liu W-Y, Yang G-J et al. The structure and cardiovascular activity of a new tetrahydroxystilbene glycoside from *Polygonum* multiflora. *Chin J Pharmaceutical Sci* 2000; 35: 906–8. https://doi.org/10.16438/j.0513-4870.2000.12.007
3. Zhang J-X, Cui Y-M. Study on the chemical composition of Chinese medicine *Fallopia multiflora*. *Chin J Chin Mater Med* 2016; 41: 3252–5.
4. Zhao H-N, Chen L-L, Huang X-J et al. A new chromogenic ketone glycoside from *Fallopia multiflora*. *Chin J Chin Mater Med* 2014; 39: 1441–4.
5. Li MJ, Wang H-S, Wang T-B et al. Effects of rhodopsin in prepared *Fallopia multiflora* on JAK2/STAT3 pathway in ApoE–/– mice atherosclerosis model. *Chin J Exp Tradit Med Form* 2018; 24: 109–14.
6. Cao X-H. *Study on Chemical Composition and its Biological Activity of Fallopia multiflora var. Ciliinervis*. Shaanxi University of Science and Technology [Dissertation]; 2018.
7. Büchter C, Liang Z, Havermann S et al. TSG (2,3,5,4′-tetrahydroxystilbene-2-O-β-D-glucoside) from the Chinese herb *Polygonum multiflora* increases life span and stress resistance of *Caenorhabditis elegans*. *Oxid Med Cell Longev* 2015; 2015: 124357–71. https://doi.org/10.1155/2015/124357
8. Choi S-G, Kim J, Sung N-D et al. Anthraquinones, Cdc25B phosphatase inhibitors, isolated from the roots of *Polygonum multiflora* Thunb. *Nat Prod Res* 2007; 21: 487–99. https://doi.org/10.1080/14786410601012265
9. Li X, Li Y, Chen J et al. Tetrahydroxystilbene glucoside attenuates MPP+-induced apoptosis in PC12 cells by inhibiting ROS generation and modulating JNK activation. *Neurosci Lett* 2010; 483: 1–5. https://doi.org/10.1016/j.neulet.2010.07.027
10. Ho T-Y, Wu S-L, Chen J-C et al. Emodin blocks the SARS coronavirus spike protein and angiotensin-converting enzyme 2 interaction. *Antiviral Res* 2007; 74: 92–101. https://doi.org/10.1016/j.antiviral.2006.04.014
11. Xu X-L, Zhu Q-Y, Zhao C et al. The effect of 2,3,4',5-tetrahydroxystilbene-2-*O*-*β*-D-glucoside on pressure overload-induced cardiac remodeling in rats and its possible mechanism. *Planta Med* 2014; 80: 130–8. https://doi.org/10.1055/s-0033-1360198
12. Han M-N, Lu J-M, Zhang G-Y et al. Mechanistic studies on the use of *Polygonum multiflora* for the treatment of hair graying. *Biomed Res Int* 2015; 19: 647–55. https://doi.org/10.1155/2015/651048
13. Schuster TM, Wilson KL, Kron KA. Phylogenetic relationships of Muehlenbeckia, Fallopia, and Reynoutria (Polygonaceae) investigated with chloroplast and nuclear sequence data. *Int J Plant Sci* 2011; 172: 1053–66. https://doi.org/10.1086/661293
14. Stalažs A. The first findings of invasive Reynoutria ×bohemica Chrtek & Chrtková (Polygonaceae) in Latvia. *Botany Lett* 2022; 1: 119–26. https://doi.org/10.1080/23818107.2021.1981438
15. Liu L. *Study on Medicinal History of Polygonum multiflora* [Dissertation]. Heilongjiang University of Chinese Medicine; 2020.
16. Peng W, Qin R, Li X et al. Botany, phytochemistry, pharmacology, and potential application of *Polygonum cuspidatum* Sieb. et Zucc.: a review. *J Ethnopharmacol* 2013; 3: 729–45. https://doi.org/10.1016/j.jep.2013.05.007
17. Li M-C, Fu Y-X, Zhang X-Y et al. Research progress on chemical constituents and pharmacological activities of *Polygonum multiflora* stems. *Yunnan J Trad Chin Med* 2018; 39: 81–4.
18. Wang Y-P, Wang Q-Y, Wang Y-Y. Summarization of medicinal plants of Polygonum in China. *Lishizhen Med Mater Med Res* 1996; 3: 47–8.
19. Liu X-J, Zhang EH, Guo H-L. Research overview of zhu shaqi. *J Shaanxi Univ Chin Med* 2003; 3: 62–3.
20. Editorial Board of Herbal China of National Administration of Traditional Chinese Medicine. *Chinese Materia Medica*. Shanghai:Shanghai Scientific & Technical Publishers,1998. p.2531–2532.
21. Hata K, Kozawa M, Baba K. A new stilbene glucoside from Chinese crude drug "Heshouwu" the roots of *Polygonum multiflora* thunb. *Yakugaku Zasshi* 1975; 95: 211–3. https://doi.org/10.1248/yakushi1947.95.2_211
22. Yuan W. *Research on the Chemical Composition of Fallopia multiflora* [Dissertation]. Beijing University of Chinese Medicine; 2017.
23. Sun Y-N, Li W, Kim J-H et al. Chemical constituents from the root of *Polygonum multiflora* and their soluble epoxide hydrolase inhibitory activity. *Arch Pharm Res* 2015; 38: 998–1004. https://doi.org/10.1007/s12272-014-0520-4
24. Zhou L-X, Lin M, Li J-B. Study on the chemical composition of the insoluble fraction of glycolic acid of *Fallopia multiflora*. *J Pharm Sci-US* 1994; 29: 107–10.
25. Li S-G, Chen L-L, Huang X-J et al. Five new stilbene glycosides from the roots of *Polygonum multiflora*. *J Asian Nat Prod Res* 2013; 15: 1145–51. https://doi.org/10.1080/10286020.2013.837454
26. Chen W-S, Yang G-J, Zhang W-D. Two new compounds from *Polygonum multiflora*. *J Pharmaceutical Sci* 2000; 35: 273–6. https://doi.org/10.16438/j.0513-4870.2000.04.009
27. Kim H-K, Choi Y-H, Choi J-S et al. A new stilbene glucoside gallate from the roots of *Polygonum multiflora*. *Arch Pharm Res* 2008; 31: 1225–9. https://doi.org/10.1007/s12272-001-2100-7
28. Chen W-S, Zhang W-D, Yang G-J. Two new glucosides from radix *Polygonum multiflora* preparata. *Chin Chem Lett* 2001; 12: 503–6.
29. Zhang J-X. *Study on Neuroprotective Active Components of Fallopia multiflora* [Dissertation]. Peking Union Medical College;2016.
30. Xiao K, Xuan L-J, Xu Y-M et al. Novel stilbene glycosides from *Polygonum multiflora*. *Acta Bot Sin* 2002; 44: 1491–4.
31. Yuan W, Gao Z-P, Yang J-B et al. Study on the chemical composition of *Fallopia multiflora*. *Chin Tradit Herbal Drugs* 2017; 48: 631–4.
32. Qi H-Y, Zhang C-F, Zhang M et al. Studies on ingredients and antifungal activity of *Polygonum multiflora* var. ciliinervis. *Chin Pharmaceutical J* 2005; 40: 819–22.
33. Hua Y, Zhou J-Y, Ni W et al. Study on chemical constituents of *Polygonum cuspidatum* [J]. *Nat Prod Res Dev.* 2001; 13: 16–8. https://doi.org/10.16333/j.1001-6880.2001.06.005
34. Luo Y-Y, Liu X-J, Liu T et al. Simultaneous determination of stilbene, anthraquinone, flavonoids, and phenolic acids in Radix et *Polygonum multiflora* by UPLC-MS/MS. *J Mass Spectrom* 2016; 37: 327–35.
35. Hegde VR, Pu H, Patel M et al. Two new bacterial DNA primase inhibitors from the plant *Polygonum cuspidatum*. *Bioorg Med Chem Lett* 2004; 9: 2275–7. https://doi.org/10.1016/j.bmcl.2004.02.006
36. Rao G-X, Xue Y-M, Hui T-T et al. Study on the chemical composition of *Polygonum multiflora* leaves. *Chin Med Mat* 2009; 32: 891–3.
37. Liu M, Li X, Liu Q et al. Preparative isolation and purification of 12 main antioxidants from the roots of *Polygonum multiflora* Thunb. using high-speed countercurrent chromatography and preparative HPLC guided by 1,1′-diphenyl-2-picrylhydrazyl-HPLC. *J Sep Sci* 2020; 43: 1415–22. https://doi.org/10.1002/jssc.201901287
38. Fan P, Hostettmann K, Lou H. Allelochemicals of the invasive neophyte *Polygonum cuspidatum* Sieb. & Zucc. (Polygonaceae). *Chemoecology* 2010; 20: 223–7. https://doi.org/10.1007/s00049-010-0052-4
39. Xiao K, Xuan L, Xu Y et al. Stilbene glycoside sulfates from *Polygonum cuspidatum*. *J Nat Prod* 2000; 10: 1373–6. https://doi.org/10.1021/np000086+
40. Grech J-N, Li Q, Roufogalis B-D et al. Novel Ca2+-ATPase inhibitors from the dried root tubers of *Polygonum multiflora*. *J Nat Prod* 1994; 57: 1682–7. https://doi.org/10.1021/np50114a010
41. Li S-G, Huang X-J, Li M-M et al. Multifloraisides A-G, dimeric stilbene glucosides with rare coupling patterns from the roots of *Polygonum multiflora* multifloraisides A-G, dimeric stilbene glucosides with rare coupling patterns from the roots of *Polygonum multiflora*. *J Nat Prod* 2018; 81: 254–63. https://doi.org/10.1021/acs.jnatprod.7b00540

42. Yang J-B et al. Multifloraisides HK, stilbene glucosides isolated from *Polygonum multiflora* and their in vitro PTP1B inhibitory activities. *Fitoterapia* 2020; 146: 104703. https://doi.org/10.1016/j.fitote.2020.104703
43. Yan S-L, Su Y-F, Chen L et al. Polygonumosides A-D, stilbene derivatives from processed roots of *Polygonum multiflora*. *J Nat Prod* 2014; 77: 397–401. https://doi.org/10.1021/np400720y
44. Yang J-B, Tian J-Y, Dai Z et al. α-Glucosidase inhibitors extracted from the roots of *Polygonum multiflora* Thunb. *Fitoterapia* 2017; 117: 65–70. https://doi.org/10.1016/j.fitote.2016.11.009
45. Chen L-L, Huang X-J, Li M-M et al. Polygonflavanol A, a novel flavonostilbene glycoside from the roots of *Polygonum multiflora*. *Phytochem Lett* 2012; 5: 756–60. https://doi.org/10.1016/j.phytol.2012.08.007
46. Zhang Z, Li Y, Cheng Q et al. Chemical constituents from the roots of *Fallopia multiflora* var. Ciliinerve. *Biochem Syst Ecol* 2021; 99: 104340. https://doi.org/10.1016/j.bse.2021.104340
47. Sa L-L. *Studies on Chemical Constituents and Quality of Polygonum cuspidatum* [Dissertation]. Shenyang: Shenyang Pharmaceutical University, 2003.
48. Zhang F-J, Zhai J-T, Wang Q. Effect of processing time on quality control of *Polygonum multiflora*. *Liaoning J Tradit Chin Med* 2018; 45: 574–6.
49. Feng J, Ren H, Gou Q et al. Comparative analysis of the major constituents in three related polygonaceous medicinal plants using pressurized liquid extraction and HPLC-ESI/MS. *Anal Methods* 2016; 8: 1557–64. http:/doi.org/10.1039/C5AY02941D
50. Li X-E, Liu J-Z, Liao ST et al. Chemical constituents from tubers of *Polygonum multiflora* Thunb. *J Trop Subtropical Botany* 2009; 17: 617–20.
51. Eom M-R, Weon J-B, Jung Y-S et al. Neuroprotective compounds from Reynoutria sachalinensis. *Arch Pharm Res* 2017; 6: 704–12. https://doi.org/10.1007/s12272-017-0918-x
52. Zhang Z-G, Lv T-S, Yao Q-Q. Study on the anthraquinone chemical composition of *Fallopia multiflora*. *Chin Tradit Herbal Drugs* 2006; 37: 1311–3.
53. Lo Y-H, Chen Y-J, Chung T-Y et al. Emoghrelin, a unique emodin derivative in Heshouwu, stimulates growth hormone secretion via activation of the ghrelin receptor. *J Ethnopharmacol* 2015; 159: 1–8. https://doi.org/10.1016/j.jep.2014.10.063
54. Yang X-W, Gu Z-M, Ma C-M. A new indole derivative isolated from the root of tuber fleece flower (*Polygonum multiflora*). *Chin Tradit Herbal Drugs* 1998; 1: 5–11.
55. Chen W-S, Fan W, Yang G-J. Study on the chemical composition of *Polygonum multiflora*. *J Second Mil Med Univ* 1999; 20: 438–40.
56. Liu X-Q, Yu L-M, Wu L-J. Studies on chemical constituents of *Polygonum cuspidatum* (I). *Chin J Chin Mater Med* 2003; 28: 47–9.
57. Liu Z-L, Li L-F, Chao Z-M. Study on the chemical composition of *Fallopia multiflora* after concoction. *Nat Prod Res Develop* 2009; 21: 239–41.
58. Kimura Y, Kozawa M, Baba K et al. New constitutents of roots of *Polygonum cuspidatum*. *Planta Med* 1983; 48: 164–8. https://doi.org/10.1055/s-2007-969914
59. Tai W, Wei Y, Zhang H-L et al. Study of anthraquinone components and sodium rhodopsin 7-sulfonate in Zhushaqi. *Chin Tradit Herbal Drugs* 1987; 18: 44.
60. Kwon B-M, Kim S-H, Baek N-I et al. Farnesyl protein transferase inhibitory components of *Polygonum multiflora*. *Arch Pharm Res* 2009; 32: 495–9. https://doi.org/10.1007/s12272-009-1403-y
61. Sun Y-N, Cui L, Li W et al. Promotion effect of constituents from the root of *Polygonum multiflora* on hair growth. *Bioorg Med Chem Lett* 2013; 23: 4801–5. https://doi.org/10.1016/j.bmcl.2013.06.098
62. Wang W-J, Zhang W-M, Dong X-L et al. Study on the chemical composition of *Fallopia multiflora* herbs from Yunnan. *J Yunnan College of Tradit Chin Med* 2005; 1: 10–2.
63. Sun Y-S, Wang J-H. Study on chemical constituents from flowers of *Polygonum cuspidatum*. *Chin Tradit Herbal Drugs* 2015; 46: 2219–22.
64. Zhang Z-G, Lv T-S, Yao Q-Q. Research progress of *Polygonum multiflora*. *Pharm J Chin PLA* 2008; 24: 62–64 + 98.
65. Zhang H, Zhang QW, Wang L et al. Two new anthraquinone malonylglucosides from *Polygonum cuspidatum*. *Nat Prod Res* 2012; 26: 1323–7. https://doi.org/10.1080/14786419.2011.578072
66. Ma P. *Pharmacognosy of Polygonum cuspidatum* [Dissertation]. Beijing: Peking Union Medical College, 2013.
67. Li J-B, Lin M. Studies on the chemical composition of *Fallopia multiflora*. *Chin Tradit Herbal Drugs* 1993; 24: 115–118 + 166.
68. Jin X-M, Jin G-Z. Chemical constituents of *Polygonum cuspidatum*. *Chin Tradit Herbal Drugs* 2007; 38: 1446–8.
69. Liang C-X, Wang S-S, Chen S-J et al. Research progress on chemical constituents and pharmacological activities of *Polygonum cuspidatum*. *Chin Tradit Herbal Drugs* 2022; 53: 1264–76.
70. Yang J, Yan Z, Ren J. Polygonumnolides A1-B3, minor dianthrone derivatives from the roots of *Polygonum multiflora* Thunb. *Arch Pharm Res* 2018; 41: 617–24. https://doi.org/10.1007/s12272-016-0816-7
71. Yang J-B, Li L, Dai Z. Polygonumnolides C1-C4; minor dianthrone glycosides from the roots of *Polygonum multiflora* Thunb. *J Asian Nat Prod Res* 2016; 18: 813–22. https://doi.org/10.1080/10286020.2016.1171758
72. Sun. W-L. *Study on the Chemical Composition of the Chinese Herbal Medicine, Ye Jiaoteng* [Dissertation]. YunnanUniversity of Chinese Medine; 2018.
73. Xu Y-L, Dong Q, Hu F-Z. Simultaneous quantitative determination of eight active components in *Polygonum multiflora* Thunb by RP-HPLC. *J Chin Pharmaceutical Sci* 2009; 18: 358–61.
74. Yoshizaki M, Fujino H, Arise A et al. Polygoacetophenoside, a new acetophenone glucoside from *Polygonum multiflora*. *Planta Med* 1987; 53: 273–5. https://doi.org/10.1055/s-2006-962703
75. Zhou L, Li J-X, Yu Y. UPLC-MS/MS method was used to determine the content of catechins in *Polygonum multiflora* from different habitats. *Chin Med Mat* 2018; 41: 1582–5.
76. Bensa M, Glavnik V, Vovk I. Leaves of invasive plants—Japanese, Bohemian and Giant Knotweed—the promising new source of flavan-3-ols and Proanthocyanidins. *Plants* 2020; 9: 118. https://doi.org/10.3390/plants9010118
77. Xiao K, Xuan LJ, Xu YM et al. Constituents from *Polygonum cuspidatum*. *Chem Pharm Bull* 2002; 50: 605–8. https://doi.org/10.1248/cpb.50.605
78. Wang H, Song L, Feng S et al. Characterization of proanthocyanidins in stems of *Polygonum multiflora* Thunb as strong starch hydrolase inhibitors. *Molecules* 2013; 18: 2255–65. https://doi.org/10.3390/molecules18022255
79. Nonaka G-I, Miwa N, Nishioka I. Stilbene glycoside gallates and proanthocyanidins from *Polygonum multiflora*. *Phytochem* 1982; 21: 429–32. https://doi.org/10.1016/s0031-9422(00)95282-8
80. Nawrot-Hadzik I, Choromańska A, Abel R et al. Cytotoxic effect of vanicosides A and B from *Reynoutria sachalinensis* against melanotic and amelanotic melanoma cell lines and in silico evaluation for inhibition of BRAFV600E and MEK1. *Int J Mol Sci* 2020; 21: 4611. https://doi.org/10.3390/ijms21134611
81. Jiang JS, Li FS, Feng ZM et al. New phenolic glycosides from *Polygonum cuspidatum*. *J Asian Nat Prod Res* 2020; 22: 17–23. https://doi.org/10.1080/10286020.2019.1646730
82. Gao S-H, Su Z-Z, Xiao X-F. Research progress on chemical composition and pharmacological effects of *Polygonum multiflora*. *J Shanxi Coll of Tradit Chin Med* 2012; 13: 74–7.
83. Xu Y-M, Ren R-N. Analysis of phospholipid composition in *Fallopia multiflora*. *J Pharmaceutical Anal* 1990; 10: 105–7.
84. Cai CQ, Luo YY, Liu XH et al. Simultaneous determination of six phospholipids in *Fallopia multiflora* by HPLC-ELSD. *Chin J New Drugs* 2018; 27: 1417–22.
85. Chen W-S, Zhang W-D, Qiao C-Z. Analysis of low-polarity oleaginous constituents of *Polygonum multiflora*. *Chin Med Mat* 2000; 11: 684–5.
86. Park S-Y, Jin M-L, Kang N-J et al. Anti-inflammatory effects of novel *polygonum multiflora* compound via inhibiting NF-κB/

MAPK and upregulating the Nrf2 pathways in LPS-stimulated microglia. *Neurosci Lett* 2017; 651: 43–51. https://doi.org/10.1016/j.neulet.2017.04.057
87. Chen W-S, Yang G-J, Zhang W-D. A new aliphatic ketone from the preparation of *Polygonum multiflora*. *Chin J Chin Mater Med* 2000; 25: 476–7.
88. Yao W, Gu C, Shao H et al. Tetrahydroxystilbene glucoside improves TNF-α-induced endothelial dysfunction: involvement of TGF-β/Smad pathway and inhibition of vimentin expression. *Am J Chin Med* 2015; 43: 183–98. https://doi.org/10.1142/s0192415x15500123
89. Yang J-B, Gao H-Y, Wang X-T et al. One new lignanamide compound in polygonum multiflorum. *Chin Tradit Herbal Drugs* 2021; 52: 5475–82.
90 Zhao J, Xu S-Z, Song F et al. 2,3,5,4′-tetrahydroxystilbene-2-O-β-D-glucoside protects human umbilical vein endothelial cells against lysophosphatidylcholine-induced apoptosis by upregulating superoxide dismutase and glutathione peroxidase. *IUBMB Life* 2015; 66: 711–22. https://doi.org/10.1002/iub.1321
91 Zhao J, Xu S-Z, Song F et al. Role of stilbene glycosides in regulating ROS-related JNK pathway on LPC-induced injury in HUVECs. *Chin Tradit Pat Med* 2015; 37: 487–92.
92 Zhang L, Rui Y-C, Qiu Y et al. Expression of VEGF in endothelial cells and the effects of 2,3,5,4′-tetrahydroxystilbene-2-*O*-beta-D-glucoside. *Acta Pharm Sin*. 2004; 39: 406–9.
93 Xu X-L, Huang Y-J, Chen X-F et al. 2,3,4',5-tetrahydroxystilbene-2-O-β-D-glucoside inhibits proliferation of vascular smooth muscle cells: involvement of NO/cGMP/PKG pathway. *Phytother Res* 2012; 26: 1068–74. https://doi.org/10.1002/ptr.3691
94 Dong Q, Xing W, Fu F et al. Tetrahydroxystilbene glucoside inhibits excessive autophagy and improves microvascular endothelial dysfunction in prehypertensive spontaneously hypertensive rats. *Am J Chin Med* 2016; 44: 7–20. https://doi.org/10.1142/s0192415x16500786
95 Zhang W, Xu X-L, Wang Y-Q et al. Effects of 2,3,4′,5-tetrahydroxystilbene-2-O-β-D-glucoside on vascular endothelial dysfunction in atherogenic-diet rats. *Planta Med* 2009; 75: 1209–14. https://doi.org/10.1055/s-0029-1185540
96 Li M-J, Wang H-S, Wang T-B et al. Effect of emodin from Polygoni Multiflori Radix on JAK2/STAT3 pathway in ApoE (–/–) mouse atherosclerosis model. *Chin J Exp Tradit Med Form* 2018; 24: 101–6. https://doi.org/10.13422/j.cnki.syfjx.20181823
97 Xian Z, Yan L, Xu W-J et al. The anti-hyperlipidemia effects of raw *Polygonum multiflora* extract in vivo. *Biol Pharm Bull* 2017; 40: 1839–45. https://doi.org/10.1248/bpb.b17-00218
98 Xing W-W, Wu J-Z, Jia M et al. Effects of polydatin from *Polygonum cuspidatum* on lipid profile in hyperlipidemic rabbits. *Biomed Pharmacother* 2009; 63: 457–62. https://doi.org/10.1016/j.biopha.2008.06.035
99 Du J, Sun L-N, Xing W-W et al. Lipid-lowering effects of polydatin from *Polygonum cuspidatum* in hyperlipidemic hamsters. *Phytomedicine* 2009; 16: 652–8. https://doi.org/10.1016/j.phymed.2008.10.001
100 Huang C, Wang Y, Wang J et al. TSG (2,3,4′,5-tetrahydroxystilbene-2-O-β-D-glucoside) suppresses induction of pro-inflammatory factors by attenuating the binding activity of nuclear factor-κB in microglia. *J Neuroinflammation* 2013; 10: 129. https://doi.org/10.1186/1742-2094-10-129
101 Shen M-Y, Liu Y-J, Don M-J et al. Combined phytochemistry and chemotaxis assays for identification and mechanistic analysis of anti-inflammatory phytochemicals in Fallopia japonica. *PLoS One* 2011; 6: e27480. https://doi.org/10.1371/journal.pone.0027480
102 Li HL, Chen HL, Li H et al. Regulatory effects of emodin on NF-kappaB activation and inflammatory cytokine expression in RAW 264.7 macrophages. *Int J Mol Med* 2005; 16: 41–7. https://doi.org/10.3892/ijmm.16.1.41
103 Park B, Jo K, Lee T-G et al. Polydatin inhibits NLRP3 inflammasome in dry eye disease by attenuating oxidative stress and inhibiting the NF-κB pathway. *Nutrients* 2019; 11: 2792. https://doi.org/10.3390/nu11112792
104 Zeng C, Xiao J-H, Chang M-J et al. Beneficial effects of THSG on acetic acid-induced experimental colitis: involvement of upregulation of PPAR-γ and inhibition of the NF-κB inflammatory pathway. *Molecules* 2011; 16: 8552–68. https://doi.org/10.3390/molecules16108552
105 Gao W-Y, Wang C-H, Yu L et al. Chlorogenic acid attenuates dextran sodium sulfate-induced ulcerative colitis in mice through MAPK/ERK/JNK pathway. *Biomed Res Int* 2019; 2019: 6769789. https://doi.org/10.1155/2019/6769789
106 Lv L-X. In vitro antioxidant study of stilbene glucosides in Radix *Polygonum multiflora*. *Food Sci* 2007; 1: 313–7.
107 Wang H-L, Gao J-P, Han Y-L et al. Comparative studies of polydatin and resveratrol on mutual transformation and antioxidative effect in vivo. *Phytomedicine* 2015; 22: 553–9. https://doi.org/10.1016/j.phymed.2015.03.014
108 Zhu W, Xue X, Zhang Z. Structural, physicochemical, antioxidant and antitumor property of an acidic polysaccharide from *Polygonum multiflora*. *Int J Biol Macromol* 2017; 96: 494–500. https://doi.org/10.1016/j.ijbiomac.2016.12.064
109 Chen L, Zhang Y, Jin L et al. Preparation, characterization and antioxidant activity of polysaccharide from *Fallopia multiflora* (Thunb.) Harald. *Int J Biol Macromol* 2018; 108: 259–62. https://doi.org/10.1016/j.ijbiomac.2017.12.020
110 Kim Y-J, Lee J-Y, Kim H-J et al. Inhibitory effect of emodin on raw 264.7 activated with double stranded RNA analogue poly i:c. *Afr J Tradit Complement Altern Med* 2017; 14: 157–66. https://doi.org/10.21010/ajtcam.v14i3.17
111 Choi S-G, Kim J, Sung N-D et al. Anthraquinones, Cdc25B phosphatase inhibitors, isolated from the roots of *Polygonum multiflora* Thunb. *Nat Prod Res* 2007; 21: 487–93. https://doi.org/10.1080/14786410601012265
112 Wu L, Cao K, Ni Z et al. Rhein reverses doxorubicin resistance in SMMC-7721 liver cancer cells by inhibiting energy metabolism and inducing mitochondrial permeability transition pore opening. *Biofactors* 2019; 45: 85–96. https://doi.org/10.1002/biof.1462
113 Li H, Shi B, Li Y et al. Polydatin inhibits cell proliferation and induces apoptosis in laryngeal cancer and HeLa cells via suppression of the PDGF/AKT signal pathway. *J Biochem Mol Toxicology.* 2017; 31: 2017. https://doi.org/10.1002/jbt.21900
114 Lee M-S, Cha E-Y, Sul J-Y et al. Chrysophanic acid blocks proliferation of colon cancer cells by inhibiting EGFR/mTOR pathway. *Phytother Res* 2011; 25: 833–7. https://doi.org/10.1002/ptr.3323
115 Chen H-S, Liu Y, Lin L-Q et al. Anti-proliferative effect of an extract of the root of *Polygonum multiflora* Thunb. on MCF-7 human breast cancer cells and the possible mechanisms. *Mol Med Rep* 2011; 4: 1313–9. https://doi.org/10.3892/mmr.2011.574
116 Sun FL, Zhang L, Zhang RY et al. Tetrahydroxystilbene glucoside protects human neuroblastoma SH-SY5Y cells against MPP+-induced cytotoxicity. *Eur J Pharmacol* 2011; 660: 283–90. https://doi.org/10.1016/j.ejphar.2011.03.046
117 Yang X-P, Liu T-Y, Qin X-Y et al. Potential protection of 2,3,5,4'-tetrahydroxystilbene-2-O-β-D-glucoside against staurosporine-induced toxicity on cultured rat hippocampus neurons. *Neurosci Lett* 2014; 576: 79–83. https://doi.org/10.1016/j.neulet.2014.05.045
118 Tao L, Li X, Zhang L et al. Protective effect of tetrahydroxystilbene glucoside on 6-OHDA-induced apoptosis in PC12 cells through the ROS-NO pathway. *PLoS One* 2011; 6: e26055. https://doi.org/10.1371/journal.pone.0026055
119 Lee S-Y, Ahn S-M, Wang Z et al. Neuroprotective effects of 2,3,5,4′-tetrahydoxystilbene-2-O-β-D-glucoside from *Polygonum multiflora* against glutamate-induced oxidative toxicity in HT22 cells. *J Ethnopharmacol* 2017; 195: 64–70. https://doi.org/10.1016/j.jep.2016.12.001
120 Jang J-Y, Kim H-N, Kim Y-R et al. Hexane extract from *Polygonum multiflora* attenuates glutamate-induced apoptosis in primary

cultured cortical neurons. *J Ethnopharmacol* 2013; 145: 261–8. https://doi.org/10.1016/j.jep.2012.10.061
121 Ahn S-M, Yu R-K, Kim H-N et al. Beneficial effects of *Polygonum multiflora* on hippocampal neuronal cells and mouse focal cerebral ischemia. *Am J Chin Med* 2015; 43: 637–51. https://doi.org/10.1142/s0192415x15500391
122 Park S-J, Jin M-L, An H-K et al. Emodin induces neurite outgrowth through PI3K/Akt/GSK-3β-mediated signal pathways in Neuro2a cells. *Neurosci Lett* 2015; 588: 101–7. https://doi.org/10.1016/j.neulet.2015.01.001
123 He Y, Wang F, Chen S et al. The protective effect of radix *Polygonum multiflora* on diabetic encephalopathy via regulating myosin light chain kinase expression. *J Diabetes Res* 2015; 29: 721–9. https://doi.org/10.1155/2015/484721
124 Zhang L, Xing Y, Ye C-F et al. Learning-memory deficit with aging in APP transgenic mice of Alzheimer's disease and intervention by using tetrahydroxystilbene glucoside. *Behav Brain Res* 2006; 173: 246–54. https://doi.org/10.1016/j.bbr.2006.06.034
125 Xu N-G, Xiao Z-J, Zou T et al. Ameliorative effects of physcion 8-*O*-β-glucopyranoside isolated from *Polygonum cuspidatum* on learning and memory in dementia rats induced by Aβ1-40. *Pharm Biol* 2015; 53: 1632–8. https://doi.org/10.3109/13880209.2014.997251
126 Qin R, Li X, Li G et al. Protection by tetrahydroxystilbene glucoside against neurotoxicity induced by MPP+: the involvement of PI3K/Akt pathway activation. *Toxicol Lett* 2011; 202: 1–7. https://doi.org/10.1016/j.toxlet.2011.01.001
127 Yu Y, Lang X-Y, Li X-X et al. 2,3,5,4′-Tetrahydroxystilbene-2-*O*-β-D-glucoside attenuates MPP+/MPTP-induced neurotoxicity in vitro and in vivo by restoring the BDNF-TrkB and FGF2-Akt signaling axis and inhibition of apoptosis. *Food Funct* 2019; 10: 6009–19. https://doi.org/10.1039/c9fo01309a
128 Li X, Matsumoto K, Murakami Y et al. Neuroprotective effects of *Polygonum multiflora* on nigrostriatal dopaminergic degeneration induced by paraquat and maneb in mice. *Pharmacol Biochem Behav* 2005; 82: 345–52. https://doi.org/10.1016/j.pbb.2005.09.004
129 Lee S-V, Choi K-H, Choi Y-W et al. Hexane extracts of *Polygonum multiflora* improve tissue and functional outcome following focal cerebral ischemia in mice. *Mol Med Rep* 2014; 9: 1415–21. https://doi.org/10.3892/mmr.2014.1943
130 Ahn S-M, Kim H-N, Yu R-K et al. Emodin from *Polygonum multiflora* ameliorates oxidative toxicity in HT22 cells and deficits in photothrombotic ischemia. *J Ethnopharmacol* 2016; 188: 13–20. https://doi.org/10.1016/j.jep.2016.04.058
131 Mu Y, Xu Z, Zhou X et al. 2,3,5,4'-tetrahydroxystilbene-2-*O*-β-D-glucoside attenuates ischemia/reperfusion-induced brain injury in rats by promoting angiogenesis. *Planta Med* 2017; 83: 676–83. https://doi.org/10.1055/s-0042-120544
132 Wang T, Gu J, Wu P-F et al. Protection by tetrahydroxystilbene glucoside against cerebral ischemia: involvement of JNK, SIRT1, and NF-κB pathways and inhibition of intracellular ROS/RNS generation. *Free Radic Biol Med* 2009; 47: 229–40. https://doi.org/10.1016/j.freeradbiomed.2009.02.027
133 Yu F, Xue W, Dong L et al. Tetrahydroxystilbene glucoside suppresses NAPDH oxidative stress to mitigate apoptosis and autophagy induced by cerebral ischemia/reperfusion injury in mice. *Evid Based Complement Alternat Med* 2019; 2019: 391–8. https://doi.org/10.1155/2019/3913981
134 Li RP, Wang Z-Z, Sun M-X et al. Polydatin protects learning and memory impairments in a rat model of vascular dementia. *Phytomedicine* 2012; 19: 677–81. https://doi.org/10.1016/j.phymed.2012.03.002
135 Wang T, Yang Y-J, Wu P-F et al. Tetrahydroxystilbene glucoside, a plant-derived cognitive enhancer, promotes hippocampal synaptic plasticity. *Eur J Pharmacol* 2011; 650: 206–14. https://doi.org/10.1016/j.ejphar.2010.10.002
136 Zhou X-X, Yang Q, Xie Y-H et al. Protective effect of tetrahydroxystilbene glucoside against d-galactose induced aging process in mice. *Phytochem Lett* 2013; 6: 372–8. https://doi.org/10.1016/j.phytol.2013.05.002
137 Hou Y, Yang Q, Zhou L et al. Tetrahydroxystilbene glucoside improves learning and (or) memory ability of aged rats and may be connected to the APP pathway. *Can J Physiol Pharmacol* 2011; 89: 801–9. https://doi.org/10.1139/y11-081
138 Liu G-S, Zhang Z-S, Yang B et al. Resveratrol attenuates oxidative damage and ameliorates cognitive impairment in the brain of senescence-accelerated mice. *Life Sci* 2012; 91: 872–7. https://doi.org/10.1016/j.lfs.2012.08.033
139 Yiu C-Y, Chen S-Y, Yang T-H et al. Inhibition of Epstein-Barr virus lytic cycle by an ethyl acetate subfraction separated from *Polygonum cuspidatum* root and its major component, emodin. *Molecules* 2014; 19: 1258–72. https://doi.org/10.3390/molecules19011258
140 Liu Z, Wei F, Chen L-J et al. In vitro and in vivo studies of the inhibitory effects of emodin isolated from *Polygonum cuspidatum* on Coxsakievirus B_4. *Molecules* 2013; 18: 11842–118583. https://doi.org/10.3390/molecules181011842
141 Lin C-J, Lin H-J, Chen T-H et al. *Polygonum cuspidatum* and its active components inhibit replication of the influenza virus through toll-like receptor 9-induced interferon beta expression. *PLoS One* 2015; 10: e0117602. https://doi.org/10.1371/journal.pone.0117602
142 Lin H-W, Sun M-X, Wang Y-H et al. Anti-HIV activities of the compounds isolated from *Polygonum cuspidatum* and *Polygonum multiflora*. *Planta Med* 2010; 76: 889–92. https://doi.org/10.1055/s-0029-1240796
143 Docherty J-J, Sweet T-J, Bailey E et al. Resveratrol inhibition of varicella-zoster virus replication in vitro. *Antivir Res* 2006; 72: 171–7. https://doi.org/10.1016/j.antiviral.2006.07.004
144 Docherty J-J, Fu M-M, Stiffler B-S et al. Resveratrol inhibition of herpes simplex virus replication. *Antivir Res* 1999; 43: 145–55. https://doi.org/10.1016/s0166-3542(99)00042-x
145 Xu J, Yin Z, Li L et al. Inhibitory effect of resveratrol against duck enteritis virus in vitro. *PLoS One* 2013; 8: e65213. https://doi.org/10.1371/journal.pone.0065213
146 Zou Y, Kong M. Tetrahydroxy stilbene glucoside alleviates palmitic acid-induced inflammation and apoptosis in cardiomyocytes by regulating miR-129-3p/Smad3 signaling. *Cell Mol Biol Lett* 2019; 24: 5–19. https://doi.org/10.1186/s11658-018-0125-x
147 Kanamori H, Takemura G, Goto K et al. Resveratrol reverses remodeling in hearts with large, old myocardial infarctions through enhanced autophagy-activating AMP kinase pathway. *Am J Pathol* 2013; 182: 701–13. https://doi.org/10.1016/j.ajpath.2012.11.009
148 Gao J-P, Chen C-X, Gu W-L et al. Effects of polydatin on attenuating ventricular remodeling in isoproterenol-induced mouse and pressure-overload rat models. *Fitoterapia* 2010; 81: 953–60. https://doi.org/10.1016/j.fitote.2010.06.023
149 Miao Q, Wang S, Miao S et al. Cardioprotective effect of polydatin against ischemia/reperfusion injury: roles of protein kinase C and mito K(ATP) activation. *Phytomedicine* 2011; 19: 8–12. https://doi.org/10.1016/j.phymed.2011.06.023
150 Zhang S-H, Wang W-Q, Wang J-L. Protective effect of tetrahydroxystilbene glucoside on cardiotoxicity induced by doxorubicin in vitro and in vivo. *Acta Pharmacol Sin* 2009; 30: 1479–87. https://doi.org/10.1038/aps.2009.144
151 Gurusamy N, Lekli I, Mukherjee S et al. Cardioprotection by resveratrol: a novel mechanism via autophagy involving the mTORC2 pathway. *Cardiovasc Res* 2010; 86: 103–12. https://doi.org/10.1093/cvr/cvp384
152 Zheng X-Y, Yang S-M, Zhang R et al. Emodin-induced autophagy against cell apoptosis through the PI3K/AKT/mTOR pathway in human hepatocytes. *Drug Des Devel Ther* 2019; 13: 3171–80. https://doi.org/10.2147/dddt.s361140
153 Koneru M, Sahu B-D, Gudem S et al. Polydatin alleviates alcohol-induced acute liver injury in mice: relevance of matrix

metalloproteinases (MMPs) and hepatic antioxidants. *Phytomedicine* 2017; 27: 23–32. https://doi.org/10.1016/j.phymed.2017.01.013

154 Lai Y, Zhou C, Huang P et al. Polydatin alleviated alcoholic liver injury in zebrafish larvae through ameliorating lipid metabolism and oxidative stress. *J Pharmacol Sci* 2018; 138: 46–53. https://doi.org/10.1016/j.jphs.2018.08.007

155 Zhang J, Tan Y, Yao F et al. Polydatin alleviates non-alcoholic fatty liver disease in rats by inhibiting the expression of TNF-α and SREBP-1c. *Mol Med Rep* 2012; 6: 815–20. https://doi.org/10.3892/mmr.2012.1015

156 Long T, Wang L, Yang Y et al. Protective effects of trans-2,3,5,4′-tetrahydroxystilbene-2-*O*-*β*-D-glucopyranoside on liver fibrosis and renal injury induced by CCl_4 via down-regulating p-ERK1/2 and p-Smad1/2. *Food Funct* 2019; 10: 5115–23. https://doi.org/10.1039/c9fo01010f

157 Wang X, Zeng J, Wang X et al. 2,3,5,4′-tetrahydroxystilbene-2-*O*-β-D-glucoside induces autophagy of liver by activating PI3K/Akt and Erk pathway in prediabetic rats. *BMC Complement Med Ther* 2020; 20: 177. https://doi.org/10.1186/s12906-020-02949-w

158 Kim J-R, Oh D-R, Cha M-H et al. Protective effect of *Polygonum cuspidatum* radix and emodin on vibrio vulnificus cytotoxicity and infection. *J Microbiol* 2008; 46: 737–43. https://doi.org/10.1007/s12275-008-0232-x

159 Paulo L, Ferreira S, Gallardo E et al. Antimicrobial activity and effects of resveratrol on human pathogenic bacteria. *World J Microb Biot.* 2010; 26: 1533–8. https://doi.org/10.1007/s11274-010-0325-7

160 Lechner D, Gibbons S, Bucar F. Plant phenolic compounds as ethidium bromide efflux inhibitors in *Mycobacterium smegmatis*. *J Antimicrob Chemother* 2008; 62: 345–8. https://doi.org/10.1093/jac/dkn178

161 Mahady G-B, Pendland S-L. Resveratrol inhibits the growth of *Helicobacter pylori* in vitro. *Am J Gastroenterol* 2000; 95: 1849. https://doi.org/10.1111/j.1572-0241.2000.02146.x

162 Augustine N, Goel A-K, Sivakumar K-C et al. Resveratrol-A potential inhibitor of biofilm formation in vibrio cholerae. *Phytomedicine* 2014; 21: 286–9.

163 Duarte A, Alves A-C, Ferreira S et al. Resveratrol inclusion complexes: antibacterial and anti-biofilm activity against *Campylobacter* spp. and *Arcobacter butzleri*. *Food Res Int* 2015; 77: 244–50. https://doi.org/10.1016/j.ijfoodmicro.2014.04.004

164 Ferreira S, Silva F, Queiroz J-A et al. Resveratrol against *Arcobacter butzleri* and *Arcobacter cryaerophilus*: activity and effect on cellular functions. *Int J Food Microbiol* 2014; 180: 62–8. https://doi.org/10.1016/j.ijfoodmicro.2014.04.004

165 Janeczko M, Masłyk M, Kubiński K et al. Emodin, a natural inhibitor of protein kinase CK2, suppresses growth, hyphal development, and biofilm formation of *Candida albicans*. *Yeast* 2017; 34: 253–65. https://doi.org/10.1002/yea.3230

166 Adrian M, Jeandet P. Effects of resveratrol on the ultrastructure of *Botrytis cinerea conidia* and biological significance in plant/pathogen interactions. *Fitoterapia* 2012; 83: 1345–50. https://doi.org/10.1016/j.fitote.2012.04.004

167 Chan M-M. Antimicrobial effect of resveratrol on dermatophytes and bacterial pathogens of the skin. *Biochem Pharmacol* 2002; 63: 99–104. https://doi.org/10.1016/s0006-2952(01)00886-3

168 Jung H-J, Hwang I-A, Sung W-S et al. Fungicidal effect of resveratrol on human infectious fungi. *Arch Pharm Res* 2005; 28: 557–60. https://doi.org/10.1007/bf02977758

169 Wang H, Song L, Feng S et al. Characterization of proanthocyanidins in stems of *Polygonum multiflora* Thunb as strong starch hydrolase inhibitors. *Molecules* 2013; 18: 2255–65. https://doi.org/10.3390/molecules18022255

170 Tang W, Li S, Liu Y et al. Anti-diabetic activities of cis- and trans-2,3,5,4′-tetrahydroxystilbene-2-*O*-β-glucopyranoside from *Polygonum multiflora*. *Mol Nutr Food Res* 2017; 61: 1. https://doi.org/10.1002/mnfr.201600871

171 Li L-C, Wu X-D, Tian W-X. Inhibition of fatty acid synthase by *Fallopia multiflora* extract. *Chin J Biochem Mol Bio* 2003; 19: 297–304.

172 Choi R-Y, Lee H-I, Ham J-R et al. Heshouwu (*Polygonum multiflora* Thunb.) ethanol extract suppresses pre-adipocytes differentiation in 3T3-L1 cells and adiposity in obese mice. *Biomed Pharmacother* 2018; 106: 355–62. https://doi.org/10.1016/j.biopha.2018.06.140

173 Fan Y-S, Li Q, Hamdan N et al. Tetrahydroxystilbene glucoside regulates proliferation, differentiation, and OPG/RANKL/M-CSF expression in MC3T3-E1 Cells via the PI3K/Akt pathway. *Molecules* 2018; 23: 2306–18. https://doi.org/10.3390/molecules23092306

174 Liu Z-P, Li W-X, Yu B et al. Effects of trans-resveratrol from *Polygonum cuspidatum* on bone loss using the ovariectomized rat model. *J Med Food* 2005; 8: 14–9. https://doi.org/10.1089/jmf.2005.8.14

175 Shin J-Y, Choi Y-H, Kim J, Park S-Y, Nam Y-J, Lee S-Y, Jeong Hoon Jeon,Mu Hyun Jin,Sanghwa Lee. *Polygonum multiflora* extract support hair growth by elongating anagen phase and abrogating the effect of androgen in cultured human dermal papilla cells. *BMC Complement Med Ther*. 2020;20:144, 2020. https://doi.org/10.1186/s12906-020-02940-5

176 Sextius P, Betts R, Benkhalifa I et al. *Polygonum multiflora* Radix extract protects human foreskin melanocytes from oxidative stress in vitro and potentiates hair follicle pigmentation ex vivo. *Int J Cosmet Sci* 2017; 39: 419–25. https://doi.org/10.1111/ics.12391

177 Park H-J, Zhang N, Park D-K. Topical application of *Polygonum multiflora* extract induces hair growth of resting hair follicles through upregulating Shh and β-catenin expression in C57BL/6 mice. *J Ethnopharmacol* 2011; 135: 369–75. https://doi.org/10.1016/j.jep.2011.03.028

178 Chen L, Duan H, Xie F et al. Tetrahydroxystilbene glucoside effectively prevents apoptosis induced hair loss. *Biomed Res Int* 2018; 2018: 1380146. https://doi.org/10.1155/2018/1380146

179 Lin L, Yuan F, Liu Y et al. Hepatotoxicity and mechanism study of chrysophanol-8-O-glucoside in vitro. *Biomed Pharmacother* 2019; 120: 109531. https://doi.org/10.1016/j.biopha.2019.109531

180 Yin C-C.*Establishment of In Vitro Evaluation Method for Early Neurotoxicity and Evaluation of Neurotoxicity of Areca nut and Polygonum cuspidatum* [Dissertation]. Zhenjiang: Jiangsu University, 2017.

181 Li C, Niu M, Bai Z et al. Screening for main components associated with the idiosyncratic hepatotoxicity of a tonic herb, *Polygonum multiflora*. *Front Med* 2017; 11: 253–65. https://doi.org/10.1007/s11684-017-0508-9

182 Quan Y, Gong L, He J et al. Aloe emodin induces hepatotoxicity by activating NF-κB inflammatory pathway and P53 apoptosis pathway in zebrafish. *Toxicol Lett* 2019; 306: 66–79. https://doi.org/10.1016/j.toxlet.2019.02.007

183 Chen B-B, Jiang A-L, Zhang Y. Advances in the pharmacological activity of the active ingredient of *Fallopia multiflora* stilbene glycosides. *Chin Clin Pharmacol Ther* 2016; 21: 710–5.

184 Yang H-L, Li X-B, Lao Z-X et al. Advances in the pharmacological effects of resveratrol. *Chin J Gerontol* 2020; 40: 3572–5.

185 Pang J-Y, Bai Z-F, Niu M et al. Comparative study on toxicity and protective effects of *Polygonum multiflora* on normal and liver injury rats . *J Pharm* 2015; 50: 973–9. https://doi.org/10.16438/j.0513-4870.2015.08.009