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Food Chemistry 128 (2011) 585–589

Contents lists available at ScienceDirect

Food Chemistry

journal homepage: www.elsevier.com/locate/foodchem

Review

# Phytoconstituents and therapeutic uses of *Rheum emodi* wall. ex Meissn

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ARTICLE INFO

*Article history:*
Received 8 January 2011
Received in revised form 18 March 2011
Accepted 20 March 2011
Available online 9 April 2011

*Keywords:*
*Rheum emodi*
Anthraquinone
Antioxidant
Antimicrobial
Hepatoprotective
Antiproliferative
Hyperglycaemia

ABSTRACT

Rhubarb (*Rheum emodi*, family Polygonaceae) has been traditionally used as diuretic, liver stimulant, purgative/cathartic, stomachic, anticholesterolaemic, antitumour, antiseptic and tonic. A number of anthraquinone derivatives including emodin, aloe-emodin, physcion, chrysophanol, rhein, emodin glycoside and chrysophanol glycoside occur as the main chemical constituents. In the past few years, new components such as sulfemodin 8-*O*-$\beta$-D-glucoside, revandchinone-1, revandchinone-2, revandchinone-3, revandchinone-4, 6-methyl-rhein and 6-methyl aloe-emodin have been reported from the same species. Anthraquinone derivatives show evidence of antifungal, anti-microbial, anti-Parkinson's, anti-proliferative, immuno-enhancing, antiviral and antioxidant activities. This review covers published work on botany, chemistry and therapeutic uses of different components from rhubarb.



**Contents**



## 1. Introduction

The word *rhubarb* originates from Latin. The ancient Romans imported rhubarb roots from unknown, barbarian lands. The lands were beyond the Volga River, sometimes known as the Rha River. *Rha* was adopted to mean rhubarb. Imported from barbarians across the Rha, the plant became *Rha barbarum* and eventually *rhabarbarum*, now considered to be Latin for rhubarb. The modern English word *rhubarb* derives its name from *rhabarbarum* (Wright, 2001).

Rhubarb has been cultivated for over 5000 years for its medicinal purposes, originating in the mountains of the North-western provinces of China and Tibet. It is first mentioned in the Chinese herbal Pen-King, which listed it as a purgative and stomachic (Foust & Clifford, 1992).

It found its way to the West *via* Turkey and Russia, and was first planted in England by an apothecary named Hayward in 1777. It soon found its way into the kitchen, where its tart flavour became popular in desserts such as rhubarb crumble, as well as in jams,

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doi:10.1016/j.foodchem.2011.03.083

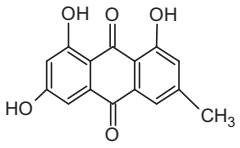
jellies and sauces. Rhubarb is a vegetable but is often thought to be a fruit (Lloyd, 2008; Newby, 2005).

Rhubarb stalk can be cooked or eaten raw with some people dipping raw stalks in sugar to remove some of the tartness. It should be noted that generally only the stalk of the plant is eaten, as its leaves contain potassium oxalate that can sometimes cause poisoning, occasionally fatal in people with susceptibility to oxalic acids.

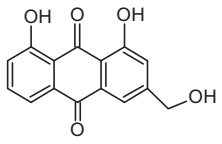
The botanical name of Himalayan rhubarb is *Rheum emodi* Wall. ex Meissn. (kingdom: Plantae; division: Magnoliophyta; class: Magnoliopsida; order: Caryophyllales; family: Polygonaceae; genus: Rheum L.). Flowering occurs in June and July (Sharma., 2009). The species is found in the temperate Himalayas, from Kashmir to Sikkim, at an elevation of 2000–3800 m. It is found in the alpine zone on rocky soil, moraines and crevices, between boulders and near streams in specific pockets. *R. emodi* is restricted to the temperate, sub-alpine, and alpine zones of the Himalayas. Well-drained, porous, humus-rich soil is suitable for its cultivation. It prefers exposed or partially shaded habitat and can be cultivated at altitudes above 1800 m.

## 2. Chemistry

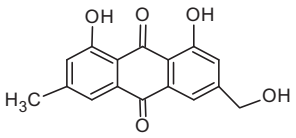
Indian Rhubarb, which is official in the Indian Pharmacopoeia, consists of the dried rhizomes of *R. emodi* (Singh, Pandey, Singh, & Agarwal, 2005). The major phytoconstituents reported to have been isolated from the rhizomes are: free anthraquinones and their glycosides. The anthraquinones, both with and without carboxyl groups are found in *R. emodi*. Anthraquinones with carboxyl group



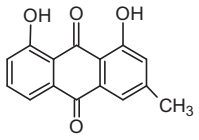
Emodin



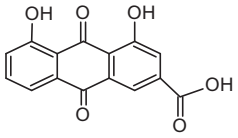
Aloe emodin



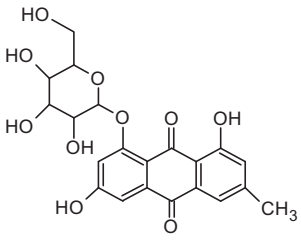
Physcion



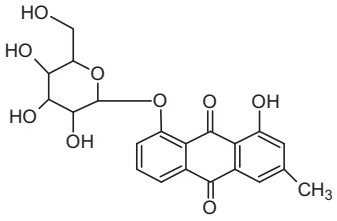
Chrysophanol



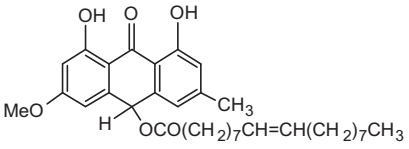
Rhein



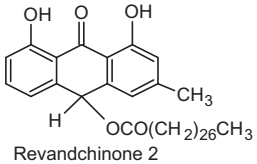
Emodin glucoside



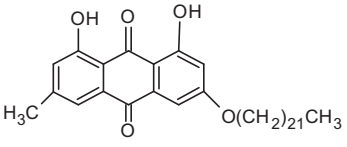
Chrysophanol glucoside



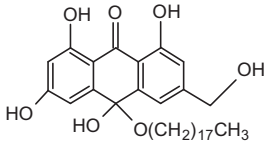
Revandchinone 1



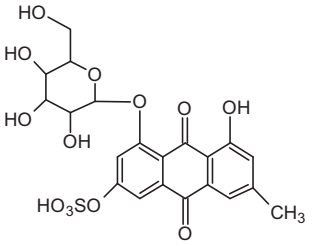
Revandchinone 2



Revandchinone 3



Revandchinone 4



Sulfemodin 8 *O* Glucoside

include rhein, while those without carboxyl group include chrysophanol, aloe-emodin, emodin, physcion (emodin monomethylether), chrysophanein and emodin glycoside (Malik et al., 2010). Some alkyl derivatives of anthraquinones, like 6-methyl rhein and 6-methyl aloe-emodin have also been reported (Singh et al., 2005).

Another chemical group which has been isolated from *R. emodi* is anthrone C-glucosides. These anthrones occur in the form of 10-hydroxycascaroside C, 10-hydroxycascaroside D, 10*R*-chrysaloin 1-*O*-*β*-D-glucopyranoside, cascaroside C, cascaroside D and cassialoin (Krenn, Pradhan, Presser, Reznicek, & Kopp, 2004). Different derivatives of oxanthrone have been isolated. These include oxanthrone ether (revandchinone-4), oxanthrone esters (revandchinone-1 and revandchinone-2), and revandchinone-3 (Babu et al., 2003; Singh et al., 2005).

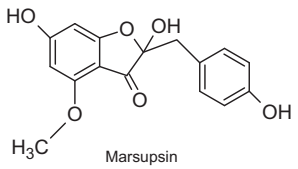
Other compounds, namely, naphthoquinones, rutin, rheinal, rhein 11-*O*-*β*-D-glucoside, torachrysone 8-*O*-*β*-D-glucoside, epicatechin, auronols (carpusin and maesopsin), the sulfated anthraquinone glycoside sulfemodin 8-*O*-*β*-D-glucoside (Krenn et al., 2003), β-asarone (Singh et al., 2005) and some stilbene compounds (e.g., rhaponticin) have also been isolated.

## 3. Bioactivity

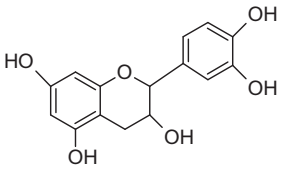
Compounds identified in *Rheum emodi* are reported to possess antioxidant, antidiabetic, antimicrobial, antifungal, cytotoxic, hepatoprotective and nephroprotective activities. The reports on pharmacological properties of different constituents from *Rheum emodi* are collected from a large number of published papers.

### 3.1. Antibacterial and antifungal action

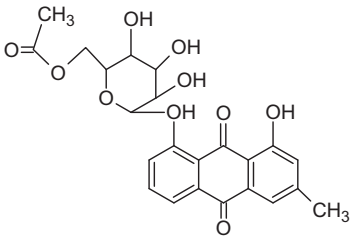
Since many bacterial and fungal strains are found to be resistant against a wide variety of antibiotics, medicinal plants have been studied for their potential to possess antimicrobial properties. Aloe-emodin, rhein and emodin obtained from commercial rhubarb possess significant antibacterial activity against four strains of methicillin-resistant *Staphylococcus aureus* (MRSA) and also a strain of methicillin-sensitive *Staphylococcus aureus* (MSSA). Aloe-emodin possesses antibacterial effects on the strains of MRSA and MSSA, with a minimum inhibitory concentration (MIC) of 2 μg/mL. Rhein possess antibacterial activity against *Escherichia coli* K12 with an MIC value of 128 μg/mL (Hatano et al., 1999). Chrysophanol, rhein, physcion and aloe-emodin exhibit antifungal activity against *Candida albicans*, *Cryptococcus neoformans*, *Trichophyton mentagrophytes* and *Aspergillus fumigatus* (MIC 25250 μg/ml) using ketoconazole as control (Agarwal, Singh, Verma, & Kumar 2000). Revandchinone-1 and 3 have shown only moderate antibacterial activity. Revandchinone-4 has been found to possess good antibacterial properties against some Gram-positive bacteria (*Bacillus subtilis*, *Bacillus sphaericus* and *Staphylococcus aureus*) using penicillin G as control, and Gram-negative bacteria (*Klebsiella aerogenes*, *Chromobacterium violaceum* and *Pseudomonas aeruginosa*) using streptomycin as control. Revandchinone-1, 3 and 4 also exhibit a moderate degree of antifungal activity against *Rhizopus oryzae* and *Aspergillus niger* using clotrimazole as control (Babu et al., 2003). The ethanolic extract has been found to possess promising activity against various strains of *H. pylori*, the strains being isolated from gastric biopsy specimens (15 from duodenal ulcer, eight from gastric ulcer, four from non-ulcer dyspepsia, and three



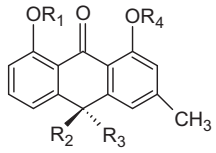
Marsupsin



Epicatechin



Glucopyranosylchrysophanol




| | $R_1$ | $R_2$ | $R_3$ | $R_4$ |
|---|---|---|---|---|
| 1 | Glu | Glu | OH | H |
| 2 | Glu | OH | Glu | H |
| 3 | H | H | Glu | Glu |
| 4 | Glu | Glu | H | H |
| 5 | Glu | H | Glu | H |
| 6 | H | OH | Glu | H |

1 = 10 hydroxycascaroside C
2 = 10 hydroxycascaroside D
3 = 10*R* chrysaloin glucopyranoside
4 = cascaroside C
5 = cascaroside D
6 = cassialoin

from gastric carcinoma) both *in vitro* and *in vivo* (Ibrahim et al., 2006).

### 3.2. Antioxidant and anticancer potential

Since oxidative stress is one of the causes for the development and progression of certain life-threatening diseases and disorders like cancer, atherosclerosis, diabetes, hyperlipidaemia, neuronal degeneration and hepatotoxicity, antioxidants from plant sources may be useful in their prevention and treatment. Instead of commonly used antioxidants like butylated hydroxyanisole (BHA) and butylated hydroxytoluene (BHT), which have been restricted, due to their toxicity and DNA damage induction potential, floral resources have received considerable attention as sources of antioxidants because of their safety in biological systems. Methanolic and aqueous extracts of the roots of *R. emodi* are reported to possess antioxidant and anticancer potential (Rajkumar, Guha, & Kumar, 2010). In Chinese folkloric medicine, *R. emodi* is used in the treatment of cancer and liver ailments. The compounds like marsupsin and maesopsin obtained from the rhizome/root extracts of *R. emodi* are found to possess antioxidant activity (Krenn et al., 2003). In a study, the anthraquinone derivatives, such as aloe-emodin, emodin, rhein, chrysophanol and physcion are reported to possess anti-angiogenic activity, by preventing blood vessel formation in zebra-fish embryos (He, He, Ma, & But, 2009). The anticancer effect of aloe-emodin has been established in two human cancer cell lines, Hep G2 and Hep 3B. Aloe-emodin inhibited cell proliferation and induced apoptosis in both examined cell lines by different antiproliferative mechanisms (Kuo, Lin, & Lin, 2002).

### 3.3. Nephroprotective activity

The effects of toxic metals on the kidney have been known for many years. Nephrotoxicity may occur as a result of occupational or therapeutic exposure to these metals. Heavy metals tend to accumulate in kidneys where they may produce a broad spectrum of morphological and functional effects (Conner & Fowler, 1993). A number of antibiotics, including the penicillins, cephalosporins, tetracyclines, as well as aminoglycosides and sulphonamides, are potential nephrotoxins. Aminoglycoside nephrotoxicity is manifested functionally by decreased urine-concentrating capacity, tubular proteinuria, lysosomal enzymuria, mild glucosuria, decreased ammonium excretion and lowering of glomerular filtration rate (Kaloyanides, & Pastoriza-Munoz, 1980). The nephroprotective activity of both the fractions (water-soluble and water-insoluble) of alcoholic extract of *R. emodi* has been established. The protective effect of water-soluble extract is pronounced on all the segments ($S_1$, $S_2$ and $S_3$) of the proximal tubule of kidney against cadmium, mercury and potassium dichromate-induced nephrotoxicity in rats. The water-insoluble fraction was found to have protective effect on $S_2$ segment only. The effect has been proposed because of the tannins present in the fraction. The nephrotoxicity was induced using cadmium chloride, mercuric chloride, potassium dichromate and gentamicin in rats and monitoring the levels of urea, nitrogen and creatinine in serum (Alam, Javed, & Jafri, 2005).

### 3.4. Hepatoprotective and antidiabetic action

According to Wang (1999) chronic and excessive ethanol consumption is associated with cellular proliferation, fibrosis, cirrhosis, and cancer of the liver. An important characteristic of alcohol-induced liver injury is an impaired vitamin A nutritional status. Studies in human Hep G2 cells have shown that ethanol is cytotoxic to Hep G2 cells, which are transduced to express P-450 2E1 (CYP 2E1) and this toxicity is apoptotic in nature (Wu & Cederbaum, 1999), predominantly in the liver. The main pathways for hepatic oxidation of ethanol to acetaldehyde involve alcohol dehydrogenase (Svensson et al., 1999) and are associated with the reduction of NAD+ to NADH (Lieber, 1997). The magnitude of derangement of liver by disease or hepatotoxins is generally measured by the level of glutamate pyruvate transaminase (ALT), glutamate oxaloacetate transaminase (AST), alkaline phosphatase (ALP), bilirubin, albumin, and whole liver homogenate.

Herbal drugs play an important role in health care programs worldwide, and there is a resurgence of interest in herbal medicines for treatment of various ailments including hepatopathy. India, the abode of Ayurvedic system of medicine, assigns much importance to the pharmacological aspects of many plants. Nearly 150 phytoconstituents from 101 plants are claimed to possess liver protecting activity (Doreswamy & Sharma, 1995). At the same time, surprisingly, we do not have satisfactory plant drugs/formulations to treat severe liver diseases. Most of the studies on hepatoprotective plants are carried out using chemical-induced liver damage in rodents as models. A few excellent reviews have appeared on this subject in the recent past (Evans, Subramoniam, Rajashekaran, & Pushpangadan, 2002). The extract from the rhizomes of *R. emodi* has shown significant hepatoprotective activity against $CCl_4$-induced liver injury both *in vitro* and *in vivo* using 50 mg/kg, p.o. (per oral) dose of silymarin as a standard (Ibrahim et al., 2008).

In a separate study it has been concluded that *R. emodi* rhizome extract exhibited antidiabetic activity by enhancing the peripheral utilisation of glucose, by correcting impaired liver and kidney glycolysis and by limiting its gluconeogenic process, similar to insulin (Radhika, Kumari, & Sudarsanam, 2010).

### 3.5. Immuno-enhancing activity

The ethyl acetate extract of rhizome of *R. emodi* has been shown to possess immuno-enhancing activity on cell lines. The effect is believed to be because of a dose-dependent increase in the release of nitric oxide and cytokine TNF-$\alpha$, IL-12 and a decrease in IL-10 by RAW 264.7 in macrophage cell lines in the presence of extract alone (Kounsar, Rather, Ganai, & Zargar, 2011).

### 3.6. Treatment of Severe Acute Respiratory Syndrome (SARS)

After screening 312 Chinese medicinal herbs, emodin, one of the main phytoconstituents in Polygonaceae family has been found to inhibit the SARS-CoV S protein and ACE2 interaction. Emodin has been found to block both the binding of SARS-CoV S protein to ACE2 and the infectivity of S protein-pseudotyped retrovirus to Vero E6 cells. These findings suggested that emodin was a novel anti-SARS-CoV compound and might be considered as a potential lead therapeutic agent in the treatment of SARS (Ho, Wu, Chen, Li, & Hsiang, 2007).

### 3.7. Prevention and treatment of Parkinson's disease

About 17 phytochemicals were examined for inhibitory activity of monoamine oxidase (MAO) A and B on rat brain mitochondria. Emodin has been found to inhibit MAO B and thus can be used as a lead for the prevention and treatment of Parkinson's disease (Kong, Cheng, & Tan, 2004).

## 4. Conclusion

*Rheum emodi* is a medicinal plant of immense importance with a diverse pharmacological spectrum. Besides having the above-mentioned pharmacological properties, it has been used as an ingredient of many herbal formulations, which are used for the treatment of various diseases, in particular the regulation of blood

fat, hepatitis and cancer. The plant could be further exploited, in order to isolate the various biologically-active constituents responsible for its activity.

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