Journal of Food Bioactives
International Society for Nutraceuticals and Functional Foods
Review
J. Food Bioact. 2019;8:42–50

Chemistry, pharmacology and processing method of rhubarb (*Rheum* species): a review

Jingwen He[a#], Jiachen Sun[a#*], Liang Wang[a], Yujia Luo[a], Weijian Gao[a], Hongxing Guo[b] and Hui Zhao[a]

[a]Tianjin Key Laboratory of Food and Biotechnology, School of Biotechnology and Food Science, Tianjin University of Commerce, Tianjin 300134, China
[b]The Third Central Clinical College, Tianjin Medical University, Jintang Road, Hedong, Tianjin 300170, China
[#]These authors contributed equally to this article.
[*]**Corresponding author:** Jiachen Sun, Tianjin Key Laboratory of Food and Biotechnology, School of Biotechnology and Food Science, Tianjin University of Commerce, Tianjin 300134, China. E-mail: sjcsunjiachen@foxmail.com
DOI: 10.31665/JFB.2019.8205
Received: July 08, 2019; **Revised:** November 11, 2019; **Accepted:** December 30, 2019
Citation: He, J., Sun, J., Wang, L., Luo, Y., Gao, W., Guo, H., and Zhao, H. (2019). Chemistry, pharmacology and processing method of rhubarb (*Rheum* species): a review. J. Food Bioact. 8: 42–50.

Abstract

Rhubarb is a Chinese traditional medicine. Ninety-four compounds belonging to five different classes of compounds (anthraquinone, anthrones, stilbenes, flavonoids and acylglucosides) have so far been identified in rhubarb. These constituents are effective in purgative, clearing heat-fire, removing toxic materials from the body, cooling blood and promoting blood circulation. Recent studies have shown that the appropriate processing methods may directly impact on its remedial activities and chemical compositions. Here, we provide a comprehensive review of the chemical compositions, pharmacological activities and processing methods of rhubarb.

Keywords: Rhubarb; Chemical composition; Pharmacological activities; Processing method.

1. Introduction

As a widely used Chinese herb, rhubarb is officially documented in Chinese Pharmacopoeia as the dried root and rhizome of *Rheum palmatum* L., *Rheum tanguticum* Maxim. ex Balf. or *Rheum officinale* Baill. (*Polygonaceae*) (China, 2015). In traditional Chinese medicine, Rhubarb is effective, short-lived and painless for the treatment of purging accumulation (*Qing-yu* in Chinese), cooling blood (*Liang-xue* in Chinese), and draining damp-heat (*Qu-nei-re* in Chinese).

The components isolated from rhubarb have been classified into five primary categories, namely, anthraquinone, anthrones, stilbenes, flavonoids and acylglucosides (Nonaka et al., 1977; Nonaka et al., 1981; Kashiwada et al., 1984; Kashiwada et al., 1986; Komatsu et al., 2006; Xing-Sheng et al., 2011). Drying, a crucial step in the post-harvest processes, can limit enzymatic degradation and microbial growth while preserving the beneficial properties of the plant material. Generally, during the drying process, the chemical compositions, content and pharmacological activities of the active principles may change, thus affecting the quality of Chinese herbal preparations. (Zhu et al., 2014). Consequently, this contribution summarizes the progress made in the chemical composition, pharmacological activities and processing methods of rhubarb in recent years.

2. Chemistry

Up to date, a variety of constituents have been isolated from *Rheum* species with their structures being elucidated. As an important traditional Chinese herb, the components of rhubarb have been classified into five primary categories, namely, anthraquinone, anthrones, stilbenes, flavonoids and acylglucosides.

2.1. Anthraquinones and anthrones

As an important type of components in rhubarb (compounds 1-30),

the free anthraquinones, such as aloe-emodin, rhein, emodin, chrysophanol and physcion, are present in nearly all *Rheum* species. In addition, the anthraquinone glycosides, such as aloe-emodin-8-*O*-β-*D*-glucoside, rhein-8-*O*-β-*D*-glucoside, chrysophanol-8-*O*-β-*D*-glucoside, emodin-8-*O*-β-*D*-glucoside and physcion-8-*O*-β-*D*-glucoside, are isolated from different species of rhubarb. In addition to those anthraquinones, the conjugated anthraquinone derivatives are responsible for their cathartic effects (Table 1), isolated from several rhubarbs.

Anthrones are less oxygenated than anthraquinones (compounds 31-56). Twenty-six anthrones were isolated from different species of rhubarb (Table 1). Among them, sennosides have been identified from *Rheum palmatum* L and include a number of anthraquinone derivatives and functioned as laxatives.

2.2. Stilbenes

Stilbenes, important components in chemotaxonomy (compounds 57-76), have been reported to show inhibit nitric oxide production, anti-bacterial, anti-fungal, anti-oxidant, anti-inflammatory, anti-cancer, and anti-malarial activities. Twenty stilbenes isolated from different species of rhubarb (Table 2) have reported in studies.

2.3. Flavonoids and acylglucosides

Being a large class of compounds that exist ubiquitously in different species of rhubarb, flavonoids contain several phenolic hydroxyl groups attached to ring structures, conferring antioxidant activity (compounds 77-82). There are four main flavonoids isolated from rhubarbs (Table 3).

Acylglucosides are considered to be important bioactive components in rhubarb (compounds 83-94). Twelve acyglucosides have been isolated from rhubarbs (Table 3) with most of them exhibiting excellent pharmacological activities.

3. Pharmacological activities

Rhubarb, the rhizome part of Rheum species including *Rheum palmatum*, *Rheum tanguticum*, *Rheum undulatum*, and *Rheum officinale*, is one of the oldest traditional medicines and is most commonly used as a purgative (Siegers et al., 1993). In addition, rhubarb has many other bioactive effects such as antibacterial, analgesic, and anti-inflammatory activities (Darias, 1987; Jong-Chol et al., 1987; Matsuda et al., 2001). Rhubarb possesses anticoagulant and anti-platelet activities have been reported and confirmed to be primarily associated with stilbene derivatives such as resveratrol, rhaponticin, and piceatannol (Aburjai, 2000; Park et al., 2002).

3.1. Purgative activities

Previous studies have suggested that diarrhea is associated with decreased Na^+/K^+-ATPase activity (Ejderhamn et al., 1989). Inhibition of this intestinal enzyme may be critical to the regulation and absorption of Na^+ and K^+ in the intestine, leading to intestinal fluid accumulation and contributing to diarrhea (Yakubu and Salimon, 2015). It showed that the purgative activities of the crude rhubarb could be determined approximately by analysis of sennoside content, whereas the correlation between purgative activity and sennoside content is not very strong, suggesting that other factors might be involved (HARIMA et al., 1994). Recent studies on the relationship between the chemical structure and functionality indicated that "Watery Diarrhea" effect induced by rhubarb was concerned with the location alteration or the expression change of Aquaporins (Li et al., 2008).

3.2. Anticancer activities

As have been demonstrated in a number of studies, as the main anthraquinones of rhubarb, emodin, aloe-emodin, and rhein could inhibit the growth and proliferation of various cancer cells. For example, emodin has been reported to inhibit proliferation in breast, lung, cervical, colorectal, and prostate cancers cells (Chan et al., 1993; Zhang et al., 1995; Chang et al., 1996; Kuo et al., 1997; Cha et al., 2005).

Emodin showed less or no cytotoxic effect in several normal cells, including HBL-100 cells derived from normal human breast tissue (Zhang et al., 1995), human fibroblast like lung WI-38 cells, and three primary cultured rat normal cells (Shieh et al., 2004). As have also been demonstrated, normal cells are more resistant to emodin-induced cytotoxicity than cancer cells. Such specificity of emodin towards malignant cells might be due to its effect targeting some oncogene signaling transductions, which are constitutively active or amplified in cancer cells (Chan et al., 1993).

Aloe-emodin was also able to inhibit cell growth in several tumor cells, including human lung carcinoma (Lee et al., 2001), hepatoma (Kuo et al., 2002), and leukemia cell lines (Chen et al., 2004). In addition, it exhibited higher cytotoxicity against oral squamous cell carcinoma and salivary gland tumor than normal human gingival fibroblasts (HGF) (Shi et al., 2001). Interestingly, high specificity for neuroectodermal tumor cells was exhibited in aloe-emodin (Pecere et al., 2003). According to Pecere' report, energy dependent incorporation of aloe-emodin may correspond to the higher sensitivity of neuroectodermal tumor cells (Pecere et al., 2000).

Rhein, another anthraquinone derivative of rhubarb, has also been reported to display an inhibitory effect on the proliferation of human breast, colon, lung, CNS, and glioma cancer cells (Cichewicz et al., 2004). In a recent study conducted by Zhou et al, rhein exhibited anti-fungal potential but was less cytotoxic than other anthraquinones in rhubarb (Zhou et al., 2006). Also, Huang et al. reported that rhein could effectively inhibit the uptake of glucose in tumor cells and induce cell necrosis (Huang et al., 2007).

Having been compared with other anthraquinone derivatives, such as emodin 1-*O*-β-*D*-glucoside, physcion, and physcion 1-*O*-β-*D*-glucoside, emodin with C1 and C3 position is believed to be important for the anti-tumor function (Kuo et al., 1997).

3.3. Hepatoprotective effect

The hepatoprotective effect of rhubarb and its components has also been documented as antagonizing α-naphthylisothiocyanate (ANIT)- and concanavalin A-induced experimental liver injury (Mase et al., 2010). A hepatoprotective effect of rhubarb against infantile cholestatic hepatitis and acute icteric hepatitis (Huang et al., 1997) have been revealed by some clinical evidence. Research has shown that free anthraquinones extracted from rhubarb, such as rhein and emodin, exhibited protective activity against ANIT-induced cholestatic liver injury by reducing the serum levels of glutamate-pyruvate transaminase, glutamic oxaloacetic transaminase and total serum bilirubin, direct bilirubin, alkaline phosphatase, γ-glutamyltransferase and total bile acids. The morpho-

Table 1. Anthraquinones and anthrone derivatives isolated from different species of rhubarb

No.	Compounds	Botanical sources	References
1	aloe-emodin	*R. officinale; R. palmatum; R. qinjingense; R. spiciforme; R. tanguticum; R. undulatum*	Xiuwei et al., 1998; Huiyan et al., 2003; Jin et al., 2006; Tan, 2006; Xu Qing et al., 2009; Gao and Liangliang, 2013
2	1-methyl-8-hydroxyl-9,10-anthraquinone-3-*O*-β-*D*-(6′-*O*-cinnamoyl) glucopyranoside	*R. glabrucaule*	Cun et al., 2010
3	6-methyl-aloe-emodin	*R. emodi*	Singh et al.
4	6-methyl-rhein	*R. emodi*	Singh et al., 2005
5	aloe-emodin-1-*O*-β-*D*-glucopyranoside	*R. undulatum*	Matsuda et al., 2001
6	aloe-emodin-3-(hydroxymethyl)-*O*-β-*D*-glucopyranoside	*R. palmatum; R. glabrucaule*	Wei et al., 2005; Xu Qing, 2009
7	aloe-emodin-8-*O*-β-*D*-glucopyranoside	*R. qinjingense; R. tanguticum*	Xiuwei et al., 1998; Jin, Ge et al., 2006
8	chrysaron	*R. rhaponticum*	Hesse, 1908
9	chrysophanol	*R. palmatum; R. tanguticum; R. officinale; R. emodi*	Suresh Babu et al., 2004; Jin, Ge et al., 2006; Tan, 2006; Xu Qing et al., 2009; Wang et al., 2010; Gao and Liangliang, 2013
10	chrysophanol-1-*O*-β-*D*-glucopyranoside	*R. palmatum*	Xu Qing et al., 2009
11	chrysophanol-8-Me ether	*R. glabrucaule*	Wei et al., 2005
12	chrysophanol-8-*O*-β-*D*-(6′-*O*-acetyl)-glucopyranoside	*R. emodi*	Krenn et al., 2004
13	chrysophanol-8-*O*-β-*D*-(6′-*O*-galloyl)-glucopyranoside	*R. undulatum*	Matsuda et al., 2001
14	chrysophanol-8-*O*-β-*D*-(6′-*O*-malonyl)-glucopyranoside	*R. qinjingense*	Xiuwei et al., 1998
15	chrysophanol-8-*O*-β-*D*-glucopyranoside	*R. palmatum; R. tanguticum; R. officinale; R. emodi; R. glabrucaule*	Suresh Babu et al., 2004; Jin et al., 2006; Tan, 2006; Wang et al., 2010; Gao and Liangliang, 2013; Xu Qing et al., 2009
16	citreorosein	*R. glabrucaule*	Wei et al., 2004
17	emodin	*R. palmatum; R. tanguticum; R. emodi; R. qinjingense; R. undulatum; R. Spiciforme*	Xiuwei et al., 1998; Huiyan et al., 2003; Suresh Babu et al., 2004; Jin et al., 2006; Xu Qing et al., 2009; Wang et al., 2010; Gao and Liangliang, 2013
18	emodin-1-*O*-β-*D*-glucopyranoside	*R. undulatum*	Ko, 2000
19	emodin-6-*O*-β-*D*-glucopyranoside	*R. palmatum*	Zhu et al., 2016
20	emodin-8-*O*-β-*D*-glucopyranoside	*R. emodi; R. glabrucaule*	Wei et al., 2005; Wang et al., 2010
21	emodin-8-*O*-β-*D*-glucopyranosyl-6-*O*-sulfate	*R. emodi*	Liselotte et al., 2004
22	emodin-gemtiobioside	*R. nanum*	Xiang et al., 2005
23	physcion	*R. palmatum; R. tanguticum; R. officinale; R. emodi; R. qinjingense*	Xiuwei et al., 1998; Suresh Babu et al., 2004; Jin et al., 2006; Tan, 2006; Xu Qing et al., 2009; Wang et al., 2010; Gao and Liangliang, 2013
24	physcion-1-*O*-β-*D*-glucopyranoside	*R. emodi*	Singh et al., 2016
25	physcion-8-*O*-β-*D*-gentiobioside	*R. officinale*	Holzschuh et al., 1982
26	physcion-8-*O*-β-*D*-glucopyranoside	*R. palmatum; R. emodi; R. qinjingense; R. undulatum*	Xiuwei et al., 1998; Ko, 2000; Xu Qing et al., 2009; Wang et al., 2010
27	revandchinone-3	*R. emodi*	Suresh Babu et al., 2004

Table 1. Anthraquinones and anthrone derivatives isolated from different species of rhubarb - *(continued)*

No.	Compounds	Botanical sources	References
28	rhein	*R. palmatum; R. tanguticum; R. undulatum; R. Spiciforme*	Xiuwei et al., 1998; Huiyan et al., 2003; Jin et al., 2006; Xu Qing et al., 2009; Gao and Liangliang, 2013
29	rhein-8-*O*-β-*D*-[6′-*O*-(3″-methoxyl malonyl)] glucopyranoside	*R. palmatum*	Cun et al., 2010
30	rhein-8-*O*-β-*D*-glucopyranoside	*R. palmatum*	Gao and Liangliang, 2013
31	10-hydroxycascaroside C	*R. emodi*	Krenn et al., 2004
32	10-hydroxycascaroside D	*R. emodi*	Krenn et al., 2004
33	10*R*-chrysaloin1-*O*-β-*D*-glucopyranoside	*R. emodi*	Krenn et al., 2004
34	cascaroside C	*R. emodi*	Krenn et al., 2004
35	cascaroside D	*R. emodi*	Krenn et al., 2004
36	cassialoin	*R. emodi*	Krenn et al., 2004
37	palmidin A	*R. palmatum*	Dequeker et al., 1964
38	palmidin B	*R. palmatum*	Dequeker et al., 1964
39	palmidin C	*R. palmatum*	Dequeker et al., 1964
40	rendin A	*R. palmatum*	LEMLI et al., 1964
41	rendin B	*R. palmatum*	LEMLI et al., 1964
42	rendin C	*R. palmatum*	LEMLI et al., 1964
43	revandchinone-1	*R. emodi*	Suresh Babu et al., 2004
44	revandchinone-2	*R. emodi*	Suresh Babu et al., 2004
45	revandchinone-4	*R. emodi*	Yamagishi et al., 1987
46	rheinoside A	*R. palmatum*	Yamagishi et al., 1987
47	rheinoside B	*R. palmatum*	Yamagishi et al., 1987
48	rheinoside C	*R. palmatum*	Yamagishi et al., 1987
49	rheinoside D	*R. palmatum*	Yamagishi et al., 1987
50	sennidin C	*R. palmatum*	Zwaving, 1965
51	sennoside A	*R. palmatum*	Oshio et al., 1974
52	sennoside B	*R. palmatum*	Oshio et al., 1974
53	sennoside C	*R. palmatum*	Oshio et al., 1974
54	sennoside D	*R. palmatum*	Oshio et al., 1974
55	sennoside E	*R. palmatum*	Oshio et al., 1974
56	sennoside F	*R. palmatum*	Oshio et al., 1974

logical alterations induced by ANIT in rats, including the necrosis of hepatocytes and biliary epithelial cells, as well as neutrophil infiltration and sinusoid congestion, were also alleviated by concurrent intragastric administration of these free anthraquinones (Zhao et al., 2009).

3.4. Anti-inflammatory activities

As have been shown in research, via activating NO/cGMP signaling, vascular smooth muscle can be dilated in aqueous extract, whose rhubarb treatment not only suppressed TNF-α-induced increase of proinflammatory and adhesion molecules in HUVECs, but also reduced the adhesion between U937 cells and HUVECs. The aqueous extract of rhubarb might have the potential to dilate vascular tissues and suppress the vascular inflammatory process, which may be closely related to the activation of vascular NO/cGMP signaling (Moon et al., 2006). Emodin exerted an anti-inflammatory effect through blocking of MAPK and PI3K pathway signaling and inhibition of the activation of NF-κB and iNOS expression (Zhu et al., 2011). Meanwhile, following severe acute pancreatitis, emodin reduced the inflammatory response in the rat lung by decreasing the expression of tumor necrosis factor-α (TNF-α) and IL-6 (Zhang et al., 2005). Rhein also showed anti-inflammation effect through inhibiting the expression of iNOS (Wang et al., 2002). Aloe-emodin might inhibit the inflammatory

Table 2. Stilbene derivatives isolated from different species of rhubarb

No.	Compounds	Botanical sources	References
57	3,4′,5-trihydroxystlbene-4′-*O*-β-*D*-(6″-*O*-galloyl) glucopyranoside	*R. palmatum; R. tanguticum; R. officinale*	Nonaka et al., 1981; Komatsu et al., 2006
58	3,4′,5-trihydroxystlbene-4′-*O*-β-*D*-glucopyranoside	*R. palmatum; R. tanguticum; R. officinale*	Nonaka et al., 1981; Komatsu et al., 2006
59	deoxyrhaponticin	*R. undulatum*	Ko, 2000
60	desoxyrhaponticin	*R. emodi; R. undulatum*	Matsuda et al., 2001; Suresh Babu et al., 2004
61	desoxyrhapontigenin	*R. undulatum*	Matsuda et al., 2001
62	gentin C	*R. nanum*	Xiang et al., 2005
63	isorhapontin	*R. undulatum*	Matsuda et al., 2001
64	maximol A	*R. palaestinum*	Shikishima et al., 2001
65	maximol B	*R. palaestinum*	Shikishima et al., 2001
66	piceatannol	*R. undulatum*	Ko et al., 1999
67	piceatannol 3′-*O*-β-*D*-glucopyranoside	*R. hotaoense; R. undulatum*	Li et al., 1998; Matsuda et al., 2001
68	piceatannol 4′-*O*-(6″-p-coumaroyl)β-*D*-glucopyranoside	*R. emodi*	Wang et al., 2010
69	piceatannol 4′-*O*-β-*D*-glucopyranoside	*R. nanum*	Xiang et al., 2005
70	piceatannol-3,4′-*O*-β-*D*-diglucopyranoside	*R. undulatum*	Ko, 2000
71	resveratrol	*R. undulatum*	Matsuda et al., 2001
72	resveratrol 4′-*O*-β-*D*-(6″-*O*-galloyl)-glucopyranoside	*R. tanguticum*	Gao and Liangliang, 2013
73	resveratrol 4′-*O*-β-*D*-glucopyranoside	*R. tanguticum*	Gao and Liangliang, 2013
74	rhaponticin	*R. tanguticum; R. undulatum; R. palaestinum*	Li, Li et al., 1998; Ko et al., 1999; Matsuda et al., 2001; Matsuda et al., 2001; Jin et al., 2006; Aburjai, 2000
75	rhapontigenin	*R. palmatum; R. tanguticum; R. emodi; R. undulatum*	Li, Li et al., 1998; Ko et al., 1999; Matsuda et al., 2001; Matsuda et al., 2001; Suresh Babu et al., 2004; Jin, Ge et al., 2006; Xu Qing et al., 2009
76	rhaponticin 2″-*O*-gallate	*R. tanguticum; R. undulatum*	Matsuda et al., 2001; Jin et al., 2006

mediators including decreasing the levels of PAF, IL-6, and TNF-α during the acute pancreatitis (AP) in rats (Chen et al., 2010).

3.5. Anti-platelet aggregation and anticoagulant activities

Being able to promote blood circulation to remove blood stasis, Rhubarb was used as an ingredient in numerous prescriptions in the medical classic "Shang-Han-Lun" by Zhongjing Zhang (Han Dynasty). In thrombotic diseases, as a multifunctional serine protease, thrombin is generated in response to vascular injury and catalyzes the proteolytic cleavage of the soluble plasma-protein fibrinogen to form soluble fibrin, leading to clot formation. In addition, thrombin also serves as a potent platelet agonist and amplifies its own generation by a several-step feedback activation process as part of the coagulation cascade (Weitz, 2003). With thrombin playing a pivotal role in thrombogenesis, its inhibitors have been used in the treatment of thrombotic diseases, which have been proved to be effective (Hanessian et al., 2008). The anti-thrombin activities of various rhubarb samples have been investigated. The inhibitory activity of smoked rhubarb (inhibition percentage of 56.34 %) was significantly higher than those of the other samples ($P < 0.05$). Also, IC_{50} values for the rhubarb samples on thrombin were determined. According to the IC_{50} values, smoked rhubarb exhibited the best thrombin inhibition activity (IC_{50} = 6.36 mg/mL) (Sun et al., 2018). The effects of anthraquinone derivatives isolated from rhubarb on platelet activity have been investigated. Among four anthraquinone derivatives isolated from rhubarb examined, chrysophanol-8-O-glucoside (CP-8-O-glc) had the most potent inhibitory effect on collagen- and thrombin-induced platelet aggregation with mice treated by it showing significantly prolonged bleeding times. Furthermore, CP-8-O-glc was found to have a significant inhibitory effect on rat platelet aggregation ex *vivo* and on thromboxane A2 formation in *vitro*. In coagulation tests, CP-8-O-glc prolonged the activated partial thromboplastin time instead of altering prothrombin time. However, CP-8-O-glc only inhibited platelet phosphatidylserine exposure without directly inhibiting intrinsic factors. This study has demonstrated the anti-platelet

Table 3. Flavonoids and acylglucosides isolated from different species of rhubarb

No.	Compounds	Botanical sources	References
77	(+)-catechin	*R. palmatum; R. tanguticum*	Nonaka et al., 1981; Lu et al., 1998; Jin et al., 2006
78	(−)epicatechin-3-O-gallate	*R. tanguticum; R. officinale*	Nonaka et al., 1981; Jin et al., 2006; Tan, 2006
79	(−)epigallocatechin-3-O-gallate	*R. officinale*	Tan, 2006
80	gallic acid	*R. palmatum*	Nonaka et al., 1981; Xu Qing et al., 2009
81	kaempferol-3-O-rhamnoside	*R. undulatum*	Ham et al., 1994
82	kaempferol-3-O-(2′,6′-di-O-rhamnopyranosyl)-β-D-galactopyra-noside	*R. undulatum*	Ham et al., 1994
83	gallic acid 3-*O*-β-*D*-glucopyranoside	*R. palmatum*	Kashiwada et al., 1986
84	gallic acid 4-*O*-β-*D*-glucopyranoside	*R. palmatum*	Kashiwada et al., 1986
85	1-*O*-galloyl-6-*O*-cinnamoyl-β-*D*-glucose	*R. palmatum*	Kashiwada et al., 1988
86	1,2-di-*O*-galloyl-6-*O*-cinnamoyl-β-*D*-glucose	*R. palmatum*	Kashiwada et al., 1988
87	1,2,6-tri-*O*-galloyglucose	*Rhei Radix et Rhizoma*	Nonaka et al., 1981
88	glucopyranosyl-galloyl-glucose	*R. palmatum*	Wang et al., 2011
89	coumaroyl-*O*-galloyl-glucose	*R. palmatum*	Wang et al., 2011
90	lindleyin	*R. tanguticum*	Gao and Liangliang, 2013
91	1′-*O*-galloylsucrose	*R. coreanum*	Kashiwada et al., 1988
92	2-*O*-galloylsucrose	*R. coreanum*	Kashiwada et al., 1988
93	6-*O*-galloylsucrose	*R. coreanum*	Kashiwada et al., 1988
94	6′-*O*-galloylsucrose	*R. coreanum*	Kashiwada et al., 1988

and anticoagulant effects of CP-8-O-glc and suggested that this compound might be of therapeutic benefit for the prevention of platelet-related cardiovascular diseases (Seo et al., 2012).

The aqueous extract of rhubarb has been reported to have an anti-platelet aggregation activity (Ko et al., 1999). Anti-platelet aggregation activity of stilbenes from *Rheum undulatum* was shown to be affected by the presence of methoxyl and free hydroxy groups of the structure. The inhibition activity on platelet aggregation induced by arachidonic acid is considered to be closely related to arachidonate metabolism. Consequently, these inhibitory effects may partially contribute to anti-blood stagnancy activity of rhubarb (Ko et al., 1999). Research suggested that rhaponticin and rhapontigenin exhibited an inhibitory effect toward platelet aggregation in *vitro* and ex *vivo* and protected the mice from thromboembolism. Among these compounds, rhapontigenin, a metabolite of rhaponticin transformed by human intestinal microflora prior to absorption in the intestine, was the more potent. Rhei Rhizoma also exhibited in *vitro* and ex *vivo* anti-platelet aggregation activity and protection against thromboembolism. Based on these findings, it is concluded that Rhei Rhizoma, particularly rhapontigenin, could prevent the development of thrombosis or its recurrence (Park et al., 2002). The phytochemical analysis of *Rheum palaestinum* revealed the presence of two stilbenes: piceid and rhaponticin, which may explain the use of this plant in traditional medicine for its anti-platelet activity as these compounds exhibited significant anti-platelet aggregation activity (Aburjai, 2000).

4. Processing methods

As one of the most important and fundamental steps in traditional Chinese medicine (TCM), drying operation is employed to maintain bioactive properties of medicinal products and cut down transport expenses as well as facilitating their consumption. The aim of drying TCM is to remove water and consequently prevent microbial and chemical decay, thus improving its shelf-life. As a result, efforts should be put on to maximizing the rate of drying through conveying heat and humidity.

Fresh crude *Rheum palmatum* was sliced and treated with the different drying methods such as sun drying, shady drying, microwave heating and various temperatures drying to choose the optimum initial processing method, and the content of anthraquinones derivatives, slicing colors and dried rates were used as evaluation indexes. Compared with traditional processing, sliced fresh crude *Rheum palmatum* had lower content of the anthraquinones derivatives and dry rates, slicing color had changed as well. For various drying methods, smoking drying was superior to sun drying, shady drying, microwave heating and various temperatures drying methods (Li et al., 2011). Due to processing-induced variations in the chemical composition, raw rhubarb samples subjected to different drying procedures have different therapeutic effects. The raw materials were processed by smoking, sun-drying, shade-drying and oven-drying at low, moderate and high temperatures. The total concentrations of twelve compounds, namely, gallic acid, catechins, epigallocatechin gallate, epicatechin, epicatechin gallate, sennoside B, sennoside A, aloe-emodin, rhein, emodin, chrysophanol, and physcion, in smoked rhubarb were higher than the concentrations of the same components in raw rhubarb and rhubarb products processed using other drying techniques. Smoked rhubarb was found to inhibit Na^+/K^+-ATPase and thrombin substantially. These results confirmed that post-harvest fresh plant materials, especially roots, were still physiologically active, and could undergo a series of anti-dehydration mechanisms, including the production of re-

lated secondary metabolites during the early stages of dehydration. Therefore, the proper design of drying processes could enhance the quality of rhubarb as well as other similar medicinal plants (Sun et al., 2018).

5. Perspectives

In the view of wide applications of rhubarb, although many studies on the chemical constituents, quality analysis, pharmacological activities, and clinical practices had been reported, there are still lots of problems to be solved. Firstly, there are about ninety-four compounds with five types of skeletons isolated from the genus Rheum, including anthraquinone, anthrones, stilbenes, flavonoids and acylglucosides (Gao et al., 2013). Most of the studies have focused on exploring the bioactivities of anthraquinones, with the precise mechanisms underlying their activities being not fully understood. Secondly, derived from long-term practices and experiences, smoking was a traditional technology primarily used for the processing of Chinese herbal medicines. A Chinese herbal medicine was baked with a small fire with the ambient temperature being between 12–18 °C, it typically took at least two weeks to reach complete dryness. This drying technique went slow, allowing the innate metabolic processes of the plant to continue after harvest. Therefore, it is imperative to study the drying mechanism based on secondary metabolism.

Acknowledgments

This study was supported by Tianjin Key R&D Program–Key Projects for Science and Technology Support (19YFZCSY00170), College Student Innovation and Entrepreneurship Training (201910069007, 201910069102), National Natural Science Foundation of China (No. 31571832), Tianjin Innovative Research Team Grant (TD13-5087), and Key Program of Tianjin Municipal Health Bureau (No. 2013-GG-05).

Conflict of interest

The authors declare no conflicts of interest.

References

Aburjai, T.A. (2000). Anti-platelet stilbenes from aerial parts of Rheum palaestinum. Phytochemistry 55(5): 407–410.

Cha, T.-L., Qiu, L., Chen, C.-T., Wen, Y., and Hung, M.-C. (2005). Emodin down-regulates androgen receptor and inhibits prostate cancer cell growth. Cancer Res. 65(6): 2287–2295.

Chan, T., Chang, C., Koonchanok, N., and Geahlen, R. (1993). Selective inhibition of the growth of ras-transformed human bronchial epithelial cells by emodin, a protein-tyrosine kinase inhibitor. Biochem. Biophys. Res. Commun. 193(3): 1152–1158.

Chang, C., Ashendel, C., Geahlen, R., McLaughlin, J., and Waters, D. (1996). Oncogene signal transduction inhibitors from medicinal plants. In Vivo 10(2): 185–190.

Chen, H., Hsieh, W., Chang, W., and Chung, J. (2004). Aloe-emodin induced in vitro G2/M arrest of cell cycle in human promyelocytic leukemia HL-60 cells. Food Chem. Toxicol. 42(8): 1251–1257.

Chen, Y.-Y., Chiang, S.-Y., Lin, J.-G., Ma, Y.-S., Liao, C.-L., Weng, S.-W., Lai, T.-Y., and Chung, J.-G. (2010). Emodin, aloe-emodin and rhein inhibit migration and invasion in human tongue cancer SCC-4 cells through the inhibition of gene expression of matrix metalloproteinase-9. Int. J. Oncol. 36(5): 1113–1120.

China, P.C.o.P.s.R.o. (2015). Pharmacopoeia of the People's Republic of China. People's Medical Publishing House, Beijing.

Cichewicz, R.H., Zhang, Y., Seeram, N.P., and Nair, M.G. (2004). Inhibition of human tumor cell proliferation by novel anthraquinones from daylilies. Life Sci. 74(14): 1791–1799.

Cun, Z., Li, L., Yong-Qing, X., Guo-Fang, T., Dong-Dong, C., Yun, W., Yu-Tian, L., and Wen-Qian, H. (2010). Two new anthraquinone glycosides from the roots of Rheum palmatum. J. Asian Nat. Prod. Res. 12(12): 1026–1032.

Darias, V. (1987). Analgesic activity of some phenolic components in rhubarb. Farmaco (Ed Sci) 33: 460–465.

Dequeker, R., Lemli, J., and Cuveele, J. (1964). Anthraquinone drugs. VII. Densitometric determination of the sennidins, rheidins and rhein in the root of rhubarb. Planta Med. 12(1): 51–56.

Ejderhamn, J., Finkel, Y., and Strandvik, B. (1989). Na, K-ATPase activity in rectal mucosa of children with ulcerative colitis and Crohn's disease. Scand. J. Gastroenterol. 24(9): 1121–1125.

Gao, L, Xu, X, and Yang, J (2013). Chemical constituents of the roots of Rheum officinale. Chem. Nat. Compd. 49(4): 603–605.

Gao, L., Xu, X., and Yang, J. (2013). Chemical constituents of the roots of Rheum officinale. Chem. Nat. Compd. 49(4): 603–605.

Ham, I.-H., Oh, I.-S., Whang, W.-K., and Kim, I.-H. (1994). Pharmaco-constituents of Korean cultivated Rhubarb leaves-the flavonoids from leaves. Yakhak Hoeji 38(4): 410–417.

Hanessian, S., Simard, D., Bayrakdarian, M., Therrien, E., Nilsson, I., and Fjellström, O. (2008). Design, synthesis, and thrombin-inhibitory activity of pyridin-2-ones as P2/P3 core motifs. Bioorg. Med. Chem. Lett. 18(6): 1972–1976.

HARIMA, S., MATSUDA, H., and KUBo, M. (1994). Study of various rhubarbs regarding the cathartic effect and endotoxin-induced disseminated intravascular coagulation. Biol. Pharm. Bull. 17(11): 1522–1525.

Hesse, O. (1908). Rhapontic root and Austrian rhubarb. J fuer Praktische Chemie (Leipzig) 77: 321–352.

Holzschuh, L., Kopp, B., and Kubelka, W. (1982). Physcion-8-O-beta-D-gentiobioside, a new anthraquinone glycoside from rhubarb roots. Planta Med. 46(3): 159–161.

Huang, Q., Lu, G., Shen, H.M., Chung, M.C., and Ong, C.N. (2007). Anti-cancer properties of anthraquinones from rhubarb. Med. Res. Rev. 27(5): 609–630.

Huang, Z., Dong, Y., and Ye, W. (1997). Clinical observation on treatment of infantile cholestatic hepatitis syndrome by rhubarb. Chinese journal of integrated traditional and Western medicine 17(8): 459–461.

Huiyan, X., Xiaofeng, Z., Huan, W., and Li, P.A.N. (2003). HPLC determination of anthraquinones from various parts of R. T anguticum, R. undulatum and R. spiciforme. Acta Bot. Boreali-Occidential Sinica 23(2): 328–331.

Jin, W., Ge, R.-L., Wei, Q.-J., Bao, T.-Y., Shi, H.-M., and Tu, P.-F. (2006). Development of high-performance liquid chromatographic fingerprint for the quality control of Rheum tanguticum Maxim. ex Balf. J. Chromatogr. 1132(1-2): 320–324.

Jong-Chol, C., Tsukasa, M., Kazuo, A., Hiroaki, K., Haruki, Y., and Yasuo, O. (1987). Anti-Bacteroides fragilis substance from rhubarb. J. Ethnopharmacol. 19(3): 279–283.

Kashiwada, Y., Nonaka, G., and Nishioka, I. (1986). Tannins and related compounds. XLVIII. Rhubarb. (7). Isolation and characterization of new dimeric and trimeric procyanidins. Chem. Pharm. Bull. (Tokyo) 34(10): 4083–4091.

Kashiwada, Y., Nonaka, G.-i., and Nishioka, I. (1988). Galloylsucroses from rhubarbs. Phytochemistry 27(5): 1469–1472.

Kashiwada, Y., Nonake, G., and Nishioka, I. (1984). Studies on Rhubarb (Rhei Rhizoma). VI. Isolation and characterization of stilbenes. Chem. Pharm. Bull. 32(9): 3501–3517.

Ko, S.K. (2000). A new stilbene diglycoside from Rheum undulatum. Arch. Pharmacal Res. 23(2): 159–162.

Ko, S.K., Lee, S.M., and Whang, W.K. (1999). Anti-platelet aggregation activity of stilbene derivatives from Rheum undulatum. Arch. Pharmacal Res. 22(4): 401–403.

Komatsu, K., Nagayama, Y., Tanaka, K., Ling, Y., Cai, S.Q., Omote, T., and Meselhy, M.R. (2006). Comparative study of chemical constituents

of rhubarb from different origins. Chem. Pharm. Bull. (Tokyo) 54(11): 1491–1499.
Krenn, L., Pradhan, R., Presser, A., Reznicek, G., and Kopp, B. (2004). Anthrone C-glucosides from Rheum emodi. Chem. Pharm. Bull. 52(4): 391–393.
Kuo, P.-L., Lin, T.-C., and Lin, C.-C. (2002). The antiproliferative activity of aloe-emodin is through p53-dependent and p21-dependent apoptotic pathway in human hepatoma cell lines. Life Sci. 71(16): 1879–1892.
Kuo, Y.-C., Sun, C.-M., Ou, J.-C., and Tsai, W.-J. (1997). A tumor cell growth inhibitor from Polygonum hypoleucum Ohwi. Life Sci. 61(23): 2335–2344.
Lee, H.-Z., Hsu, S.-L., Liu, M.-C., and Wu, C.-H. (2001). Effects and mechanisms of aloe-emodin on cell death in human lung squamous cell carcinoma. Eur. J. Pharmacol. 431(3): 287–295.
LEMLI, J., Bequeker, R., and Cuveele, J. (1964). SENNIDIN C, REIDIN B AND REIDIN C, HETERODIANTHRONES OF THE FRESH ROOTS OF RHUBARB. Pharm. Weekbl. 99: 613.
Li, F., Wang, S., Wang, X., Ren, Q., Wang, W., Shang, G., Zhang, L., and Zhang, S. (2008). Novel exploration of cathartic pharmacology induced by rhubarb. China J. Chin. Mater. Med. 33(4): 481–484.
Li, J., Li, J., and He, W. (1998). Studies on the non-anthraquinones of Hotao rhubarb (Rheum hotaoense). Chinese Traditional and Herbal Drugs 29: 721–722.
Li, Y., Miao, X., Wu, P., Li, Y., Liu, F., and Wei, S. (2011). Influences of different initial processing methods on Rheum palmatum. J. Chin. Med. Mater. 34(8): 1196–1199.
Liselotte, K., Riddhi, P., Armin, P., Gottfried, R., and Brigitte, K. (2004). Anthrone C-glucosides from Rheum emodi. Cheminform 35(37): 391.
Lu, K., Tong, W., and Hu, R. (1998). Studies on the chemical constituents of rheum's Callus. Chin. Tradit. Herb. Drugs 29: 438–440.
Mase, A., Makino, B., Tsuchiya, N., Yamamoto, M., Kase, Y., Takeda, S., and Hasegawa, T. (2010). Active ingredients of traditional Japanese (kampo) medicine, inchinkoto, in murine concanavalin A-induced hepatitis. J. Ethnopharmacol. 127(3): 742–749.
Matsuda, H., Shimoda, H., Morikawa, T., and Yoshikawa, M. (2001). Phytoestrogens from the roots of Polygonum cuspidatum (Polygonaceae): structure-requirement of hydroxyanthraquinones for estrogenic activity. Bioorg. Med. Chem. Lett. 11(14): 1839–1842.
Matsuda, H., Tomohiro, N., Hiraba, K., Harima, S., Ko, S., Matsuo, K., Yoshikawa, M., and Kubo, M. (2001). Study on anti-Oketsu activity of rhubarb II. Anti-allergic effects of stilbene components from Rhei undulati Rhizoma (dried rhizome of Rheum undulatum cultivated in Korea). Biol. Pharm. Bull. 24(3): 264–267.
Moon, M.K., Kang, D.G., Lee, J.K., Kim, J.S., and Lee, H.S. (2006). Vasodilatory and anti-inflammatory effects of the aqueous extract of rhubarb via a NO-cGMP pathway. Life Sci. 78(14): 1550–1557.
Nonaka, G., Minami, M., and Nishioka, I. (1977). Studies on rhubarb (Rhei rhizoma). III. Stilbene glycosides. Chem. Pharm. Bull. (Tokyo) 25(9): 2300–2305.
Nonaka, G., NISHIOKA, I., NAGASAWA, T., and OURA, H. (1981). Tannins and related compounds. I. Rhubarb (1). Chem. Pharm. Bull. 29(10): 2862–2870.
Oshio, H., IMAI, S., FUJIOKA, S., SUGAWARA, T., MIYAMOTO, M., and TSUKUI, M. (1974). Investigation of Rhubarbs. III. New purgative constituents, sennosides E and F. Chem. Pharm. Bull. 22(4): 823–831.
Park, E.-K., Choo, M.-K., Yoon, H.-K., and Kim, D.-H. (2002). Antithrombotic and antiallergic activities of rhaponticin from Rhei Rhizoma are activated by human intestinal bacteria. Arch. Pharmacal Res. 25(4): 528–533.
Pecere, T., Gazzola, M.V., Mucignat, C., Parolin, C., Dalla Vecchia, F., Cavaggioni, A., Basso, G., Diaspro, A., Salvato, B., and Carli, M. (2000). Aloe-emodin is a new type of anticancer agent with selective activity against neuroectodermal tumors. Cancer Res. 60(11): 2800–2804.
Pecere, T., Sarinella, F., Salata, C., Gatto, B., Bet, A., Dalla Vecchia, F., Diaspro, A., Carli, M., Palumbo, M., and Palù, G. (2003). Involvement of p53 in specific anti-neuroectodermal tumor activity of aloe-emodin. Int. J. Cancer 106(6): 836–847.
Seo, E.J., Ngoc, T.M., Lee, S.-M., Kim, Y.S., and Jung, Y.-S. (2012). Chrysophanol-8-O-glucoside, an anthraquinone derivative in rhubarb, has antiplatelet and anticoagulant activities. J. Pharmacol. Sci. 118(2): 245–254.
Shi, Y.-Q., Fukai, T., Sakagami, H., Kuroda, J., Miyaoka, R., Tamura, M., Yoshida, N., and Nomura, T. (2001). Cytotoxic and DNA damage-inducing activities of low molecular weight phenols from rhubarb. Anticancer Res. 21(4A): 2847–2853.
Shieh, D.-E., Chen, Y.-Y., Yen, M.-H., Chiang, L.-C., and Lin, C.-C. (2004). Emodin-induced apoptosis through p53-dependent pathway in human hepatoma cells. Life Sci. 74(18): 2279–2290.
Shikishima, Y., Takaishi, Y., Honda, G., Ito, M., Takeda, Y., Kodzhimatov, O.K., and Ashurmetov, O. (2001). Phenylbutanoids and stilbene derivatives of Rheum maximowiczii. Phytochemistry 56(4): 377–381.
Siegers, C., von Hertzberg-Lottin, E., Otte, M., and Schneider, B. (1993). Anthranoid laxative abuse--a risk for colorectal cancer? Gut 34(8): 1099–1101.
Singh, P., Pant, G.J.N., and Rawat, M. (2016). Phytochemistry and Biological Activity Perspectives of Rheum Species. Natural Products Journal 6(2): 84–93.
Singh, S.S., Pandy, S.C., Singh, R., and Agarwal, S.K. (2005). 1,8-Dihydroxyanthraquinone derivatives from rhizomes of Wall. Indian J. Chem. 43B: 1494–1496.
Sun, J., Wu, Y., Dong, S., Li, X., and Gao, W. (2018). Influence of the drying method on the bioactive compounds and pharmacological activities of rhubarb. J. Sci. Food Agric. 98(9): 3551–3562.
Suresh Babu, K., Tiwari, A.K., Srinivas, P.V., Ali, A.Z., China Raju, B., and Rao, J.M. (2004). Yeast and mammalian α-glucosidase inhibitory constituents from Himalayan rhubarb Rheum emodi Wall.ex Meisson. Bioorg. Med. Chem. Lett. 14(14): 3841–3845.
Tan, J. (2006). Research on the Anti-viral Chemical Constituents of Rheum officinale Bail. Hubei Traditional Chinese Medicine, Wuhan.
Wang, A., Li, J., and Li, J. (2010). Chemical constituents of Rheum emodi. Chin. Tradit. Herb. Drugs 41(3): 343–347.
Wang, C.-C., Huang, Y.-J., Chen, L.-G., Lee, L.-T., and Yang, L.-L. (2002). Inducible nitric oxide synthase inhibitors of Chinese herbs III. Rheum palmatum. Planta Med. 68(10): 869–874.
Wang, J.-b., Kong, W.-j., Wang, H.-j., Zhao, H.-p., Xiao, H.-y., Dai, C.-m., Xiao, X.-h., Zhao, Y.-l., Jin, C., and Zhang, L. (2011). Toxic effects caused by rhubarb (Rheum palmatum L.) are reversed on immature and aged rats. J. Ethnopharmacol. 134(2): 216–220.
Wei, Y.H., Zhang, C.Z., Chong, L.I., and Tao, B.Q. (2004). Chemical constituents of Rheum glabricaule (I). Chin. Tradit. Herb. Drugs 35(7): 732–734.
Weitz, J.I. (2003). A novel approach to thrombin inhibition. Thromb. Res. 109: S17–S22.
Xiang, L., Liu, X., and Fan, G. (2005). Chemical constituents from Rheum nanum Siev. ex Pall.(II). Chin Tradit Herb Drugs 36: 1306–1309.
Xing-Sheng, F.U., Chen, F., Liu, X.H., Hu, X.U., and Zhou, Y.Z. (2011). Progress in research of chemical constituents and pharmacological actions of Rhubarb. Chin. J. New Drugs 20(16): 1534–1538+1568.
Xiuwei, Y., Jing, Z., and Yan, Z. (1998). Studies on Rhubarb I. A New Malonylanthraquinone Glycoside from the Rhizomes of Qinling Rhubarb (Rheum qinlingense). Chin. Tradit. Herb. Drugs 5: .
Xu Qing, Q.Y., Su, X.J., and Luo, W.S. (2009). Chemical constituents in Rheum palmatum. Chin. Tradit. Herb. Drugs 40(04): 533–536.
Yakubu, M., and Salimon, S. (2015). Antidiarrhoeal activity of aqueous extract of Mangifera indica L. leaves in female albino rats. J. Ethnopharmacol. 163: 135–141.
Yamagishi, T., Nishizawa, M., Ikura, M., Hikichi, K., Nonaka, G.-I., and Nishioka, I. (1987). New Laxative Constituents of Rhubarb. Isolation and Characterization of Rheinosides A, B, C and D. Chem. Pharm. Bull. (Tokyo) 35(8): 3132–3138.
Wei, Y, Wu, X, Zhang, C., and Li, C. (2005). Studies on Chemical Constituents of Rheum glabricaule Sam. J. Chin. Med. Mater. 28(8): 658–660.
Zhang, L., Chang, C.-j., Bacus, S.S., and Hung, M.-C. (1995). Suppressed transformation and induced differentiation of HER-2/neu-overexpressing breast cancer cells by emodin. Cancer Res. 55(17): 3890–3896.
Zhang, X.-P., Li, Z.-F., Liu, X.-G., Wu, Y.-T., Wang, J.-X., Wang, K.-M., and Zhou, Y.-F. (2005). Effects of emodin and baicalein on rats with severe acute pancreatitis. World Journal of Gastroenterology: WJG 11(14): 2095.
Zhao, Y.L., Wang, J.B., Zhou, G.D., Shan, L.M., and Xiao, X.H. (2009). Investigations of Free Anthraquinones from Rhubarb Against α-Naphthylisothiocyanate-induced Cholestatic Liver Injury in Rats.

Basic Clin. Pharmacol. Toxicol. 104(6): 463–469.
Zhou, X., Song, B., Jin, L., Hu, D., Diao, C., Xu, G., Zou, Z., and Yang, S. (2006). Isolation and inhibitory activity against ERK phosphorylation of hydroxyanthraquinones from rhubarb. Bioorg. Med. Chem. Lett. 16(3): 563–568.
Zhu, B., Lin, Y., Zhu, C.-F., Zhu, X.-L., Huang, C.-Z., Lu, Y., Cheng, X.-X., and Wang, Y.-J. (2011). Emodin inhibits extracellular matrix synthesis by suppressing p38 and ERK1/2 pathways in TGF-β1-stimulated NRK-49F cells. Mol. Med. Report. 4(3): 505–509.
Zhu, T., Liu, X., Wang, X., Cao, G., Qin, K., Pei, K., Zhu, H., Cai, H., Niu, M., and Cai, B. (2016). Profiling and analysis of multiple compounds in rhubarb decoction after processing by wine steaming using UHPLC-Q-TOF-MS coupled with multiple statistical strategies. J. Sep. Sci. 39(15): 3081–3090.
Zhu, Y., Pu, B.-Q., Xie, G.-Y., Tian, M., Xu, F.-Y., and Qin, M.-J. (2014). Dynamic changes of flavonoids contents in the different parts of rhizome of Belamcanda chinensis during the thermal drying process. Molecules 19(7): 10440–10454.
Zwaving, J. (1965). Separation and isolation of anthraquinone glycosides of Rheum palmatum. Planta Med. 13(4): 474–484.