· Reviews ·

Review of Rhubarbs: Chemistry and Pharmacology

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Abstract: Rhubarb is a perennial herb belonging to the genus *Rheum* L. (Polygonaceae). *Rhei Radix* et *Rhizoma* (rhubarb roots and rhizomes) is one of the most popular Chinese materia medica and has been widely used for strong laxative function. About 200 compounds with six different types of skeletons (anthraquinone, anthrone, stilbene, flavonoids, acylglucoside, and pyrone) have so far been isolated from eighteen species of the genus *Rheum* L. These constituents showed extensive pharmacological activities including cathartic, diuretic, anticancer, hepatoprotective, anti-inflammatory, and analgesic effects, as well as toxicological effects. Chemical fingerprint, LC-MS, and other analytical techniques have been used for the quality control of rhubarb. This comprehensive review summarizes the researches into the isolation, pharmacological activities, and phytochemical analysis reported since investigations began in the late 1940s. In addition, pharmacokinetic studies and clinical application of rhubarb are also discussed in present paper.

Key words: pharmacokinetic studies; pharmacological activities; quality control; *Rheum* L.; rhubarb
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Introduction

Rhubarb refers to any of several species of the genus *Rheum* L. in the family Polygonaceae. The genus *Rheum* L., consisting of about 60 herbaceous perennial plants growing from short and thick rhizomes, is distributed in the temperate and sub-tropical regions. China is the distribution center of the genus with 41 species and two variants accounting for three-quarters of the genus. Rhubarb is mainly found in the northwest and southwest regions of China (The Flora of China Editorial Committee, 1998). It is traditionally acknowledged that Qinghai, Sichuan, and Gansu provinces are the producing areas of rhubarbs in China.

Rhei Radix et *Rhizoma* (RRR, the roots and rhizomes of rhubarb) is one of the well-known Chinese materia medica (CMM) and has been widely used as a strong laxative agent in China for over 2000 years. Rhubarb has been gradually spreading to India, Russia, Europe, and North America (Xiao *et al*, 1984). The ancient practitioner used rhubarb as an effective, short-lived and painless cathartic with highly significant therapeutic effects. Because purging one's system was one of many important treatments under the guidance of traditional Chinese medicine (TCM) theory, the usage of roots and rhizomes of rhubarb was frequently featured in the traditional Chinese pharmacopeia, e.g. *Shennong Ben Cao Jing* and *Ben Cao Gang Mu*. In addition, fleshy and thorny stalks (petioles) of some species (eg *R. rhabarbarum*) are also used for food in some countries such as US and England. The modern research for the

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development of rhubarb as an herbal medicine has been carried out in China since the late 1940s. The academician LOU Zhi-cen developed a bioassay method for the botanical purgative agent called Lou's Method with world-wide recognition (Zheng and Guo, 2007). Since then, researchers in Peking University Medical College have been engaged in rhubarb investigation with the great achievements, which laid firm foundation for successive research on rhubarb. In *Chinese Pharmacopoeia 2010*, there are three authorized rhubarbs, namely *R. palmatum* L., *R. tanguticum* Maxim. ex Balf, and *R. officinale* Bail (Pharmacopoeia Committee of P. R. China, 2010). The roots and rhizomes of these species, generally called official rhubarbs, are commonly used in the clinic. It is estimated that there is rhubarb formulated in more than 800 kinds of CMM preparation. Commercial rhubarbs mainly include Qinghai rhubarbs (*R. palmatum* and *R. tanguticum*), Gansu rhubarb (*R. palmatum*), Sichuan Ya-huang (*R. tanguticum* and *R. palmatum*), Korean rhubarb (*R. coreanum* Nakai), and Japanese rhubarb (Imo-Daio). Because of the increasing requirement both domestically and abroad and the short supply of official rhubarb, other *Rheum* L. species, such as *R. hotaoense* C. Y. Cheng et Kao and *R. franzenbachil* Miinter have been also used as commercial substitutes in some regions (Zheng and Guo, 2007).

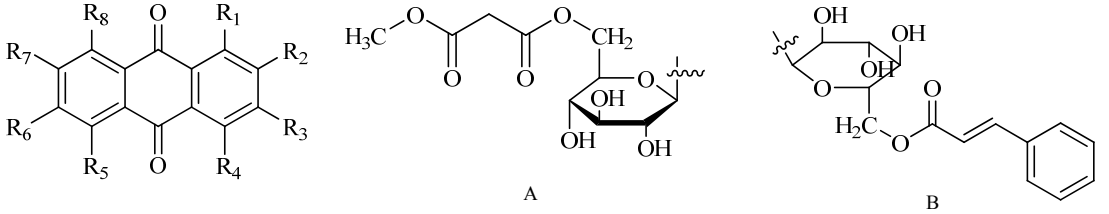
So far, phytochemical investigation on the eighteen species of the genus *Rheum* L. has led to the isolation of about two hundred constituents. Rhein, emodin, aloe-emdin, and so on are reportedly responsible for biological activities such as cathartic, diuretic, antidiarrhea, antidiabetic, and antitumor effects (Ding, Zou, and Li, 2011). Chemical fingerprint**,** LC-MS, and other analytical techniques have been widely used for the qualitative and quantitative analysis of constituents in rhubarb. In this review, we summarized the researches reported over the past decades on the isolation, pharmaceutical activity, quality control, pharmacokinetic study, and clinical application of rhubarbs to provide the scientific evidence for the better utilization of rhubarbs.

Phytochemical investigation

To date, about 200 compounds mainly in six skeletal types (including anthraquinone, anthrone, stilbene, flavonoids, acylglucoside, and pyrone) have been isolated from the eighteen species of the genus *Rhuem* L.

Anthraquinones

Anthraquinones are an important type of components in rhubarb (Fig. 1). The free anthraquinones—rhein, emodin, physcion, and chrysophanol, are present in nearly all species. The conjugated anthraquinone derivatives are responsible for the cathartic effects. Compounds **1**—**31**) were isolated from the species of the genus *Rheum* L. (Table 1), most of which showed good pharmacological activities.



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3 R_1=R_6=R_8=OH R_2=R_4=R_5=R_7=H R_3=CH_3
4 R_1=R_8=OH R_2=R_4=R_5=R_6=R_7=H R_3=CH_2OH
5 R_1=R_8=OH R_2=R_4=R_5=R_7=H R_3=COOH
6 R_1=R_2=R_5=R_8=H R_3=R_4=R_6=OH R_7=CH_3
7 R_1=CH_3 R_2=COOH R_3=R_6=R_8=OH R_4=R_5=R_7=H
8 R_1=R_3=R_8=OH R_2=R_4=R_5=R_7=H R_6=CH_2OH
9 R_1=R_8=OH R_2=R_4=R_5=R_7=H R_3=CH_3 R_6=OH
10 R_1=OH R_2=R_4=R_5=R_6=R_7=H R_3=CH_3 R_8=OCH_3
11 R_1=OGlu R_2=R_4=R_5=R_7=H R_3=CH_3 R_8=OH
12 R_1=OH R_2=R_4=R_5=R_6=R_7=H R_3=CH_3 R_8=OGlu
13 R_1=OH R_2=R_4=R_5=R_6=R_7=H R_3=CH_3 R_8=OGlu-G
14 R_1=OH R_2=R_4=R_5=R_6=R_7=H R_3=CH_3 R_8=OGlu-M
15 R_1=OH R_2=R_4=R_5=R_6=R_7=H R_3=CH_3 R_8=OGlu-A
16 R_1=OGlu R_2=R_4=R_5=R_7=H R_3=CH_3 R_6=R_8=OH
17 R_1=R_8=OH R_2=R_4=R_5=R_7=H R_3=CH_3 R_6=OGlu
18 R_1=OH R_2=R_4=R_5=R_6=R_7=H R_3=CH_3 R_8=OGlu
19 R_1=OH R_2=R_4=R_5=R_7=H R_3=CH_3 R_6=OSO_3H R_8=OGlu
20 R_1=R_6=OH R_2=R_4=R_5=R_7=H R_3=CH_3 R_8=OGlu-Glu
21 R_1=R_8=OH R_2=R_4=R_5=R_7=H R_3=CH_2OH R_6=CH_3
22 R_1=OGlu R_2=R_4=R_5=R_6=R_7=H R_3=CH_2OH R_8=OH
23 R_1=OH R_2=R_4=R_5=R_6=R_7=H R_3=CH_2OH R_8=OGlu
24 R_1=R_8=OH R_2=R_4=R_5=R_6=R_7=H R_3=CH_2OGlu
25 R_1=R_8=OH R_2=R_4=R_5=R_7=H R_3=COOH R_6=CH_3
26 R_1=OH R_2=R_4=R_5=R_6=R_7=H R_3=COOH R_8=OGlu
27 R_1=OGlu R_2=R_4=R_5=R_7=H R_3=CH_3 R_6=OCH_3 R_8=OH
28 R_1=OH R_2=R_4=R_5=R_7=H R_3=CH_3 R_6=OCH_3 R_8=OGlu
29 R_1=OH R_2=R_4=R_5=R_7=H R_3=CH_3 R_6=OCH_3 R_8=OGlu-Glu
30 R_1=OH R_2=R_4=R_5=R_6=R_7=H R_3=COOH R_8=OA
31 R_1=CH_3 R_2=COOH R_3=OB R_4=R_5=R_6=R_7=H R_8=OH

Fig. 1 Structures of anthraquinone derivatives isolated from plants in *Rheum* L.

Table 1 Anthraquinone derivatives isolated from plants in *Rheum* L.

No.	Compounds	Botanical sources	References
1	chrysophanol	a, b, c, d, e, g, h, i, j, k ,l, m, n, o	Xiong *et al*, 2003; Gao *et al*, 2011; Kang *et al*, 2002; Wang, Li, and Li, 2010; Liu, Yang, and Wang, 2007; Yang *et al*, 1998; Wei *et al*, 2004; Li *et al*, 2000; Hu *et al*, 1997; Jin , 2006; Min *et al*, 1998; Zong, 2008; Xiang *et al*, 2001; Zhao, Chang, and Du, 2002; Song *et al*, 2003; Tang, 2009; Xu *et al*, 2009; Cai *et al*, 2004; Ko, Whang, and Kin, 1995; Wang, Li, and Wu, 2003; Babu *et al*, 2004; Choi *et al*, 2005; Tan, 2006
2	physcion	a, b, c, d, e, f, g, h, l, i k, m, n, o	Gao *et al*, 2011; Kang *et al*, 2002; Wang, Li, and Li, 2010; Liu, Yang, and Wang, 2007; Yang *et al*, 1998; Wei *et al*, 2004; Li *et al*, 2000; Hu *et al*, 1997; Jin, 2006; Min *et al*, 1998; Zong, 2008; Xiang *et al*, 2001; Song *et al*, 2003; Tang, 2009; Xu *et al*, 2009; Cai *et al*, 2004; Ko, Whang, and Kin, 1995; Wang, Li, and Wu, 2003; Babu *et al*, 2004
3	emodin	a, b, c, d, e, f, g, h, i, j, k, l, m, n, o	Xiong *et al*, 2003; Gao *et al*, 2011; Kang *et al*, 2002; Wang, Li, and Li, 2010; Liu, Yang, and Wang, 2007; Yang *et al*, 1998; Wei *et al*, 2004; Li *et al*, 2000; Hu *et al*, 1997; Jin, 2006; Min *et al*, 1998; Zong, 2008; Xiang *et al*, 2001; Zhao, Chang, and Du, 2002; Zhang *et al*, 2005; Tang, 2009; Xu *et al*, 2009; Cai *et al*, 2004; Ko, Whang, and Kin, 1995; Wang, Li, and Wu, 2003; Babu *et al*, 2004; Choi *et al*, 2005
4	aloe-emodin	a, b, c, e, f, h, k ,l, n, o	Xiong *et al*, 2003; Gao *et al*, 2011; Kang *et al*, 2002; Yang *et al*, 1998; Wei *et al*, 2004; Li *et al*, 2000; Hu *et al*, 1997; Jin, 2006; Zong, 2008; Zhang *et al*, 2005; Xu *et al*, 2009; Cai *et al*, 2004; Tan, 2006
5	rhein	a, b, c, h, m, n, o	Xiong *et al*, 2003; Gao *et al*, 2011; Li *et al*, 2000; Hu *et al*, 1997; Jin, 2006; Zong, 2008; Tang, 2009; Xu *et al*, 2009; Cai *et al*, 2004; Wang, Li, and Wu, 2003
6	chrysaron	q	Hesse, 1908
7	laccaic acid D	r	Oshio, Naruse, and Tsukui, 1978
8	citreorosein	I, e, l	Kang *et al*, 2002; Wei,Wu, and Zhang, 2005; Xiang *et al*, 2001
9	revandchinone-3	d	Babu *et al*, 2003
10	chrysophanol-8-Me ether	l	Wei, Wu, and Zhang, 2005
11	chrysophanol-1-*O*-β-*D*-glucopyranoside	a, c, h, j	Li *et al*, 2000; Zhao, Chang, and Du, 2002; Xu *et al*, 2009; Cai *et al*, 2004
12	chrysophanol-8-*O*-β-*D*-glucopyranoside	a, b, c, d, e, g, h, l, k, n	Gao *et al*, 2011; Kang *et al*, 2002; Wang, Li, and Li, 2010; Liu *et al*, 2007; Yang *et al*, 1998; Wei, Wu, and Zhang, 2005; Li *et al*, 2000; Hu *et al*, 1997; Jin, 2006; Min *et al*, 1998; Zong, 2008; Song *et al*, 2003; Xu *et al*, 2009; Cai *et al*, 2004; Ko, Whang, and Kin, 1995; Babu *et al*, 2004; Zhang *et al*, 2011
13	chrysophanol-8-*O*-β-*D*-(6′-*O*-galloyl)-glucopyranoside	h, n	Li *et al*, 2000; Matsuda *et al*, 2000
14	chrysophanol-8-*O*-β-*D*-(6′-*O*-malonyl)-glucopyranoside	f	Yang *et al*, 1998
15	chrysophanol-8-*O*-β-*D*-(6′-*O*-acetyl)-glucopyranoside	d	Krenn *et al*, 2004

(To be continued)

(Continued Table 1)

No.	Compounds	Botanical sources	References
16	emodin-1-*O*-β-*D*-glucopyranoside	c, n	Cai *et al*, 2004; Ko, 2000; Babu *et al*, 2004; Zhang *et al*, 2011
17	emodin-6-*O*-β-*D*-glucopyranoside	a	Romanova *et al*, 1966
18	emodin-8-*O*-β-*D*-glucopyranoside	d, l, g, i, k, m, n	Wang, Li, and Li, 2010; Liu, Yang, and Wang, 2007; Wei *et al*, 2006; Min *et al*, 1998; Xiang *et al*, 2001; Song *et al*, 2003; Ko, Whang, and Kin, 1995; Wang, Li, and Wu, 2003; Zhang *et al*, 2011
19	emodin-8-*O*-β-*D*-glucopyranosyl-6-*O*-sulfate	d	Krenn *et al*, 2003
20	emodin-gemtiobioside	e	Kang *et al*, 2002
21	6-methyl-aloe-emodin	d	Singh *et al*, 2005
22	aloe-emodin-1-*O*-β-*D*-glucopyranoside	n	Matsud *et al*, 2000
23	aloe-emodin-8-*O*-β-*D*-glucopyranoside	f, h, b, i, n	Yang *et al*, 1998; Li *et al*, 2000; Jin, 2006; Xiang *et al*, 2001; Ko, Whang, and Kin, 1995; Zhang *et al*, 2011
24	aloe-emodin-3-(hydroxymethyl)-*O*-β-*D*-glucopyranoside	a, l	Wei *et al*, 2006; Xu *et al*, 2009; Zhang *et al*, 2011
25	6-methyl-rhein	d	Singh *et al*, 2005
26	rhein-8-*O*-β-*D*-glucopyranoside	a	Zhang *et al*, 2011
27	physcion-1-*O*-β-*D*-glucopyranoside	d	Wang, Li, and Wu, 2010
28	physcion-8-*O*-β-*D*-glucopyranoside	a, c, d, f, h, m, n	Wang, Li, and Li, 2010; Yang *et al*, 1998; Li *et al*, 2000; Zong, 2008; Xu *et al*, 2009; Wang *et al*, 2003; Ko, 2000; Zhang, 2011
29	physcion-8-*O*-β-*D*-gentiobioside	c	Holzschuh, Kopp, and Kubelka, 1982
30	rhein-8-*O*-β-*D*-[6′-*O*-(3″-methoxyl malonyl)] glucopyranoside	a	Zhang *et al*, 2010
31	1-methyl-8-hydroxyl-9,10-anthraquinone-3-*O*-β-*D*-(6′-*O*-cinnamoyl) glucopyranoside	a	Zhang *et al*, 2010

Note: a: *R. palmatum*; b: *R. tanguticum*; c: *R. officinale*; d: *R. emodi*; e: *R. nanum*; f: *R. qinjingense*; g: *R. wittrochii*; h: *R. hotaoense*; i: *R. sublanceolatum*; j: *R. rhizastachyum*; k: *R. uninrrre*; l: *R. glabrucaule*; m: *R. franzenbachil*; n: *R. undulatum*; o: *R. Spiciforme*; p: *R. palmatum*; q: *R. rhaponticum*; r: Shin-Shu Daio (a hybrid between *R. coreanum* and *R. palmatum*)

Anthrones

Anthrones are less oxygenated than anthraquinones and 26 anthrones (compounds **32**—**57**) have been isolated from the species of this genus so far (Fig. 2 and Table 2). Among them, sennosides are a number of anthraquinone derivatives as laxatives.

Stilbenes

Stilbenes are considered to be important components in chemotaxonomy. The distinction between high- and low-quality rhubarbs could be defined based on the presence or absence of stibene glucoside, rhaponticin, which is believed to only occur in rhubarbs of low-quality (Kashiwada, Nonaka, and Nishioka, 1984a). So far, 35 stilbenes (compounds **58**—**92**) have been isolated from the plants in genus *Rheum* L. (Fig. 3 and Table 3).

Condensed tannins and related flavonoids

Flavonoids are a type of flavonoids and forty-five flavonoids (compounds **93**—**137**) have been isolated from official rhubarbs and commercial species (Fig. 4 and Table 4).

Acylglucosides

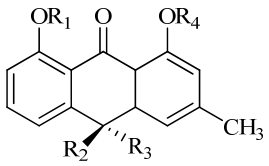
Thirty-three acyglucosides (compounds **138**—**172**) are isolated from rhubarbs (Fig. 5 and Table 5).

Pyranones and some flavonoids

Fourteen pyranones (compounds **173**—**187**) were isolated from *R. hotaoense*, *R. glabricaule*, *R. undulatum*, and commercial rhubarbs (Fig. 6 and Table 6).

Others

Three naphthalene glycosides, such as torachrysone-8-*O*-β-*D*-glucopyranoside (**187**), torachrysone-8-*O*-β-*D*-(6′-*O*-oxalyl)-glucopyranoside (**188**) (Gao *et al*, 2011), and 6-hydroxymusizin-8-*O*-β-*D*-glucopyranoside (**189**) (Xiang *et al*, 2001), were isolated from rhubarbs. In addition, polysaccharides, organic acid, and volatile oil were investigated (Zhao 2011; Xie, Li, and Ma, 2010; Hu *et al*, 2011; Wang, Zheng, and Chen, 1995).



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33 R_1=R_3=Glu R_2=OH R_4=H
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35 R_1=R_2=Glu R_3=R_4=H
36 R_1=R_3=Glu R_2=R_4=H
37 R_1=R_4=H R_2=OH R_3=Glu
38 R_1=R_2=Glu R_2=OH R_4=H
39 R_1=R_3=Glu R_2=OH R_4=H
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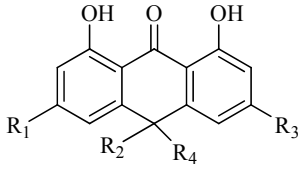
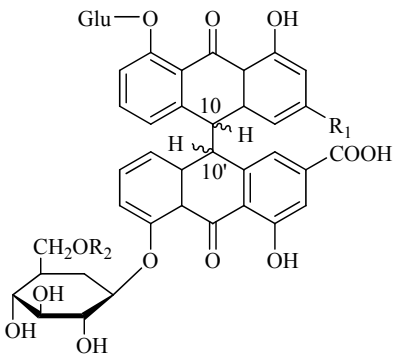
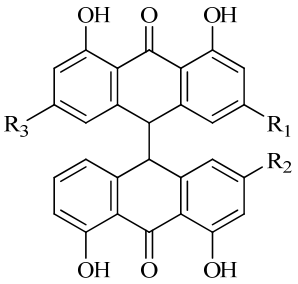


55 R_1=OCH_3 R_2=H R_3=CH_3 R_4=O-CO-$(CH_2)_7$-CH_3
58 R_1=R_2=H R_3=CH_3 R_4=O-CO-$(CH_2)_{26}$-CH_3
57 R_1=R_2=OH R_3=CH_2OH R_4=O-$(CH_2)_{17}$-CH_3



42 R_1=COOH R_2=H 10-10′ trans
43 R_1=COOH R_2=H 10-10′ meso
44 R_1=CH2OH R_2=H 10-10′ trans
45 R_1=CH2OH R_2=H 10-10′ meso
46 R_1=COOH R_2=Oxalyl 10-10′ *trans*
47 R_1=COOH R_2=Oxalyl 10-10′ meso



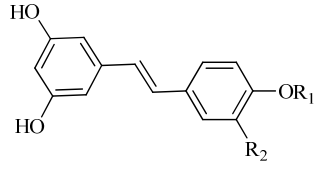
48 R_1=CH_3 R_2=CH_2OH R_3=OH
49 R_1=CH_3 R_2=CH_2OH R_3=H
50 R_1=CH_3 R_2=CH_3 R_3=OH
51 R_1=CH_3 R_2=COOH R_2=OH
52 R_1=CH_3 R_2=COOH R_3=H
53 R_1=CH_3 R_2=COOH R_3=OCH_3
54 R_1=COOH R_2=CH_2OH R_3=H

Fig. 2 Structures of anthrone derivatives isolated from plants in *Rheum* L.

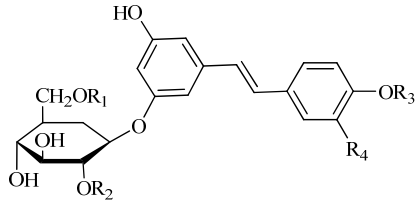
Table 2 Anthrone derivatives isolated from plants in *Rheum* L.

No.	Compounds	Botanical sources	References
32	10-hydroxycascaroside C	b	Krenn *et al*, 2004
33	10-hydroxycascaroside D	b	Krenn *et al*, 2004
34	10*R*-chrysaloin1-*O*-β-*D*-glucopyranoside	b	Krenn *et al*, 2004
35	cascaroside C	b	Krenn *et al*, 2004
36	cascaroside D	b	Krenn *et al*, 2004
37	cassialoin	b	Krenn *et al*, 2004
38	rheinoside A	a	Yamagishi *et al*, 1987
39	rheinoside B	a	Yamagishi *et al*, 1987
40	rheinoside C	a	Yamagishi *et al*, 1987
41	rheinoside D	a	Yamagishi *et al*, 1987
42	sennoside A	c	Oshio *et al*, 1974; Miyamoto *et al*, 1967
43	sennoside B	c	Oshio *et al*, 1974; Miyamoto *et al*, 1967
44	sennoside C	c	Oshio *et al*, 1974; Miyamoto *et al*, 1967
45	sennoside D	c	Oshio *et al*, 1974; Miyamoto *et al*, 1967
46	sennoside E	c	Oshio *et al*, 1974; Miyamoto *et al*, 1967
47	sennoside F	c	Oshio *et al*, 1974
48	palmidin A	a	Dequeker, Lemli, and Cuveeie, 1964; Zwaving *et al*, 1965
49	palmidin B	a	Dequeker, Lemli, and Cuveeie, 1964
50	palmidin C	a	Dequeker, Lemli, and Cuveeie, 1964
51	rendin A	a	Lemili, Bequeker, and Cuveele, 1964.
52	rendin B	a	Lemili, Bequeker, and Cuveele, 1964
53	rendin C	a	Lemili, Bequeker, and Cuveele, 1964
54	sennidin C	a	Zwaving *et al*, 1965
55	revandchinone-1	b	Babu *et al*, 2003
56	revandchinone-2	b	Babu *et al*, 2003
57	revandchinone-4	b	Babu *et al*, 2003

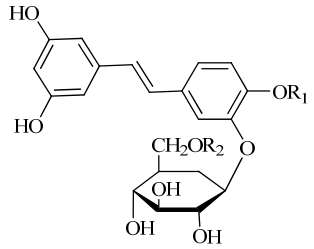
Note: a: *R. palmatum*; b: *R. emodi*; c: *R. palmatum*



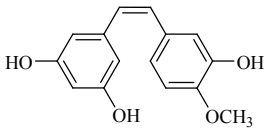
58 R_1=CH_3 R_2=OH
59 R_1=H R_2=OH
60 R_1=CH_3 R_2=H
61 R_1=H R_2=H
62 R_1=Glu_6 R_2=H
63 R_1=Glu-G R_2=H



65 R_1=R_2=R_3=R_4=H
66 R_1=R_2=H R_3=CH_3 R_4=OH
67 R_1=R_2=R_3=H R_4=OH
68 R_1=G R_2=H R_3=CH_3 R_4=OH
69 R_1=H R_2=G R_3=CH_3 R_4=OH
70 R_1=H R_2=*p*-coum R_3=CH_3 R_4=OH
71 R_1=R_2=R_4=H R_3=CH_3
72 R_1=R_2=R_3=H R_4=OCH_3
73 R_1=R_2=R_4=H R_3=CH_3
74 R_1=G R_2=R_4=H R_3=CH_3
75 R_1=R_2=H R_3=Glu R_4=OH



76 R_1=OCH_3 R_2=H
77 R_1=H R_2=H
78 R_1=H R_2=G



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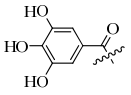
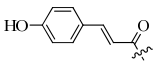
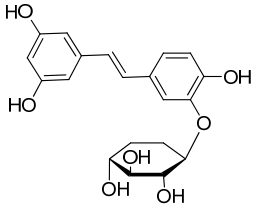
G:



p-coum:





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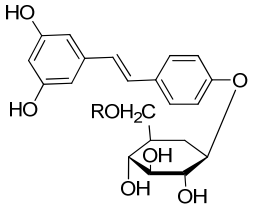
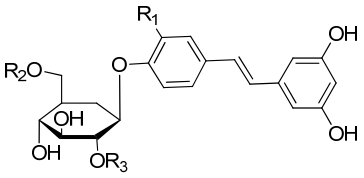
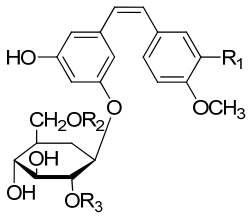


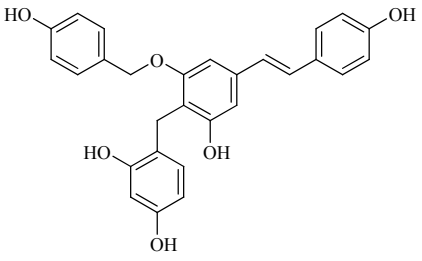
80 R=H
81 R=G



82 R_1=OH R_2=R_3=H
83 R_1=OH R_2=G R_3=H
84 R_1=R_3=H R_2=*p*-coum
85 R_1=R_2=H R_3=G



86 R_1=OH R_2=R_3=H
87 R_1=OH R_2=G R_3=H
88 R_1=R_2=R_3=H
89 R_1=OH R_2=H R_3=G



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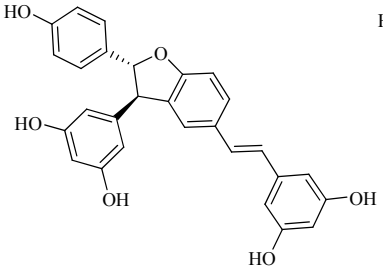

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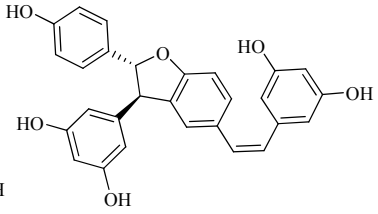

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Fig. 3 Structures of stilbene derivatives isolated from plants in *Rheum* L.

Table 3 Stilbene derivatives isolated from plants in *Rheum* L.

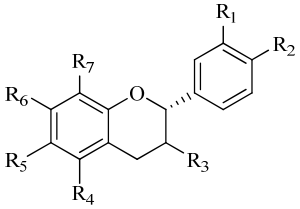
No.	Compounds	Botanical sources	References
58	rhapontigenin	a, b, d, g, j, k	Kashiwada, Nonaka, and Nishioka, 1984b; Matsuda *et al*, 2000; Wang, Li, and Wu, 2001; Ko, Lee, and Whang, 1999; Jin, 2006; Xu *et al*, 2009; Matuda *et al*, 2001; Babu *et al*, 2004; Li *et al*, 1998
59	piceatannol	d, f, j, k, n	Kashiwada, Nonaka, and Nishioka, 1984c; Matsuda *et al*, 2000; Wang, Li, and Wu, 2001; Ko, Lee, and Whang, 1999; Xiang *et al*, 2001; Min *et al*, 1998; Xiang *et al*, 2005
60	desoxyrhapontigenin	d, k, j	Matsuda *et al*, 2000; Wang, Li, and Wu, 2001; Ko, Lee, and Whang, 1999; Babu *et al*, 2004; Choi *et al*, 2005

(To be continued)

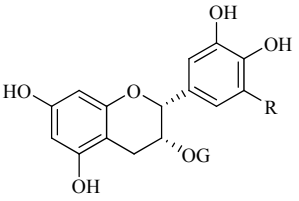
(Continued Table 3)

No.	Compounds	Botanical sources	References
61	resveratrol	f, k	Min *et al*, 1998; Matuda *et al*, 2001; Matsuda *et al*, 2000
62	resveratrol 4′-*O*-β-*D*-glucopyranoside	b	Gao *et al*, 2011
63	resveratrol 4′-*O*-β-*D*-(6″-*O*-galloyl)-glucopyranoside	b	Gao *et al*, 2011
64	*cis*-3,3′,5-trihydroxy-4′-methoxystilbene	n	Kashiwada, Nonaka, and Nishioka, 1984a
65	*trans*-resveratrol-3-*O*-β-*D*-glucopyranoside	m	Aburjai, 2000
66	rhaponticin	b, c, g, k, j, m, n	Aburjai, 2000; Kashiwada, Nonaka, and Nishioka, 1984b; Matsuda *et al*, 2000; Wang, Li, and Wu, 2001; Ko, Whang, and Kin, 1995; Ko, Lee, and Whang 1999; Jin, 2006; Zong, 2008; Matuda *et al*, 2001; Li *et al*, 1998
67	piceatannol 3-*O*-β-*D*-glucopyranoside	n	Kashiwada, Nonaka, and Nishioka, 1984c
68	rhaponticin 6″-*O*-gallate	b, k, n	Kashiwada, Nonaka, and Nishioka, 1984a; Matsuda *et al*, 2000; Jin, 2006; Matuda *et al*, 2001
69	rhaponticin 2″-*O*-gallate	b, k, n	Kashiwada, Nonaka, and Nishioka, 1984b; Matsuda *et al*, 2000; Jin, 2006; Matuda *et al*, 2001
70	rhaponticin 2″-*p*-coumarate	n	Kashiwada, Nonaka, and Nishioka, 1984c
71	desoxyrhaponticin	c, d, f, j, k, n	Kashiwada, Nonaka, and Nishioka, 1984a; Matsuda *et al*, 2000; Min *et al*, 1998; Wang, Li, and Wu, 2001; Zong, 2008; Matuda *et al*, 2001; Babu *et al*, 2004
72	isorhapontin	k	Matsuda *et al*, 2000
73	deoxyrhaponticin	f, k	Ko, 2000; Min *et al*, 1998
74	desoxyrhaponticin 6″-*O*-gallate	n	Kashiwada, Nonaka, and Nishioka, 1984b
75	piceatannol-3,4'-*O*-β-*D*-diglucopyranoside	k	Ko, 2000
76	rhapontidenin 3′-3-*O*-β-*D*-glucopyranoside	n	Kashiwada, Nonaka, and Nishioka, 1988a
77	piceatannol 3′-*O*-β-*D*-glucopyranoside	g, j, k, n	Kashiwada, Nonaka, and Nishioka, 1984; Matsuda *et al*, 2000; Wang, Li, and Wu, 2001; Matuda *et al*, 2001; Ko, Whang, and Kin, 1995; Li *et al*, 1998
78	piceatannol 3-*O*-β-*D*-(6″-*O*-galloyl)glucopyranoside	n	Kashiwada, Nonaka, and Nishioka, 1988b
79	piceatannol 3′-*O*-β-*D*-xylopyranoside-	n	Kashiwada, Nonaka, and Nishioka, 1988c
80	3,4′,5-trihydroxystlbene-4′-*O*-β-*D*-glucopyranoside	a, b, c	Komatsu *et al*, 2006; Nonaka *et al*, 1981
81	3,4′,5-trihydroxystlbene-4′-*O*-β-*D*-(6″-*O*-galloyl) glucopyranoside	a, b, c, n	Komatsu *et al*, 2006; Nonaka *et al*, 1981; Kashiwada, Nonaka, and Nishioka, 1984a
82	piceatannol 4′-*O*-β-*D*-glucopyranoside	d, f, o	Xiang *et al*, 2005; Min *et al*, 1998; Kashiwada *et al*, 1988
83	piceatannol 4′-*O*-(6″-*O*-galloyl)β-*D*-glucopyranoside	o	Kashiwada, Nonaka, and Nishioka, 1988
84	piceatannol 4′-*O*-(6″-p-coumaroyl)β-*D*-glucopyranoside	d	Wang, Li, and Li, 2010
85	3,4′,5-trihydroxystlbene-4′-*O*-β-*D*-(2″-*O*-galloyl)glucopyranoside	o	Kashiwada, Nonaka, and Nishioka, 1986
86	*cis*-3,3′,5-trihydroxy-4′-methoxystilbene 3-*O*-β-*D*-glucopyranoside	n	Kashiwada, Nonaka, and Nishioka, 1988
87	*cis*-3,3′,5-trihydroxy-4′-methoxystilbene 3-*O*-β-*D*-(6″-*O*-galloyl)glucopyranoside	n	Kashiwada, Nonaka, and Nishioka, 1988
88	*cis*-3,5-dihydroxy-4′-methoxystilbene 3-*O*-β-*D*-glucopyranoside	n	Kashiwada, Nonaka, and Nishioka, 1988
89	*cis*-3,3′,5-trihydroxy-4′-methoxystilbene 3-*O*-β-*D*-(2″-*O*-galloyl) glucopyranoside	n	Kashiwada, Nonaka, and Nishioka, 1988
90	gentin C	e	Xiang *et al*, 2005
91	maximol A	m	Shikishima *et al*, 2001
92	maximol B	m	Shikishima *et al*, 2001

Note: a: *R. palmatum*; b: *R. tanguticum*; c: *R. officinale*; d: *R. emodi*; e: *R. nanum*; f: *R. wittrochii*; g: *R. hotaoense*; h: *R. sublanceolatum*; i: *R. uninrrre*; j: *R. franzenbachil*; k: *R. undulatum*; l: *R. maximowiczii*; m: *R. palaestinum*; n: commercial rhubarbs; o: *R. palmatum*

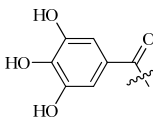


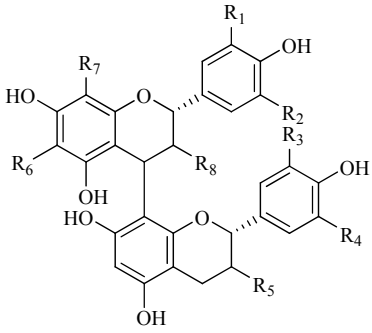
93 R_1=R_2=R_3=R_4=R_6=OH R_5=R_7=H
94 R_1=R_2=R_3=R_6=OH R_4=O-Glu R_5=R_7=H
95 R_1=R_2=R_3=R_4=OH R_5=R_7=H R_6=O-Glu
96 R_1=O-Glu R_2=R_3=R_4=R_6=OH R_5=R_7=H
97 R_1=R_3=R_4=R_6=OH R_2=O-Glu R_5=R_7=H
98 R_1=R_6=O-Glu R_2=R_3=R_4=OH R_5=R_7=H
99 R_1=R_4=O-Glu R_2=R_3=R_6=OH R_5=R_7=H
100 R_1=R_3=R_6=OH R_2=R_4=O-Glu R_5=R_7=H
101 R1=R_2=O-Glu R_3=R_4=R_6=OH R_5=R_7=H
102 R_1=R_2=R_3=R_6=OH R_5=H R_7=-Glu
103 R_1=R_2=R_3=R_4=R_6=OH R_5=Glu R_7=H



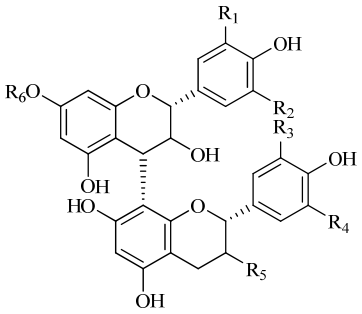
104 R=H
105 R=OH

G:

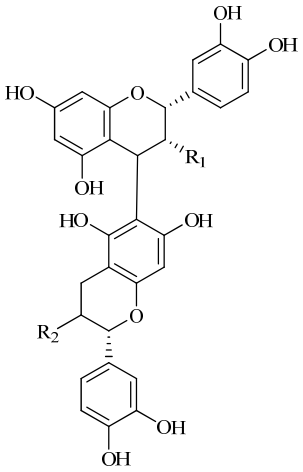




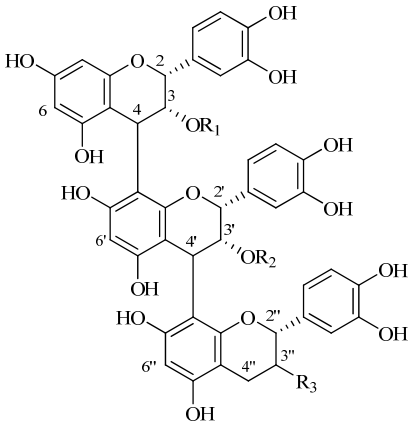
106 R_1=R_3=OH R_2=R_4=R_6=H R_5=β-OH R_7=Glu R_8=α-OH
107 R_1=R_3=OH $_{R2}$=R_4=R_7=H R_5=β-OH R_6=Glu R_8=α-OH
108 R_1=OH R_2=R_4=R_6=H R_3=OH R_5=R_8=α-OH R_8=Glu
109 R_1=R_3=OH R_2=R_4=R_7=H R_5=R_8=α-OH R_6=Glu
110 R_1=R_3=R_6=R_7=H R_2=R_4=OH R_5=β-OH R_8=α-OH
111 R_1=R_3=R_6=R_7=H R_2=R_4=OH R_5=R_8=α-OH
112 R_1=R_3=R_6=R_7=H R_2=R_4=OH R_5=R_8=α-OH
113 R_1=R_3=R_6=R_7=H R_2=R_4=OH R_5=R_8=α-OH
114 R_1=R_3=R_6=R_7=H R_2=R_4=OH R_5=R_8=α-OG



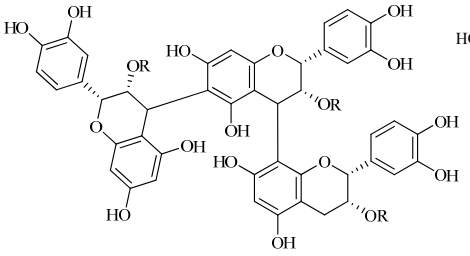
115 R_1=R_3=OH R_2=R_4=H R_5=β-OH R_6=Glu
116 R_1=R_3=R_6=H R_2=R_4=OH R_5=β-OH
117 R_1=R_3=R_6=H R_2=R_4=OH R_5=α-OH
118 R_1=R_3=R_6=H R_2=R_4=OH R_5=α-OG



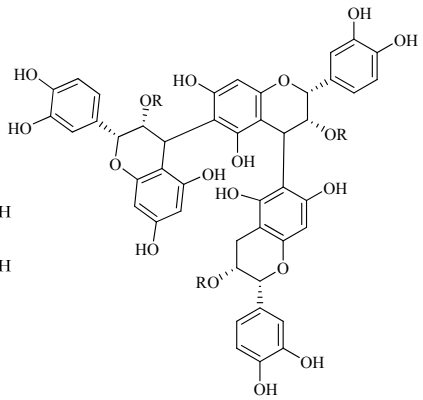
119 R_1=OH R_2=β-OH
120 R_1=OG R_2=β-OH
121 R_1=OG R_2=α-OG
122 R_1=OH R_2=α-OH



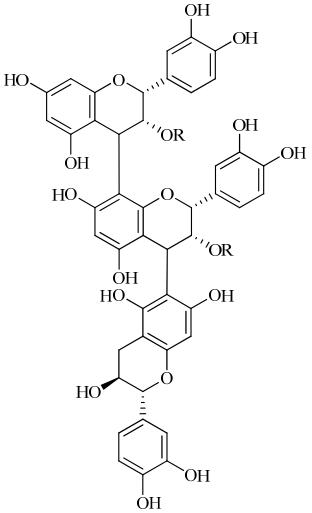
123 R_1=R_2=H R_3=β-OH
124 R_1=R_2=G R_3=α-OG
125 R_1=R_2=G R_3=α-OG
126 R_1=R_2=G R_3=β-OH
127 R_1=R_2=H R_3=α-OH



128 R=H
129 R=G



130 R=H
131 R=G



132 R=H
133 R=G

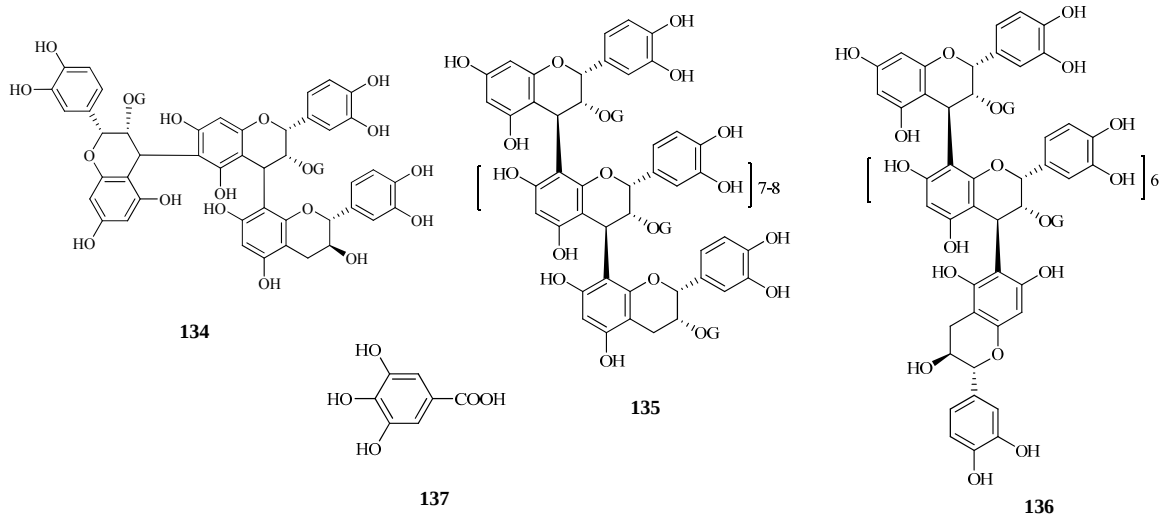


Fig. 4 Strutures of flavonoids isolated from plants in *Rheum* L.

Table 4 Flavonoids isolated from plants in *Rheum* L.

No.	Compounds	Botanical sources	References
93	(+)-catechin	a, b, d, g	Jin, 2006; Lu *et al*, 1998; Wang, Li, and Wu, 2003; Nonaka *et al*, 1981; Komatsu *et al*, 2006
94	(+)-catechin-5-*O*-β-*D*-glucopyranoside	f	Kashiwada, Nonaka, and Nishioka, 1986; Nonaka and Nishioka, 1983
95	(+)-catechin-7-*O*-β-*D*-glucopyranoside	f	Kashiwada, Nonaka, and Nishioka, 1986; Nonaka and Nishioka, 1983
96	(+)-catechin-3′-*O*-β-*D*-glucopyranoside	f	Kashiwada, Nonaka, and Nishioka, 1986
97	(+)-catechin-4′-*O*-β-*D*-glucopyranoside	f	Kashiwada, Nonaka, and Nishioka, 1986
98	(+)-catechin-3′,7-di-*O*-β-*D*-glucopyranoside	f	Kashiwada, Nonaka, and Nishioka, 1986
99	(+)-catechin-3′,5-di-*O*-β-*D*-glucopyranoside	f	Kashiwada, Nonaka, and Nishioka, 1986
100	(+)-catechin-4′,5-di-*O*-β-*D*-glucopyranoside	f	Kashiwada, Nonaka, and Nishioka, 1986
101	(+)-catechin-3′,4′-di-*O*-β-*D*-glucopyranoside	f	Kashiwada, Nonaka, and Nishioka, 1986
102	(+)-catechin-8-*C*-β-*D*-glucopyranoside	f	Kashiwada, Nonaka, and Nishioka, 1986
103	(+)-catechin-6-*C*-β-*D*-glucopyranoside	f	Kashiwada, Nonaka, and Nishioka, 1986
104	(−)epicatechin-3-*O*-gallate	b, c, g	Tan, 2006; Komatsu *et al*, 2006; Nonaka *et al*, 1981; Jin, 2006
105	(−)epigallocatechin-3-*O*-gallate	c	Tan, 2006
106	procyanidin B-1-8-*C*-β-*D*-glucopyranoside	f	Kashiwada, Nonaka, and Nishioka, 1986; 1984
107	procyanidin B-1-6-*C*-β-*D*-glucopyranoside	f	Kashiwada, Nonaka, and Nishioka, 1986
108	procyanidin B-2-8-*C*-β-*D*-glucopyranoside	f	Kashiwada, Nonaka, and Nishioka, 1986
109	procyanidin B-2-6-*C*-β-*D*-glucopyranoside	f	Kashiwada, Nonaka, and Nishioka, 1986
110	procyanidin B-1	f	Kashiwada, Nonaka, and Nishioka, 1986
111	procyanidin B-2	f	Kashiwada, Nonaka, and Nishioka, 1986
112	procyanidin B-1-3-*O*-gallate	f	Kashiwada, Nonaka, and Nishioka, 1986; Nonaka *et al*, 1981
113	Procyanidin B-2-3′-*O*-gallate	f, g	Komatsu *et al*, 2006; Kashiwada, Nonaka, and Nishioka, 1986
114	procyanidin B-2-3,3′-di-*O*-gallate	f, g	Komatsu *et al*, 2006; Kashiwada, Nonaka and Nishioka, 1986; Nonaka *et al*, 1981
115	procyanidin B-3-7-*O*-β-*D*-glucopyranoside	f	Kashiwada, Nonaka, and Nishioka, 1986
116	procyanidin B-3	f	Kashiwada, Nonaka, and Nishioka, 1986
117	procyanidin B-4	f	Kashiwada, Nonaka, and Nishioka, 1986

(To be continued)

(Continued Table 4)

No.	Compounds	Botanical sources	References
118	procyanidin B-4-3′-*O*-gallate	f	Kashiwada, Nonaka, and Nishioka, 1986
119	procyanidin B-7	f	Kashiwada, Nonaka, and Nishioka, 1986
120	procyanidin B-7-3-*O*-gallate	f	Kashiwada, Nonaka, and Nishioka, 1986
121	procyanidin B-5-3,3′-di-*O*-gallate	f	Kashiwada, Nonaka, and Nishioka, 1986
122	procyanidin B-5	f	Kashiwada, Nonaka, and Nishioka, 1986
123	epicatechin-(4β→8)-epicatechin-(4β→8)-catechin	f	Kashiwada, Nonaka, and Nishioka, 1986
124	procyanidin C-1-3,3′-di-*O*-gallate	f	Kashiwada, Nonaka, and Nishioka, 1986
125	procyanidin C-1-3,3′,3″-tri-*O*-gallate	f	Kashiwada, Nonaka, and Nishioka, 1986
126	3-*O*-galloylepicatechin-(4β→8)-3-*O*-galloylepicatechin-(4β→8)-catechin	f	Kashiwada, Nonaka, and Nishioka, 1986
127	procyanidin C-1	f	Kashiwada, Nonaka, and Nishioka, 1986
128	epicatechin-(4β→6)-epicatechin-(4β→8)-catechin	f	Kashiwada, Nonaka, and Nishioka, 1986
129	3-*O*-galloylepicatechin-(4β→6)-3-*O*-galloylepicatechin-(4β→8)-catechin	f	Kashiwada, Nonaka, and Nishioka, 1986
130	epicatechin-(4β→6)-epicatechin-(4β→6)-catechin	f	Kashiwada, Nonaka, and Nishioka, 1986
131	3-*O*-galloylepicatechin-(4β→6)-3-*O*-galloylepicatechin-(4β→6)-catechin	f	Kashiwada, Nonaka, and Nishioka, 1986
132	epicatechin-(4β→8)-epicatechin-(4β→6)-catechin	f	Kashiwada, Nonaka, and Nishioka, 1986
133	3-*O*-galloylepicatechin-(4β→8)-3-*O*-galloylepicatechin-(4β→6)-catechin	f	Kashiwada, Nonaka, and Nishioka, 1986
134	3-*O*-galloylepicatechin-(4β→6)-3-*O*-galloylepicatechin-(4β→8)-catechin	f	Kashiwada, Nonaka, and Nishioka, 1986
135	rhatannin	g	Nonaka *et al*, 1981; Komatsu *et al*, 2006
136	RG-tannin	g	Komatsu *et al*, 2006
137	gallic acid	a, d, e, g	Komatsu *et al*, 2006; Nonaka *et al*, 1981; Wang, Li, and Wu, 2003; Xu *et al*, 2009; Zhao, Chang, and Du, 2002

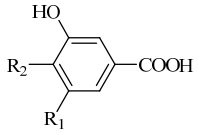
Note: a: *R. palmatum*; b: *R. tanguticum*; c: *R. officinale*; d: *R. franzenbachii*; e: *R. rhizastachyun*; f: *Choukichio*; g: *Daio*

Pharmacological activities

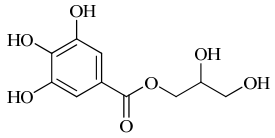
Studies have demonstrated that rhubarb exhibited comprehensive biological activites *in vitro* such as cathartic, anticancer, hepatoprotective, anti-inflammatory, analgesic, antibacterial, anti-oxidative, and antimutagenic effects. In addition, rhubarb also showed a positive effect on diabetic nephropathy (DN) in the clinic.

Cathartic effect

Rhubarb is well-known for its strong cathartic and diuretic effects, which are closely correlated with water adjustment of colon and kidney by the theory of TCM. Recent studies on the relationship between the formation and the effects indicated that anthraquinone glycosides with 1,8-di-hydroxy and without hydroxyl at the 2, 3, 6, and 7 positions, such as emodin, rhein, and chrysophanol, had fairly obvious effects of "Watery Diarrhea". Aquaporins (AQPs) are a group of conveying membrane proteins associated with the transmembrane aquatic transport. AQPs are abundantly expressed in colonic epithelial cells. The abnormal expression of AQPs could lead to the less absorption of water in colon and / or the more secretion of intestinal juice, suggesting that AQPs might be one kind of the effector molecules (Li *et al*, 2008). For example, chrysophanol and emodin inhibited the genetic transcription and the translation of AQP2 gene in LoVo cells, indicating that the cathartic effect of rhubarb might be due to the changes of AQP2 expression regulated by chrysophanol. It is likely that the expression of AQP2 is regulated through PKA signal pathway (Zhang, Li, and Bao, 2008; Liu *et al*, 2009). At the same time, total anthraquinone of rhubarb could effectively inhibit the expression of AQP4 in rat's proximal colon, and rhein-emodin could suppress the AQP4 express in LoVo cells *in vitro*. One mechanism of cathartic effect of



138 R1＝O-Glu R2＝H
139 R1＝H R2＝O-Glu
140 R1＝O-Glu-(6′-O-G) R2＝OH
141 R1＝OH R2＝O-Glu-(6′-O-G)



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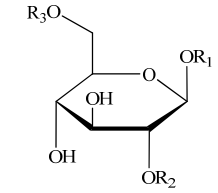
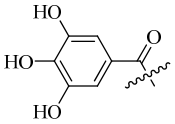
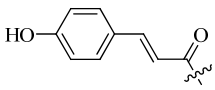


glucopyranosyl-galloyl-

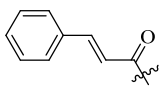
G:



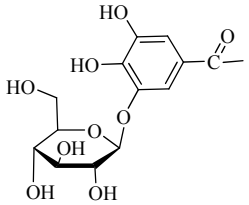
p-coum:



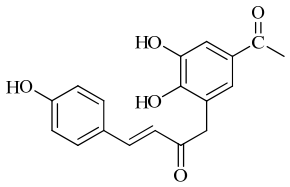
Cinn:



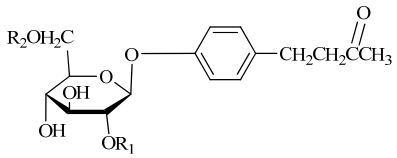
coumaroyl-*O*-galloyl-



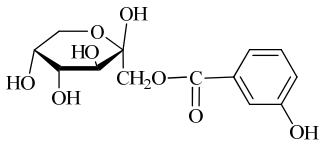
143 R_1＝R3＝H R_2＝Cinn
145 R_1＝G R_2＝*p*-coum R_3＝H
147 R_1＝H R_2＝R_3＝G
149 R_1＝R_2＝H R_3＝Cinn
151 R_1＝R_3＝G R_2＝Coum
153 R_1＝R_2＝R_3＝G
155 R_1＝R_2＝H R_3＝G
157 R_1＝R_2＝G R_3＝H
159 R_1＝R_2＝R_3＝coumaroyl-galloyl



144 R_1＝R_3＝G R_2＝Cinn
146 R_1＝G R_2＝Cinn R_3＝H
148 R_1＝G R_2＝H R_3＝Cinn
150 R_1＝R_2＝G R_3＝Coum
152 R_1＝G R_2＝coum R_3＝H
154 R_1＝R_3＝G R_2＝H
156 R_1＝G R_2＝R_3＝H
158 R_1＝R_2＝R_3＝glucopyranosyl-galloyl



160 R_1＝R_2＝G
161 R_1＝G R_2＝*p*-coum R_3＝H
162 R_1＝G R_2＝*p*-coum
163 R_1＝H R_2＝G
164 R_1＝G R_2＝H
165 R_1＝H R_2＝H



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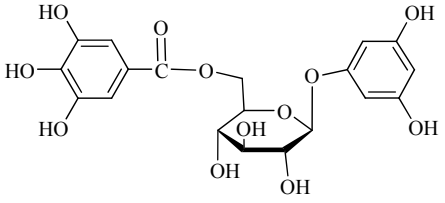

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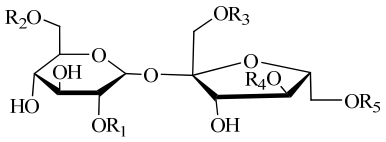

168 R_1＝R_2＝R_3＝R_4＝H R_5＝G
169 R_1＝R_2＝R_3＝R_5＝H R_4＝G
170 R_1＝R_2＝R_3＝R_5＝H
171 R_1＝R_4＝H R_5＝R_2＝R_3＝G
172 R_1＝G R_2＝R_3＝R_4＝R_5＝H

Fig. 5 Strctures of acylglucosides isolated from plants in *Rheum* L.

Table 5 Acylglucosides isolated from plants in *Rheum* L.

No.	Compounds	Botanical sources	References
138	gallic acid 3-*O*-β-*D*-glucopyranoside	c	Kashiwada, Nonaka, and Nishioka, 1986
139	gallic acid 4-*O*-β-*D*-glucopyranoside	c	Kashiwada, Nonaka, and Nishioka, 1986
140	gallic acid 3-*O*-β-*D*-(6′-*O*-galloyl)glucopyranoside	d	Nonaka and Nishioka, 1983
141	gallic acid 4-*O*-β-*D*-(6′-*O*-galloyl)-glucopyranoside	d	Nonaka and Nishioka, 1983
142	1-*O*-galloylycerol	d	Nonaka and Nishioka, 1983
143	2-*O*-cinnamoyl-β-*D*-glucose	e	Kashiwada, Nonaka, and Nishioka, 1984
144	2-*O*-cinnamoyl-1,6-di-*O*-galloy-β-*D*-glucose	e	Kashiwada, Nonaka, and Nishioka, 1984
145	2-*O*-p-coumaroyl-1-*O*-galloy-β-*D*-glucose	e	Kashiwada, Nonaka, and Nishioka, 1984
146	2-*O*-cinnamoyl-1-*O*-galloy-β-*D*-glucose	e	Kashiwada, Nonaka, and Nishioka, 1984
147	2,6-di-*O*-galloyglucose	f	Kashiwada, Nonaka, and Nishioka, 1984
148	1-*O*-galloyl-6-*O*-cinnamoyl-β-*D*-glucose	g	Kashiwada, Nonaka, and Nishioka, 1988
149	1,2-di-*O*-galloyl-6-*O*-cinnamoyl-β-*D*-glucose	g	Kashiwada, Nonaka, and Nishioka, 1988
150	1,2-di-*O*-galloyl-6-*O*-*p*-coumaroyl-β-*D*-glucose	h	Kashiwada, Nonaka, and Nishioka, 1988
151	1,6-di-*O*-galloyl-2-*O*-*p*-coumaroyl-β-*D*-glucose	i	Kashiwada, Nonaka, and Nishioka, 1988
152	2-*O*-galloyl-β-*D*-glucose	i	Kashiwada, Nonaka, and Nishioka, 1988
153	1,2,6-tri-*O*-galloyglucose	k	Nonaka *et al*, 1981
154	1,6-di-*O*-galloylycerol-β-*D*-glucopyranoside	d, e	Nonaka and Nishioka, 1983 ; Kashiwada, Nonaka, and Nishioka, 1984
155	6-*O*-galloylglucose	d, f	Nonaka and Nishioka, 1983; Kashiwada, Nonaka, and Nishioka, 1984
156	1-*O*-galloyl-β-*D*-glucose	e	Kashiwada, Nonaka, and Nishioka, 1984
157	1,2-di-*O*-galloyl-β-*D*-glucose	g, h, i	Kashiwada, Nonaka, and Nishioka, 1988
158	glucopyranosyl-galloyl-glucose	l	Wang *et al*, 2011
159	coumaroyl-*O*-galloyl-glucose	l	Wang *et al*, 2011
160	4′-*O*-β-*D*-(2″,6″-di-*O*-galloyl)-glucopyranoside	d	Kashiwada, Nonaka, and Nishioka, 1986
161	4-(4′-hydtoxyphenyl)-2-butanone 4′-*O*-β-*D*-(2″-*O*-galloyl-6″-*O*-cinnamoyl)-glucopyranoside	d	Kashiwada, Nonaka, and Nishioka, 1986
162	4-(4′-hydtoxyphenyl)-2-butanone (2″-*O*-galloyl-6″-*O*-*p*-coumaroyl)-glucopyranoside	d	Kashiwada, Nonaka, and Nishioka, 1986
163	lindleyin	a, d	Nonaka *et al*, 1981; Gao *et al*, 2011; Kashiwada, Nonaka, and Nishioka, 1986
164	isolindleyin	d	Nonaka and Nishioka, 1983; Kashiwada, Nonaka, and Nishioka, 1986
165	4-(4′-hydtoxyphenyl)-2-butanone 4′-*O*-β-*D*-glucopyranoside	a, d	Kashiwada, Nonaka, and Nishioka, 1986; Gao *et al*, 2011
166	1-*O*-galloyfructose	e, f	Kashiwada, Nonaka, and Nishioka, 1984
167	3,5-dihydroxyphenol 1-*O*-β-*D*-(6-*O*-galloyl)-glucopyranoside	f	Kashiwada, Nonaka, and Nishioka, 1984
168	6′-*O*-galloylsucrose	b, j	Kashiwada, Nonaka, and Nishioka, 1988
169	4′-*O*-galloylsucrose	j	Kashiwada, Nonaka, and Nishioka, 1988
170	6-*O*-galloylsucrose	b, j	Kashiwada, Nonaka, and Nishioka, 1988
171	1′-*O*-galloylsucrose	b, j	Kashiwada, Nonaka, and Nishioka, 1988
172	2-*O*-galloylsucrose	b	Kashiwada, Nonaka, and Nishioka, 1988

Note: a: *R. tanguticum*; b: *R.coreanum*; c: *R. palmatum*; d: commercial rhubarbs; e: Batei-Daio; f: Imo-Daio; g: *R. palmatum*; h: Japanese rhubarb; i: North Korean rhubarbs; j: Chong-Gi-Huang; k: *Rhei Radix* et *Rhizoma*; l: *R. palmatum*

rhubarb anthraquinone was possibly related to its ability to down-regulate AQP4 expression (Zhang *et al*, 2008). AQP2 and AQP4 expression regulated by rhubarb presented a synchronous effect in the colon and kidney of rats, which was probably one mechanism of multiply effectiveness. In addition, rhubarb's drastic effect was highly associated with the increasing of 5-HT and content of 5-HT receptor in duodenum (Zhao *et al*, 2002).

Anticancer effect

A number of studies have shown that the main anthraquinones of rhubarb, such as emodin, aloe-emodin,

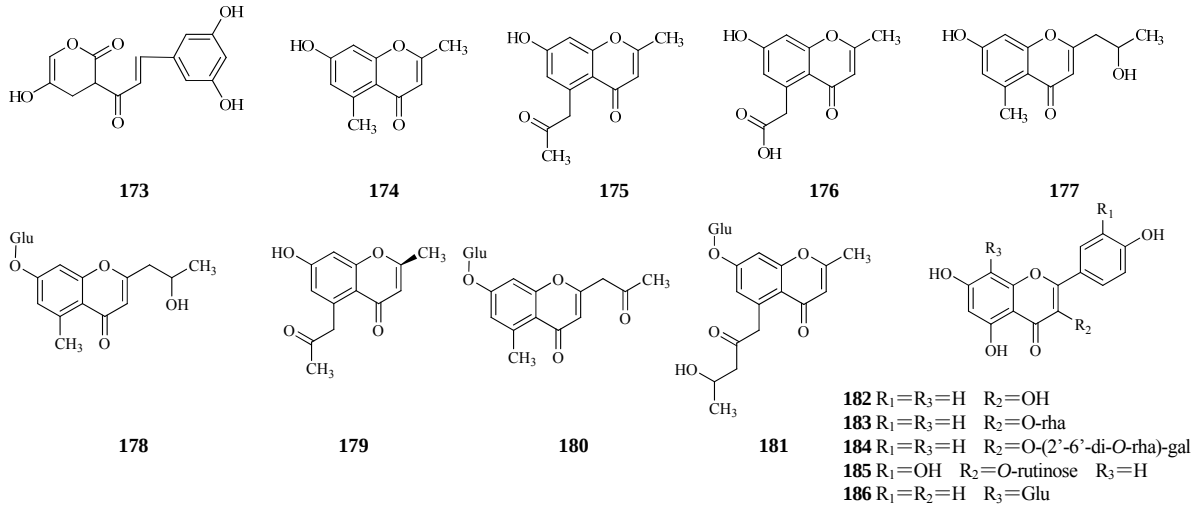

Fig. 6 Structures of pyrones isolated from plants in *Rheum* L.

Table 6 Pyranones isolated from plants in *Rheum* L.

No.	Compounds	Botanical sources	References
173	3-(3′,5′-dihydroxyl-*trans*-cinnamoyl)-5-hydroxyl-△^{5}-α-pyranone	a	Li *et al*, 1998
174	2,5-dimethyl-7-hydroxychromone	b, d	Wei, Wu, and Zhang, 2005; Kashiwada, Nonaka, and Nishioka, 1984
175	2-methyl-5-acetonyl-7- hydroxychromone	d	Kashiwada, Nonaka, and Nishioka, 1984
176	2-methyl-5-carboxymethyl-7-hydroxychromone	d	Kashiwada, Nonaka, and Nishioka, 1984
177	2-(2′-hydroxypropyl)-5-methyl-7-hydroxychromone	d	Kashiwada, Nonaka, and Nishioka, 1984
178	2-(2′-hydroxypropyl)-5-methyl-7-hydroxychromone-7-*O*-β-*D*-glucopyranoside	d	Kashiwada, Nonaka, and Nishioka, 1984
179	2-methyl-5-carboxymethyl-7-hydroxychromone	d	Kashiwada, Nonaka, and Nishioka, 1984
180	aloesone-7-*O*-β-*D*-glucopyranoside	d	Kashiwada, Nonaka, and Nishioka, 1990
181	2-methyl-5-(2′-oxo-4′-hydroxypentyl)-7-hydroxychromone-7-*O*-β-*D*-glucopyranoside	d	Kashiwada, Nonaka, and Nishioka, 1990
182	kaempferol	d	Kashiwada, Nonaka, and Nishioka, 1984; Han *et al*, 1994
183	kaempferol-3-*O*-rhamnoside	c, d	Han, Oh, and Whang1994
184	kaempferol-3-*O*-(2′,6′-di-*O*-rhamnopyranosyl)-β-*D*-galactopyra-noside	c	Han *et al*, 1994
185	quercetin-3-*O*-rutinoside	d	Kashiwada, Nonaka, and Nishioka, 1990
186	apigenin-8-*O*-β-*D*-glucoside	d	Kashiwada, Nonaka, and Nishioka, 1990

Note: a: *R. hotaoense*; b: *R. glabricaule*; c: *R. undulatum*; d: commercial rhubarb

and rhein could inhibit the growth and the proliferation of various cancer cells. Emodin reportedly inhibited the proliferation of ovarian, breast, lung, liver, and prostate cancer cells. Emodin could induce the apoptosis alone and sensitize the ovarian cancer cells to paclitaxel induced apoptosis. At the same time, emodin could inhibit the tumor invasion ability by down-regulating the expression of macrophage migration inhibitory factor (MIF), matrix metalloproteinase-2 (MMP-2), and matrix metalloproteinase-9 (MMP-9) in ovarian cancer cells (Li, 2009). Emodin could also induce the apoptosis of CBRH-7919 cells *in vitro* by up-regulating the expression of apoptosis-inducing factor (AIF) and endonuclease G (EndoG), and emodin combined with 5-fluorouracil (5-Fu) could sensitize HepG2 cells to induce apoptosis in a time-dependent manner (Zhang, Guang, and Yang, 2007; Li *et al*, 2009). In prostate cancer cell line, LNCaP, emodin inhibited the proliferation by androgen receptor (AR) and p53-p21 pathways, and induced the apoptosis via mitochondrial pathway (Yu *et al*, 2009). Emodin showed the inhibition on the growth, metastasis, and angiogenesis of pancreatic cancer, possibly via the down-regulation of nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB), and the inhibition of NF-κB regulated factors, vascular endothelial growth factor (VEGF), MMP-2, MMP-9, eNOS, and survivin excretion (Lin, 2011). Besides, emodin had the effect of

reducing tumor cell's adhesion to HUVECs by down-regulating the expression of adhesion molecules (Zeng, Ke, and Zhu, 2008). Moreover, emodin induced the apoptotic death in murine leukemia WEHI-3 cells and enhanced the phagocytosis in the leukemia animal model (Chang *et al*, 2011). These data suggested that emodin was potentially useful in cancer therapy. However, emodin (120 and 80 μg/mg) showed a weak mutagenicity in TK gene mutation analysis (Zhu, Chen, and Zhang, 2011).

Aloe-emodin was also able to inhibit the cell growth in several tumor cells including human lung carcinoma (Lee *et al*, 2001; Yeh, Wu, and Lee, 2003), lung adenocarcinoma (Wu, 2007), hepatoma (Kuo, Lin, and Lin, 2003), gastric cancer (Fu, 2006; Xiao *et al*, 2008), and leukemia cell lines (Chen *et al*, 2004). Pecere *et al* (2000; 2003) reported that aloe-emodin had a specific *in vitro* and *in vivo* antineuroectodermal tumor activity. Aloe-emodin could interact with DNA by intercalation and have potential genetic toxicity (Li *et al*, 2010).

Rhein had also been reported to display synergistic antitumor effects. Recent study demonstrated for the first time that cell cycle S-phase arrest was one of the mechaisms of rhein in the inhibition of human hepatocelluar carcinoma BEL-7402 cells. Rhein played the antitumor effects via down-regulation on oncogene c-Myc and apoptosis through the caspase-dependent pathway (Shi, Huang, and Chen, 2008). Many studies suggested that rhein induced the apoptosis in SCC-4-cells via caspase, reactive oxygen species (ROS), and mitochondrial death pathways (Lai *et al*, 2009; Liu, Fujii, and Hou, 2003). However, because of the poor aqueous solubility, the antitumor efficacy of rhein was limited *in vivo*. Lin *et al* observed the antitumor activity of rhein-lysinate *in vivo* and investigated its mechanism. The results suggested that rhein lysinate inhibited the proliferation of ovarian cancer (SKOV-3) and breast cancer cells (MCF-7M, SK-Br-3, and MDA-MB-231). Rhein lysinate inhibited the phosphorylation of epidermal growth factor receptor and extracellular signal-regulated kinase (MEK and ERK) with or without epidermal growth factors (EGF) stimulation, as a result, increased the antitumor activity of Taxol *in vitro* and in athymic mice (Lin and Zhen, 2009; Lin *et al*, 2009). The results of these studies indicated that emodin, aloe-emodin, and rhein might be the active components for cancer chemoprevention and/or chemo-therapeutics. On the other hand, although sharing very similar chemical structure, physcion and chrysophanol showed no significant effect on the inhibition of cancer cell proliferation (Kuo *et al*, 1997; Chen *et al*, 2002).

Hepatoprotective effect

The ethanolic extract of rhubarb could prevent and treat hyperlipidemia and fatty liver in rabbits via reducing blood lipid. It was found that the administration of rhubarb extacts to rabbits could decrease total cholesterol (TC) and low-density lipoprotein cholesterol (LDL-C) in serum, increase high-density lipoprotein cholesterol (HDL-C) in serum, reduce liver fatty degeneration, and protect liver cell function (Xu *et al*, 2007). Sheng *et al* (2011) tested the effect of rhein on non-alcoholic fatty liver disease (NAFLD)-associated hepatic steatosis, insulin resistance, and the T helper (Th)1/Th2 cytokine inbalance in high-fat diet-induced obese (DIO) mice. The results indicated that rhein ameliorated NAFLD and associated disorders through LXR-mediated negative energy balance, metabolic regulatory pathways, and immunomodulatory activities involved in hepatic steatosis. The combinded effects of rhein to target hepatic metabolic and immune pathways might be beneficial for complex metabolic diseases such as NAFLD (Sheng *et al*, 2011). On the other hand, rhein could improve lipid metabolic disorder and insulin resistance, along with the status of hepatocyte steatosis and inflammatory cell infiltration, which indicated that rhein could prevent the development of nonalcoholic steatohepatitis (Li, Ying, and Zhu, 2007). Besides, rhein could inhibit the adipocyte differentiation and adipogenesis in the cultured cells and in rodent models of obesity by down-regulating the mRNA levels of PPARγ and C/EBPα, and their downstream target genes are reported to be important transcription factors for adipogenesis, lipogenesis, glucose metabolism, and fatty acid synthesis. The evidences implied that rhein was a potential candidate for preventing the mebabolic disorders (Liu *et al*, 2011). In addition, rhaponticin from RRR alleviated liver steatosis and improved blood glucose and lipid profiles in KK/Ay diabetic mice, which indicated that rhaponticin could be potentially

used as a new agent to treat type 2 diabetes mellitus and its complications (Chen *et al*, 2009).

Rhubarb also showed the protective effect against liver injury. It was reported that high dosage (40 g/kg) of rhubarb exhibited a significant protective effect on CCl_4-injured liver by reversing the biochemical parameters and histopathological changes. However, this hepatoprotective effect would be weakened, even be transferred to toxicity with increasing of the dose and administration times of rhubarb (Xing *et al*, 2011). In addition, aloe-emodin in the concentration of 10^{-4}—10^{-7} mol/L could significantly improve the number of cell viability and the level of glutathione (GSH). Meanwhile, it could also prevent the increase of alanine aminotransferase (ALT) and malondialdehyde (MDA) caused by CCl_4. Therefore, aloe-emodin could protect primary cultured rat hepatocytes from CCl_4-induced injury (Luo, 2003). Besides, rhein could also protect hepatocyte from CCl_4-induced and pig serum-induced injury, which suggested that rhein played a role in anti-oxidation, anti-inflammation by inhibiting the expression of transforming growth factor-β1 (TGF-β1) and connective tissue growth factor (CTGF) and suppressing the activation of hepatic stellate cells (Guo, 2003; Wang, 2009). Rhein might have the inhibitory activity on apoptosis of L-02 cell induced by tumor necrosis factor-α (TNF-α) and triglyceride (TG). The mechanism of effect might be due to up-regulating the expression of Bcl-2 or down-regulating the expression of Bax expression (Wang *et al*, 2006). Rhein, aloe-emodin, and physione all exhibited the protective effects on hepatocytes and cholangiocytes against alpha-naphthylisothio-cyanate-induced damage, whereas emodin and chrysophanol provided partial protection (Zhao *et al*, 2009). Besides anthraquinones, the polysaccharide extracted from *R. Tanguficum* increased the survival rate in thioacetamide model and decreased the malondialdehyde level in liver and the activities of alanine aminotransferase and glutamic-oxaloacetic transaminase in serum significantly. These protective actions might relate to its anti-oxidation (Liu *et al*, 2001).

Anti-inflammatory and analgesic activities

Yang *et al* (2003) investigated the effect of rhein and aloe-emodin on single cell [Ca^{2+}] dynamics and TNF-α production in normal and lipopolysaccharide (LPS)-stimulated peritoneal macrophages (PMφ) of rats. These results indicated that rhein could reduce the increase of [Ca^{2+}], and be the key of signal transduction pathway by inhibiting the TNF-α production in LPS-stimulated PMφ, whereas, aloe-emodin showed the complex effects on LPS-stimulated PMφ in a dose-dependent manner. At low concentration, aloe-emodin could attenuate the transient increase of $[Ca^{2+}]_i$ induced by LPS. The inhibitory effect of aloe-emodin on LPS-induced TNF-α production decreased with the increasing of concentration. Rhein could enhance the inhibitory activity of aloe-emodin on the increase of [Ca^{2+}] induced by LPS (Liu *et al*, 2001; Chen *et al*, 2007). Aloe-emodin blocked phytohemagglutinin (PHA)- and IL-2-induced proliferation of T lymphocytes and the mechanism for these might be due to its inhibition on [Ca^{2+}] mobilization (Li *et al*, 2008; 2010). On the other side, aloe-emodin could significantly inhibit LPS-induced nitric oxide (NO) production through suppressing inducible NO synthase (NOS) expression at mRNA level in a dose- and time-dependent manner to exert anti-inflammatory effects (Li *et al*, 2010). Aloe-emodin might also inhibit the inflammatory mediators to decrease the levels of PAF, IL-6, and TNF-α during the acute pancreatitis (AP) in rats (Li *et al*, 2009). Meanwhile, emodin reduced inflammatory response in the rat lung following severe acute pancreatitis by negatively modulating the mRNA expression of IL-1β and IL-6 and positively modulating the mRNA expression of IL-10 (Cha, 2005). Yin *et al* (2010) studied the protective effect of rhein-arginine on rat's ankylenteron and explored the anti-inflammatory mechanism. The results showed that rhein-arginine could significantly relieve the experimental testinal adhesion, obviously decrease the levels of IL-1β and TNF-α, and inhibit the hyperplasia of fibrous connective tissue. That is to say, rhein-arginine could effectively prevent the formation of postoperative ankylenteron by inhibiting the expression of inflammatory cytokines and reducing the inflammatory response.

Diabetic nephropathy

Diabetic nephropathy (DN) is one of the main complications in patients with diabetes. The patho-physiological mechanism for the development and progression of DN is not clear, but it had been

suggested that DN was influenced by some genetic factors like apolipoprotein E (Eto, 2002), the overexpression of glucose transporter 1 (GLUT1) in mesangial cells (Brosius and Heiling, 2005; Wang *et al*, 2010), and the over-activity of the hexosamine pathway (Zheng *et al*, 2008). Clinical trial showed that rhubarb had positive effect on DN. As the main active ingredients of rhubarb, rhein exhibited protective effects on kidney. Choi *et al* (2006) investigated the antidiabetic action of 70% ethanol extract of RRR in streptozotocin-induced diabetic mice. The results showed that the crude extract improved the glucose intolerance by enhancing insulin-stimulated glucose uptake and decreasing carbohydrate digestion via inhibiting alpha-glucoamylase activity. Rhein and rhaponticin were potential candidates for hypoglycemic agents. The renal gene expression profile of DN in db/db mice was explored and the candidate genes through which effects of rhein on DN were revealed (Liu *et al*, 2002). Gao *et al* (2010) found that, compared with the simvastatin group, the urinary albumin excretion (UAE) was reduced after eight weeks of treatment and the levels of extracellular matrix (ECM) decreased significantly after the full treatment in the rhein group. More powerful effects of rhein on decreasing the transforming growth factor-beta 1 (TGF-β1) and fibronectin immunohistochemistry expression in renal tissue were also observed. Besides, the plasma level of cholesterol (Chol), TG, LDL-C, and ApoE were all decreased. These results suggested that rhein could regulate dyslipidemia. Therefore, rhein could be a potential new drug candidate to decrease the lipid level and protect the cell against DN progression in a different fashion (Gao *et al*, 2010). The effect of rhein on cell hypertrophy and accumulation of ECM in the renal tubular epithelial cells was investigated as well. The results indicated that rhein could inhibit the cell hypertrophy and ECM accumulation in LLC-PK-1 cells induced by TGF-β1 (Guo *et al*, 2001). TGF-β1 stimulated the glucose uptake in mesangial cells through upregulation of GLUT 1 expression. Many researches showed that rhein antagonized the effect of TGF-β1 in mesangial cells (Liu *et al*, 2001; Zhang *et al*, 1999; Liu, Li, and Zhang, 1999; Zhu, Liu, and Li, 2001). Rhein in combination with benazepril could reduce the urinary albumin excretion of mice after 4-week treatment and lower the plasma creatinine level significantly. Furthermore, after administration of the combined drug, all the body weight, plasma glucose, Chol, TG, and LDL decreased. Histological morphometric analysis revealed that the whole glomerular area and ECM area were significantly reduced by comparing to the control group. Using techniques of immunohistochemistry, Jia *et al* (2007) also found that the expression of fibronectin and TGF-β1 decreased by comparing with the control group. This demonstrated that rhein and benazepril might have a similar renal protective effect in DN. This result also suggested that compound drug of rhein and angiotensin-converting enzyme inhibitor (ACEI) provided a more effective therapy for DN than separate agent.

Other

Rhein could inhibit adipocyte differentiation and adipogenesis in the cultured cells and in the rodent models of obesity, and was a potential candidate for preventing metabolic disorders (Liu *et al*, 2011). Rhubarb could be used to protect gut barrier, maintain intestinal micro-ecological environment, and prevent bacterial translocation (Chen, Ma, and Liu, 2009; Chen and Wang, 2009). Emodin was found to have anti-herpes simplex virus (HSV) activity *in vitro* and *in vivo*, and thus was a promising agent in the clinical therapy of HSV infection (Xiong *et al*, 2011). Emodin inhibited TNF-α-induced human aortic smooth-muscle cell (HASMC) proliferation via a caspase- and mitochondrial-dependent apoptotic pathway. This indicated that emodin had the potential to be an anti-atherosclerosis agent (Heo *et al*, 2008). The hypothesis was confirmed by an experiment in which systemic administration of aloe-emodin, immediately before (0.5 h) and after intervention, could effectively inhibit myointimal proliferation after balloon injury of the rabbit iliac artery *in vivo* and might be useful in the vascular remodeling. It seemed that this agent might be useful in the prevention from coronary restenosis (Yin, Xu, and Wang, 2005). In addition, Yang *et al* (2004) suggested that natural anthraquinone deriatives could be used as ROS generators to increase the susceptibility of tumor cells to cytotoxic therapertic agents. The results of Zhang's experiment showed that rhapontigenin protected V79-4 cells against oxidative damage by enhancing the cellular anti-oxidant activity

and modulating the celluar signal pathways (Zhang *et al*, 2007). The anti-oxidant activity of chloroform and methanol extracts from the roots and stems of *R. ribes* was investigated (Öztük *et al*, 2007).

Toxicological effects

Wang *et al* (2009) assessed the value and toxic potential of rhubarb to treat the chronic renal failure (CRF), and the result indicated that there was an evidence of protective effect to CRF rats while the incidences of hepatotoxicity with the minimal to mild hyaline droplets were also observed in normal rats. With canonical correlation analysis the sequence of hepatic and renal toxicity of constituents in rhubarb was found as follows: total anthraquinones glucosides (AQGs) > tannins (Tns) > total anthraquinones (AQs); aloe-emodin (AE) > physcione (Ph) > rhein (Rn) > emodin (Ed) > chrysophanol (Ch) and AEG > PhG > ChG > EdG > RnG of glycosyl-anthraquinones (Wang *et al*, 2009). Different processings (i.e. alcohol- and vinegar-processing, steaming, and carbonization) could cause the decline of the contents of both anthraquinone glycosides and tannins, and thus attenuate the toxicity of crude drug of rhubarb. It was also suggested that the alanine aminotransferase and creatine in serum would be useful to monitor the hepatic and renal toxixity of rhubarb. In addition, raw rhubarb had more tissue toxicity than steamed rhubarb and rhein might be one of the major poisonous ingredients (Fang *et al*, 2011a).

Quality evaluation

Because multiple components are responsible for the therapeutic effects, quality control is indispensable for ensuring the safety and efficacy of rhubarbs. A variety of analytical techniques are currently applied for quality evaluation. Sun and Zeng (2000) separated the anthraquinones in free and combining state by using thin layer chromatography (TLC) and determined their cotents by TLC-scanning method. In a similar way, Zhu, Fu, and Han (2001) determined emodin in raw and processed rhubarb, as well as their extractions. The results showed that the contents of emodin were significantly different, and the clinical usage of them should be differentiated. The main chemical constituents, including anthraquinones, mono-glycosides, water-soluble anthraquinone glycosides, phenybutanones, stilbenes, tannins, and related compounds, were analyzed by HPLC technique. The active tannins, amino acids, volatile oil, and trace elements were also analyzed (Zheng and Guo, 2007). Wang *et al* (2005) investigated the differences of the active components in the different parts of rhubarb (the head, the body, and the end part of the root) from genuine medicinal materials in Gansu province. The results showed that the significant differences exhibited in the HPLC fingerprints of different parts of rhubarb. The contents of the active components, such as emodin and chrysophanol, decreased progressively from the head and body parts to the end part of root. The chemical constituent pattern of different rhubarbs was also clearly characterized by quantification of 30 major constituents from the different botanical origins in rhubarb using a new HPLC method (Komatsu *et al*, 2006). Besides, a cyclodextrin-modified micellar electrokinetic chromatographic (CD-MEKC) method was established to determine five hydroxyl-anthraquinoids in rhubarb. This proposed method was validated and successfully applied for the determination of components in two commercial rhubarb samples (Shang *et al*, 2002). Microemulsion electrokinetic chromatography (MEEKC) is another kind of method that has been developed for the analysis of nine anthraquinones and bianthrones in rhubarb (Sun *et al*, 2005). Wang *et al* (2011) developed a simple and rapid ultra-performance liquid chromatography method coupled with photo-diode array (UPLC-PDA) to simultaneously determine seven anthraquinones (sennoside B, sennoside A, aloe-emodin, rhein, emodin, chrysophanol, and physcion) in aqueous extract of rhubarb. Using a facile method based on LC-MS^n, a total of 107 phenolic compounds from official (*R. officinale*, *R. palmatum*, and *R. tanguticum*) and unofficial species (*R. franzenbachii*, *R. hotaoense*, and *R. emodi*), were identified or tentatively characterized based on their mass spectra. The results showed that there were some significant differences in chemical composition of rhubarbs, and it was advisable that different species should be used separately in clinical practice (Ye *et al*, 2007).

Pharmacokinetic studies

Wang *et al* (2011) evaluated the intestinal absorption characteristic of the mixture from rhubarb

free anthraquinones (aloe-emodin, rhein, emodin, physcion, and chrysophanol) in rats and the rat single-pass intestinal perfusion experimental result showed that anthraquinones were absorbed in the different segments of intestine. Yan and Ma (2007) established and validated a sensitive HPLC method with fluorescence detection (excitation 435 nm and emission 515 nm) for the quantification of five anthraquinones (aloe-emodin, rhein, emodin, physcion, and chrysophanol) in rat plasma. This method was suitable for the simultaneous quantification of five anthra-quinones in rat plasma and thus determining the pharmacokinetics of anthraquinones in Xiexin decoction. Fang *et al* (2011b) determined the concentration of free anthraquinones in different tissues and evaluated their toxic effects on the liver or kidney in normal rats and in rats with CCl_4-induced liver damage. The results suggested that the tissue toxicity caused by accumulation of anthraquinones was higher in normal animals than that in pathological models. In order to provide some references for clinical use, an attempt was made to access the safety of rhubarb to both immature and aged rats. The immature and aged rats showed reversed responses to the toxic potential of rhubarb extract. Elderly subjects were susceptible to the toxicity of high-dose rhubarb, which drove rigorous consideration on rational use of rhubarb to aged people (Wang *et al*, 2011). Wu *et al* (2009) studied the comparison of pharmacokinetic characteristics of different particle diameters in rhubarb powder in rabbits and suggested that the rhubarb ultra-fine powder could promote the absorption of active ingredients in rhubarb and increase bioavailability of rhubarb powder. Tang *et al* (2006) found that the pharmacokinetics of chrysophanol after iv administration showed a rapid distribution and effect, the elimination was main process, and the retention time was long. Peng and Deng (2010) established a simple method for simultaneous determination of rhein and emodin in mouse plasma by RP-HPLC, which could be used for the analysis of biological samples containing rhein and emodin and for pharmacokinetic study. Raal *et al* (2009) showed that *trans*-resveratrol alone and hydroxylstilbenes of rhubarb (*R. rhaponticum* L.) root reduce liver damage induced by chronic ethanol administration.

Application and development in clinical therapy

RRR, together with *Ginseng Radix*, *Rehmannia Radix*, and *Aconitum Radix*, is one of the most popular CMM and has a wide range of clinical applications and development potentials not only in the single herb but also in official Chinese patent medicines containing rhubarb. To the best of our knowledge, about 800 prescriptions containing rhubarb such as *Dachengqi* Decoction, *Taohechengqi* Decoction, *Maziren* Pill, and *Daxianxiong* Decoction are recorded in *Chinese Pharmacopoeia* and local drug standards. Modern clinical research has proved that rhubarbs combined with other drugs possess the positve effects on many diseases. For instance, rhubarb compound prescriptions had a significant effect on infantile pneumonia medicines and effectively treated vertigo (Feng, Sun, and Tian, 2011). Other than a cathartic, rhubarb roots were used to cure stomach ailments and used as a poultice to reduce fevers and relieve edema. Moreover, rhubarbs are also used in the treatment of digestive disease such as intestinal obstruction, constipation, dyspepsia, infantile anorexia, and hemobila. In the treatment of urinary disorders, rhubarbs are found to have therapeutic effect for chronic prostatitis, ovulation dysfunction, diabetes, and kidney disease azotemia. For the high cholesterol disease, oral rhubarb could improve the status of hemorheology property of blood, decrease blood viscosity, and lower the cholesterol and triglyceride levels. The lipid-lowering efficacy is superior to inositol nicotinate (Lu and Liu, 2003; Ding and Xu, 2004). Animal experiments have proved that rhubarb had the effect on reducing the fat and weight (Jiao *et al*, 1998). The roots of *R. rhaponticum* contain lindleyin possessing estrogen-like properties and its extract has been used as an effective treatment for menopausment.

Future perspectives

Rhubarb is one of the oldest and most frequently used herbal medicines in China, Korea, Japan, and other Asian countries. In the view of far-ranging applications of rhubarb, although many studies on the chemical constitutients, quality analysis, pharmacological activities, and clinical practices had been reported, there are still lots of questions waiting to be solved.

Up to date, there are about 200 compounds isolated from rhubarb, including anthraquinones, anthrones, stilbenes, flavonoids, acylglucosides, and pyrones, and most of the studies have focused on exploring the bioactivities of anthraquinones. However, the precise mechanisms underlying their activities are not fully understood. The studies on the bioactivities of other components, such as acylglucosides and tannins have rarely been reported. Given the complex bioactivities of CMM that might interact with multiple targets simultaneously, further studies on the synergistic mechanism of chemical compositions from rhubarb, and the potential toxic effects are still required.

To better evaluate the quality of rhubarb, suitable analytical methods need to be developed for the analysis of active ingredients in rhubarb. Sennoside A as an anthraquinone derivative is a typical laxative component in rhubarb, which is commonly used as one of the markers for the quality evaluation of rhubarb by means of chromatography or hyphenated techniques. However, such evaluation is incomplete because other constituents could possess different effects. Therefore, the development of a comprehensive analytical method for the characteristic of bioactive constituents in rhubarb is still necessary. The chromatographic fingerprints of CMM with the relatively unified criterion of the characteristics may be promising. In addition, futher studies on the quality evaluation based on bioassay are also required.

Finally, with the growing demand for rhubarb in domestic and international markets, excessive and predatory exploration has resulted in not only sharp drop in wild resources of rhubarb but also damage to the environment, which could affect the sustainability of regional economic development in the long term. In some regions, non-official rhubarbs have been used as commercial substitutes. However, considering that the quality of these rhubarbs varies widely, using these substitutes containg uncharacterized components could greatly affect the effectiveness of herbal medicines and even cause safety concerns. Therefore, the protection of wild resources and standard cultivation of rhubarb is also imperative.

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Latest Progress in Tianjin Press of Chinese Herbal Medicines

Four journals including *Chinese Traditional and Herbal Drugs* (CTHD), *Chinese Herbal Medicines* (CHM), *Drugs & Clinic* (DC), and *Drug Evaluation Research* (DER) are edited and published by Tianjin Press of Chinese Herbal Medicines.

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