



## Therapeutic effects of *Rheum palmatum* L. (Dahuang): A systematic review

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### ABSTRACT

*Rheum palmatum* L. (Dahuang) is a wild rebus, erect, glabrous, perennial aromatic herb, which grows up to 120 to 200 cm high. The flowers are 1 to 2 mm in diameter, all hermaphrodites and Petals are yellow and produced in compound umbels. While this plant has lots of properties, the aim of this study is to overview its therapeutic effects than its nutritive and industrial effects. This review article was carried out by searching studies in PubMed, Medline, , Web of Science, and Iran Medex databases up to 2016. totally, of 94 found articles, 40 articles (42 in vitro and 5 animal studies) were included. The search terms were “Calendula. ”, “therapeutic”, “pharmacological”. Various studies have shown that *Rheum palmatum* L. (Dahuang). Possess Antioxidant Effect, Effect-enhancing and toxicity-reducing, Anti-viral effect, Liver failure Effect ,Anti-metastatic effects ,Hepatitis and renal failure Effect ,Metabolic syndrome treatment Effect ,Antipyretic and reducing plasma concentration Effect ,Inhibitory effect ,Hepatotoxicity Effect ,Anti-SARS coronavirus Effect ,Anti-liver effect ,Anti-stress Effect ,Anti-liver and hepatic Effect ,Anti HBV effect ,Anthracene derivatives ,Increasing intelligence Effect ,Anti-inflammation Effect ,Anthracene derivatives production Effect ,Homogenate of *Candida utilis* Effect *Rheum palmatum* L. (Dahuang) is widely used for therapeutic and purposes that trigger its significant value. Various combinations and numerous medicinal properties of its extract, essential oils, its stems and leaves demand further and more studies about the other useful and unknown properties of this multipurpose plant.

**Keywords:** *Rheum palmatum* L. (Dahuang), “therapeutic”, “pharmacological”

### INTRODUCTION

It is proved that herbal medicine is effective in the treatment of many diseases [1-10].

*Rheum palmatum*, commonly called Chinese rhubarb, ornamental rhubarb, Turkish rhubarb, Turkey rhubarb, Indian rhubarb, Russian rhubarb or rhubarb root [and within Chinese herbal medicine da-huang] [11, 12].

The species *R. tanguticum* and *R. officinale*, also under the categorical term of the Chinese drug da-huang, are closely related to *R. palmatum*. Today, these three species are regarded as superior in performance to other species-existing rhubarbs. Though *R. palmatum* is commonly misinterpreted to be one in the same with the familiar *R. rhabarbarum* garden rhubarb we eat, there are several facets falsifying this assumption. Size is the most evident of the facets used to differentiate these two closely related species. While most garden species only grow to a mere few feet in height, Chinese rhubarb can produce as high as a “six to ten foot jointed stalk,” with loosely branched clusters of flowers along the tips that mature red in color from their often yellow or white blooms [13, 14].

Its leaves are rather “large, jagged and hand – shaped,” growing in width of at least two to three feet. It is important to recognize that only those species of *Rheum* with lobed leaves are accredited for their medicinal use. Subsequently, garden rhubarb, *R. rhubarb barum*, as well as any other variety of species with either “wavy” or “undulating leaves” are not founded for any medicinal purpose. Additionally, one can decipher Chinese rhubarb by its rather thick, deep roots whereas the perennial garden plant is composed predominantly of “fleshy rhizomes and buds.

Of the numerous herbs renowned for their medicinal benefits in early civilizations, Chinese rhubarb remains one of few still used today in both “conventional and herbal medicine.” The very first accounts are found in ancient Chinese writings, dating back to 2700 B.C.....A study of Chinese history shows that it was known, even back then, for its purging effects, as well as its ability to suppress feverish conditions (Foster): it was taken by an emperor in the Liang dynasty (557-579) for fever, used as gift-bearing means to an emperor of the Tang dynasty (618-907), used to combat the plague in the years which the Song dynasty ruled (960-1127), and used as a suicidal measure by a general of the Ming dynasty (1368–1644). With a variety of medicinal uses, it wasn’t long before this potent plant began making its way to other parts of the world. In fact, it became one of the most prominent items traded along the Silk Road. A rhubarb monopoly initiated in Imperial Russia in 1731, stiffly regulating its trade from “China via the Asian steppes to Moscow and St. Petersburg, where its root was shipped to the rest of Europe.” For 125 years thereafter, rhubarb-root imports were governed solely by what was known as the “Rhubarb Office.” This, “office” ceased to exist once China opened its ports to the Western nations, allowing for free trade. Some of the common names associated with *Rheum palmatum*: “Russian rhubarb”, “Turkey rhubarb,” and “Indian rhubarb,” are directly affiliated with the trade routes for rhubarb from China[15].

In ancient China, rhubarb root was taken and recognized as a means to cure stomach ailments and as a “cathartic” [an agent used to relieve severe constipation], as well as its use as a poultice [a preparation of fresh, moistened, or crushed dried herbs, applied externally] for “fevers and edema” [swelling caused by fluid retention in the tissues of the body]. It was given its Latin name by the renowned Carolus Linnaeus in the year 1759, and made to augment its proliferation to British botanical gardens around 1762 [13, 16, 17].

Today, Rhubarb festivals persist in areas “all over the U.S., Canada, England, and Australia These “gatherings” appeal to both travellers and “rhubarb buffs” all around the world. For instance, the first International Symposium on Rhubarb was held in China in 1990 [Foster]. Its objective was to verify the scientific data and treatment of Chinese Rhubarb used by Chinese pharmacopoeias[18].

#### **Effect-enhancing and toxicity-reducing.**

The study is conducted to investigate the influence of Dahuang on the pharmacokinetics of Fuzi. Fuzi diterpene alkaloids pharmacokinetics was greatly influenced by Dahuang which may account for the compatibility mechanism of effect-enhancing and toxicity-reducing [19].

#### **Anti-viral effect**

The antiviral activities of emodin (an ingredient of *Rheum palmatum*) against CVB5 and RSV infections, in an attempt to discover new antiviral agents for virus infection was examined. emodin could decrease the mRNA expression of IFN- $\alpha$  but enhance TNF- $\gamma$  expression significantly compared to the viral controls *in vitro*. Our results provide a molecular basis for development of emodin as a novel and safe antiviral agent for human enterovirus and respiratory virus infection in the clinical therapy [20].

#### **Liver failure**

the regulation effect of *Rheum palmatum* (*R. palmatum*) L. on NF- $\kappa$ B signaling pathway of ALF mice was explored. Through NF- $\kappa$ B signaling pathway, the *R. palmatum* L. could reduce the content of enzyme of liver function and inflammation factor in the serum of ALF mice, regulate the expression of cell apoptosis-related protein and improve the symptoms of ALF mice [21].

#### **Anti-metastatic effects**

The effect of RP ethanol extract (RPE) on the highly metastatic human MDA-MB-231 breast cancer cells *in vitro* was assessed. Results showed that RPE down-regulated the levels of extracellular matrix degradation-associated proteins, including MMP-2/-9, uPA and uPAR, and up-regulated PAI-1. In addition, RPE affected NF- $\kappa$ B by degrading I $\kappa$ B $\alpha$ , and affected the mitogen-activated protein kinase signal transduction pathway by depressing the

activation of p38, ERK and Akt. These results suggest that RPE has potential anti-metastatic activity and warrants further investigation [22].

#### **Hepatitis and renal failure**

potential differences in the chemical markers between batches of raw and processed *R. palmatum* and to develop a deeper understanding of the underlying mechanisms responsible for the enhanced efficacy and reduced toxicity of the processed material. UPLC/Q-TOF-MS represents an efficient method for exploring the chemical markers in the raw and processed *R. palmatum* material, as well as investigating the mechanisms associated with the processing, quality control, and safe application of *R. palmatum* [23].

The mechanism of the antipyretic effect of *Rheum palmatum* L. and *Coptis chinensis* Franch. from the perspective of transient receptor potential vanilloid 1 and transient receptor potential melastatin 8 expression on yeast-induced pyrexia rat model was examined. The antipyretic effect of *Rheum palmatum* L. and *Coptis chinensis* Franch might result, at least in part, from the regulation of transient receptor potential vanilloid 1 and melastatin 8 expressions. Result showed that wide use of cold-natured traditional Chinese medicine such as *Rheum palmatum* L. and *Coptis chinensis* Franch in China as a traditional antipyretics [24].

#### **Metabolic syndrome treatment**

the effect of compound FF16, compatibility of *Rhodiola crenulata*, *Cordyceps militaris*, and *Rheum palmatum*, on obesity was investigated. The results showed that the body weights and the energy uptake were markedly reduced by compound FF16 in both IRF mice in dose-dependent manner and KKAY mice, respectively. Meanwhile, with the administration of FF16, the hypercholesterolemia and the hypertriglyceridemia were improved significantly in KKAY mice; and the levels of serum cholesterol and fatty index were decreased obviously, and the value of serum HDL-C was increased significantly in IRF mice, respectively. Moreover, the activity of  $\alpha$ -glycosidase was inhibited by compound FF16 in vitro. In conclusion, FF16 could improve the obesity by inhibiting  $\alpha$ -glycosidase activity [25].

#### **Antipyretic and reducing plasma concentration**

the antipyretic and anti-inflammatory effects in rats of Rhein, a major component in rhubarb was examined. there was a difference in pharmacokinetic process of Rhein between the impact of normal saline and LPS. So, it can be concluded that the targets of regulating NO production and BT after RD administration may be at the same location. Not only do that, the antipyretic effect induced by RD maybe completely manifest through reducing the plasma concentration of NO [26].

#### **Inhibitory effect**

The antiviral effect of an ethanol extract from the roots and rhizoma of *Rheum palmatum* (*R. palmatum*, one of the Chinese Rhubarbs) was determined against CVB(3) in tissue culture cells and in a mouse model. The ethanol extract treated mice showed alleviated clinical signs, better survival rate, prolonged MTD and decreased viral titers compared to the virus control group. Our results indicate that the ethanol extract from *R. palmatum* has the anti-CVB(3) activity in vitro and in vivo and thus provides a re-evaluation of this old remedy with a broad therapeutic potential [27].

#### **Hepatotoxicity**

the bidirectional potential of rhubarb was illustrated and demonstrates the feasibility of using factor analysis to study the dose-response relationships between herbal medicines and hepatotoxicity or the healing effects of these herbs by extracting the underlying interrelationships among a number of functional bio-indices in a holistic manner [28].

#### **Anti-SARS coronavirus**

The inhibitive effect of the compounds from *Rheum palmatum* L. on the SARS-3CL protease was clarified. Result showed that extracts from *Rheum palmatum* L. have a high level of inhibitory activity against 3CL protease, suggesting that extracts from *Rheum palmatum* L. may represent a potential therapeutic for SARS [29].

#### **Antioxidant activity**

The metabolism and pharmacokinetics of anthraquinones in RP decoction in rats was investigated. It was found that the glucuronides of aloe-emodin, rhein, emodin and chrysophanol were predominant in the blood, whereas their aglycones were not detected except for rhein. In conclusion, the anthraquinones were subject to a rapid and

extensive conjugation metabolism in rats and the serum metabolites of RP exhibited a potential free radical scavenging effect on AAPH-induced hemolysis at pharmacologically relevant concentrations [30].

#### **Anti-liver effect**

The possible interactions between TCM and drugs, the effect of water and ethanol extracts of DG, CX and DH on cytochrome P450 were studied in rats was assessed. All extract treatments had significant effects on CYP isoforms activities, whether induction or inhibition, compared with the blank control. Thus, caution should be paid to possible drug interactions of DG, CX, DH and CYP substrates (31).

The effect of four concentrations of calcium ions on the production of anthracene derivatives by means of the callus and suspension cultures of *Rheum palmatum* L. (Polygonaceae) was assessed. the production was stimulated by 44% and 17%, respectively. After an addition of calcium ions to the elicited callus culture, no positive influence on the production was observed [32].

#### **Anti-stress**

the effect of four concentrations of jasminic acid on the production of anthracene derivatives by a three-year-old tissue culture was examined. The results show that the optimal effect of jasminic acid on the production of callus culture was manifested after a 12-hour application of the strongest concentration of 5 mM, and on the production of suspension culture after a 48-hour application of a concentration of 0.05 mM, when the photometric determination according to PhBs 4 demonstrated the maximal content of anthracene derivatives (1.26%) and the production was stimulated by 109% in comparison with the control [33].

#### **Anti-liver and hepatic**

The preventive, therapeutic effect and the possible mechanism of extract from *Rheum palmatum* (ERP) on hepatic encephalopathy (HE) in rats with acute liver failure was investigated. ERP significantly prevents and treats HE in rats with thioacetamide-induced acute liver failure [34].

#### **AntiHBV effect**

The anti HBV effect of *Rheum palmatum* Volatile oil was studied by using 2215 cell line transfected with HBV DNA. At the same time MTT method was applied for the detection of cytotoxicity of drugs, selecting acyclovir (ACV) as control medicine. This shows *Rheum palmatum* Volatile oil possesses the effect of antiHBV in vitro [35].

#### **Anthracene derivatives**

the effects of five concentrations of salicylic acid on the production of anthracene derivatives by a three-year and a nine-year old culture derived from the root of the intact plant *Rheum palmatum* L was examined. It follows from the results that increase in production after elicitation is higher in the three-year old culture than in the nine-year old one and elicitation of suspension culture is more successful than elicitation of callus culture [36].

#### **Increasing intelligence**

Thenootropic effect of *Rheum palmatum* decoction in mice was observed. *Rheum palmatum* decoction contains the substances of increasing intelligence which may be substantial basis of the decoctions mainly containing *Rheum palmatum* therapig aphasia from apoplexy, senile dysmnesis, sequel from brain trauma, etc [37].

#### **Anti-inflammation**

the clinical significance of urinary interleukin-6 (IL-6) level in chronic renal failure (CRF) patients was assessed and the effect of *Rheum palmatum* (RP) in treating it. Determination of urinary IL-6 level is useful in studying the severity of immune inflammation of CRF. RP improves renal function by inhibiting the production of IL-6 and lowering immune inflammation [38].

#### **Anthracene derivatives production**

the effect of 6, 12, 24, 48, 72, and 168 hours lasting action of four concentrations of the biotic elicitor chitosan was investigated on the production of anthracene derivatives by the callus and suspension culture of *Rheum palmatum* L. The maximal content of anthracene derivatives (1.181%), found by photometric determination according to PhBs 4, as demonstrated after 24-hour action of a chitosan solution of a concentration of 1 mg/30 ml of the medium. In contrast to the suspension culture, the production of anthracene derivatives in the callus culture was influenced by elicitation only in the minimal way [39].

**Homogenate of *Candida utilis***

The effect of the homogenate of *Candida utilis* on the production of anthracene derivatives was studied by the callus and suspension culture of *Rheum palmatum* L. of different age and origin. Result showed that the content of anthracene derivatives was lower than in the eight-year-old culture. In contrast to the suspension culture, the production of anthracene derivatives in the callus culture was influenced by elicitation only in the minimal extent [40].

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