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REVIEW ARTICLE

Medicinal importance of Genus *Rheum* -A review

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Abstract

Genus *Rheum* is medicinally important as it has hepatoprotective, spasmolytic, anticholesterolaemic, antitumor, antiseptic, antifungal, antimicrobial, anti-Parkinson's, anti-proliferative, immuno-enhancing, antiviral and antioxidant properties. A huge array of bioactive compounds have been so far isolated from *Rheum*. This emphasizes on the need of extensive study for the survey of literature regarding the information on the medicinal importance of various species of genus *Rheum*.

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INTRODUCTION

The genus *Rheum* L. commonly called as 'Indian Rhubarb', 'Gilgiti Rubarb', 'Small Himalayan Rubarb' belongs to family Polygonaceae is represented by 60 species and is mainly distributed in mountains and desert regions in Asia and Europe (Kao and Cheng 1975, Li 1998). Diverse bioactivities have been attributed to this genus like anticholesterolaemic, antitumour, antiseptic (Zargar et al., 2011) antioxidant (Krenn et al., 2003), antitumour and antiangiogenic (Srinavas et al., 2007). Its pharmacologically active ingredients include emodin, aloe-emodin, physcion, chrysophanol, rhein, emodin glycoside, chrysophanol glycosides and anthraquinones (Nadkarni 1996). In the present case extensive literature has been reviewed to find out the medicinal importance of some of the plant species of this genus

Rheum webbianum Royle

Rheum webbianum Royle, an important medicinal plant of this family is commonly known as Pambhakh (leaves) or Pambchalan (roots). It is found in China, India, Pakistan and Nepal at an altitude of 2,400-4,300 m asl. In India it occurs in Jammu & Kashmir, & Himachal Pradesh.

The rhizome of *Rheum webbianum* has been traditionally used as a medicine since ancient times. It is used for the treatment of indigestion, abdominal disorders, boils, wounds and flatulence (Chaurasia et al., 2009). *Rheum webbianum* root contains a large proportion of chrysophanic acid, sometimes called chrysophan, an allied substance emodin, a glycoside rhaponticin, a tannin called rheo-tannic-acid, several resins, an albuminoid principle, mucilage, extracts, tannic and gallic acids, sugars, starch, pectin, lignin, calcium oxalate, oxalic acid and various inorganic salts (Nadkarni.1996). Abe et al., 2000 found that *Rheum webbianum* is a potential source of dietary fiber with lipid lowering effect. It is suggested that rhubarb exerts its effect on cholesterol by inhibition of enzyme squalene epoxidase. This enzyme is thought to catalyze the rate limiting step of cholesterol biogenesis. The main secondary

metabolites present in *Rheum webbianum* to which it owes its medicinal importance are anthraquinones like rhein, emodin, aloemodin, physcion and chrysophanol. Besides anthraquinones various stilbene glycosides like rhaponticin and tannins like sennosides, catechins, gallic acid and cinnamic acid are also present. Due to the presence of these active components it is used to cure various diseases like cancer, renal disorders, and hyperlipidemia and improves the memory of senile patients. (Tayade et al., 2012). Srinavas et al., 2007 found that the action of anthraquinones present in *Rheum webbianum* is helpful in managing cancer. Rhubarb extract has been found to have antitumor and antiangiogenic action. Apoptosis and cell cycle inhibition of many human cancer cell lines has been observed in vitro. Rhubarb extract is also suggested as an adjunct to chemotherapy.

***Rheum emodi* Wall.**

Rheum emodi Wall is one of the oldest and best known Indian herbal medicinal plant. It is used as a purgative, stomachic, astringent and tonic as well as in certain skin diseases (Kapoor et al., 1990; Prasad et al., 2001). This herbal medicine is also administered in biliousness, piles, lumbago, chronic bronchitis and asthma. Rhizomes of *R. emodi* contain a large number of hydroxyanthraquinone derivatives such as physcion, chrysophanol, emodin, aloemodin, rhein and their glycosides (Agarwal et al., 2000; Babu et al., 2003) which are reportedly known for various biological activities including anti-oxidant (Yen et al., 2000 and Cai et al., 2004), cytotoxic (Kubo et al., 1992), casein kinase II inhibitory (Yim et al., 1999), anti-viral (Semple et al., 2001) and nephroprotective activities (Alam et al., 2005). In addition, these hydroxyanthraquinone derivatives are also used in preserving food stuffs (Yen et al., 2000) and in textile dyeing as safe and eco friendly natural dyes (Kala 2002). *Rheum emodi* is an important medicinal plant, which finds an extensive use in Ayurvedic and Unani systems of medicine. The anthraquinone derivatives like emodin, aloemodin, physcion, chrysophanol, rhein, emodin glycoside and chrysophanol glycosides are the active components present in the rhizomes of this species and due to the presence of these anthraquinones this plant is having antimicrobial, anti-tumor and anti-inflammatory properties (Wealth of India, 1972). The roots are astringent, tonic and purgative; the tuber is pungent, bitter, with diuretic effect, and reported to be useful in chronic bronchitis, asthma, sore eyes and bruises. It is also used as a blood purifier. Besides its medicinal properties, it is used as a natural dye in cosmetics, textiles and as food colorant (Malik et al., 2009).

Zargar et al., 2011 have reported the presence of components such as sulfemodin 8-O- β -D-glucoside, revandchinone-1, revandchinone-2, revandchinon-3, revandchione-4, 6-methyl-rhein and 6-methyl aloemodin from the same species. Revandchinones belong to a new class of compounds called as oxanthrone esters. Due to the presence of the huge array of compounds *Rheum emodi* is found to be liver stimulant, purgative, anticholesterolaemic, anti-tumor, antiseptic and tonic. Anthraquinone derivatives show evidence of antifungal, antimicrobial, anti-Parkinson's (Kong et al., 2004). The rhizome of *Rheum emodi* possesses hepatoprotective principles that can prevent and treat liver damage due to paracetamol (Akthar et al., 2009).

Hassan et al., 2008 assessed the effect of aqueous and alcoholic extracts of *Rheum emodi* Wall. against carbon tetrachloride induced hepatic injury. The crude extract of *Rheum emodi* affords a significant protection against carbon tetrachloride induced hepatotoxicity in rats when given before the metabolic activation of the toxin.

Ho et al., 2007 have observed that emodin blocks 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 can be a novel anti-SARS-CoV compound and might be considered as a potential lead therapeutic agent in the treatment of SARS. *R. emodi* rhizome extract has been found to exhibit 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, et al., 2010). Alam, et al., 2005 reported that *Rheum emodi* extract possesses nephroprotective properties due to the presence of tannins in it so it can be used against antibiotic induced nephrotoxicity. Methanolic and aqueous extracts of the roots of *R. emodi* are reported to possess antioxidant and anticancer potential (Rajkumar, et al., 2010). Kuo et al., 2002 studied the anti-cancer effect of *Rheum emodi* in two human cell lines Hep G2 and Hep 3B. The anti-cancer effect of this species is attributed to the presence of aloemodin which inhibited cell proliferation and induced apoptosis in both examined cell lines by different antiproliferative mechanisms

***Rheum palaestinum* Feinbr.**

Rheum palaestinum a rare plant belonging to family Polygonaceae is a perennial hemicryptophyte that grows during the rainy winter in desert mountainous areas in Israel and Jordan that receive an average annual rainfall of 75 mm. This plant is a wild species locally known as Atrafan. It is mainly found in the Syrian Desert and Eastern Desert of Jordan with a distribution extending to the Southern part of Palaestine and Sinai (Al-Eisawi 1982 and

Zohary 1966). It is a perennial herb, 15-40 cm long, with underground woody stem. Leaves are rounded, huge, 20-50 cm in diameter, with wrinkled surface. Flowers are greenish, not showy, producing triangular fruits with broad wings (Al-Eisawi, 1998). *Rheum palaestinum* remains in use as a laxative, especially in powdered form (Bruneton 1995). It produces a variety of secondary phenolic metabolites, i.e. anthraquinones, naphthalenes, stilbenes, chromones, avonoids, and related compounds (Kashiwada and Nonaka, 1984 and Bruneton, 1995). Since ancient times the aqueous extract of the rhizome of *R. palaestinum* is used as a coloring agent in the preparation of sheep butter among Bedouins (Al-Khalil and Al-Eisawi 1993). Further information provided by the rural inhabitants and some herbalists indicated that the extract of this plant exhibits anti-platelet activity and increases the time of clotting. Early works on *R. palaestinum* reported the isolation of only chrysophanol and emodin from the roots and aerial parts of the plant (Al-Khalil and Al-Eisawi 1993), which is not sufficient to explain its use in traditional therapy as anti-platelet aggregation agent. Later on other chemical compounds like resveratrol-3-O-b-d- glucopyranoside and its corresponding aglycon, resveratrol has been isolated from this plant which act as anti-platelet aggregation agents (Kimura et al., 1985, Chung et al., 1992 and Orsini et al., 1997). Moreover, resveratrol also acts as coronary vasodilator (Fremont 2000), anti-leukemia (Mannila et al., 1993), and anti-fungal agent (Lang- cake et al., 1979). Other stilbenes isolated from *Rheum palaestinum* act as glucosidase inhibitory agents (Kubo et al., 1991). Aburjai 2000 carried out the chemical characterization of *Rheum palaestinum* and isolated two stilbene derivatives (trans-resveratrol-3-O-b- d-glucopyranoside and rhaponticin (rhapontigenin-3-O-b-d-glucopyranoside) from this plant. These compounds are reported to have anti- platelet activity on human platelet rich plasma (PRP) aggregation.

***Rheum ribes* Linn.**

Rheum ribes Linn another species of this genus, locally known as “Iskin, usgun or, Ucgun” is distributed in Eastern Turkey, Lebanon and Iran. This is the only species of *Rheum* growing in Turkey (Cullen 1996). *Rheum ribes* is the source of one of the most important crude drugs in the Middle East (Kashiwada, et al., 1988). Young shoots and petioles of *R. ribes* are used against diarrhea as well as stomachic while juice of some parts of the plant is used against hemorrhoids, measles, smallpox and cholagogue (Baytop 1999). Its fresh stems and petioles are consumed as vegetable, and stems are also eaten fresh, which act as digestive and appetizer while the roots are used to treat diabetes, hypertension, obesity, ulcer, diarrhea (Tabata et al., 1994 and Abu-Irmaileh & Afifi 2003), as antihelmintic, anti-psoriatic (Shokravi & Agha Nasiri, 1997) and expectorant (Tabata et al., 1994). The decoction of *R. ribes* roots possesses blood sugar lowering activity (Naqishbandi et al., 2009). *R. ribes*, grown in Iran, is reported to have antimicrobial activity against gram negative pathogens such as *Escherichia coli*, *Klebsiella pneumoniae*, *Proteus* spp., *Pseudomonas aeruginosa* and *Neisseria gonorrhoeae* (Bazzaz et al., 2010). It has also an inhibitory effect on Herpes Simplex Virus (Hudson 2000). *Rheum ribes* is a good source of vitamin A, C and E and the antioxidant potential is found to be more in the plants growing at high altitude (Munzuroglu et al 2000). Ozturk et al 2007 studied the antioxidant potential of chloroform and methanol extracts of roots and stems of *Rheum ribes* using different antioxidant tests. Total antioxidant activity was also measured according to the β -carotene bleaching method, and all four extracts exhibited stronger activity than known standards, namely butylated hydroxytoluene (BHT) and α -tocopherol. Methanolic extract of *Rheum ribes* leaves is reported to have anti-ulcer activity and the effect of the extract in preventing the formation of gastric ulcers is comparable to the standard anti-ulcer drug cimetidine (Sindhu et al. 2010).

***Rheum palmatum* Linn.**

Rheum palmatum Linn, commonly known as “Turkish Rhubarb”, is distributed in Western China, Northern Tibet and Mongolian Plateau. This plant is medicinally very important due to the presence of various bioactive compounds like anthraquinones, flavinoids, tannins, phenolic acids, oxalic acid etc (Chevallier and Andrew 2000). The extracts of the root of this plant are used to cure stomach ailments, as cathartic as well as poultice for fevers and edema. However the extra dosage of the extracts may prove fatal due to oxalic acid crystals which cause the swelling of breathing canal (Chmelik and Stefan 1999). The extract of *R. palmatum* has strong antibacterial activities (Dictionary of Traditional Chinese Medicine 1997) and the major active components in it are considered to be five hydroxyanthraquinones (HAQs), namely aloe-emodin, rhein, emodin, chrysophanol and physcion (Pharmacopoeia of the People’s Republic of China 2005a, 2005b). Emodin (1,3,8-trihydroxy-6-methyl-anthraquinone), an active component contained in the rhizome of *R. palmatum* was found to have antitumor, antibacterial, diuretic and vasorelaxant effects (Tsai and Chen 1992, Liang et al., 1993, Koyama et al., 1998, Zhou and Chen, 1988 and Huang et al., 1991). Emodin has also been reported to sensitize HER-2/neu-overexpressing lung cancer cells to chemotherapeutic drugs and to repress transformation and metastasis-associated properties of HER-2/neu over- expressing breast cancer cells (Zhang and Hung 1996 and Zhang et al., 1998). *Rheum palmatum* is also reported to have antagonistic effect against hepatitis B virus (Kim 2001). Kang et al. 2008 reported that emodin and

aloe-emodin present in *Rheum palmatum* have estrogenic properties and thus could be a good natural estrogen alternative and anti-cancer agents for breast cancer. Yang et al. 2005 reported that the extracts of *Rheum palmatum* could be useful in the treatment of skin or soft tissue infections or those located within oral cavity, caused by Staphylococci such as potentially pathogenic *S. aureus*, *S. epidermidis*, and by other Gram-positive bacteria.

***Rheum undulatum* Linn.**

Rheum undulatum, Linn. commonly known as “Korean Rhubarb”, a perennial herb mainly distributed and cultivated in South Korea has been used in Chinese herbal medicine since ancient times. It has been traditionally used as a controlling agent for dental diseases in Korea (Hur 1994). Rhizomes of *Rheum undulatum* are medicinally very important as they contain suitable quantities of anthraquinones, stilbene derivatives like rhaponticin, piceatannol 3-O- β -D-glucopyranose, rhapontigenin, etc. and due to the presence of these active compounds the rhizome extracts have anti-bacterial, anti-fungal, antioxidant, anti-inflammatory, anti-cancer, and anti-malarial activities (Boonlaksiri et al 2000). *Rheum undulatum* is considered to be less purgative than other *Rheum* species but is more effective in case of blood stagnation syndrome (Kubo et al., 1997). Choi 2005 found that the stilbene derivative (desoxyrhapontigenin) and anthraquinones (emodin and chrysophanol) isolated from this plant have inhibitory effect on hyperglycemia and therefore can be used as a substitute for anti-diabetic drugs. Song et al. 2006 reported that the extract of *Rheum undulatum* root has antibacterial activity against *Streptococcus mutans* and *Streptococcus sobrinus* indicating that it can be used for the control of dental plaque formation and prevention of dental cavities. Mastuda et al., 2004 reported that rhizome extract of *Rheum undulatum* have anti-allergic properties as it causes the inhibition of antigen-induced degranulation of rat basophilic leukemia (RBL-2H3) cells. The anti-allergic properties are due to the presence of hydroxystilbenes. Cheong et al., 1999) concluded that the anti-allergic activity decreases in proportion to the number of methoxyl groups, and hydroxyl substituents on the benzene rings might be important for the anti-allergic activity.

***Rheum officinale* Baill.**

Rheum officinale Baill. (Dahuang in Chinese), an important traditional Chinese medicinal herb is distributed to North Western and Central regions of China (Gao et al 2000). Chinese “Rhubarbs” possess antibacterial, anti-inflammation, antiviral, and anticancer effects. Traditionally, this plant is used for remedies of digestive system diseases, such as constipation (as a purgative agent), dysentery, gastritis, enteritis, gastric ulcer, and hepatitis, and also for treatment of various hemorrhages and trauma. Major active components in *R. officinale* are hydroxyanthraquinones and their derivatives together with tannins (Shen et al., 1997). Yizhong et al., 2004 demonstrated the radical scavenging activity of *Rheum officinale*. The radical scavenging activity is attributed to the presence of hydroxyanthraquinones. Hydroxy groups on one benzene ring of anthraquinone structure were essential for the hydroxyanthraquinones to show activity, the ortho-dihydroxy structure in the hydroxyanthraquinone molecules could greatly enhance their radical scavenging effect, and glycosylation of the hydroxyanthraquinones reduced the activity.

Discussion

The main aim of the present review is to present comprehensive information of the medicinal importance of genus *Rheum*. Though about 60 species of this genus have been identified but the medicinal importance of only a few species is available in the literature. The reason for the chemical profiling of only a few species may be the occurrence of most of the species of this genus in the alpine areas which are inaccessible. However, it is evident from the survey of literature during the present study that genus *Rheum* is a potential source of various secondary metabolites like anthraquinones, stilbenes, tannins, etc. Studies have shown that the secondary metabolites present in *Rheum* have various pharmacological properties like anti cancer, anti microbial, anti ulcer, anticholesterolaemic, anti Parkinson, hepatoprotective, laxative etc.

Conclusion

The presence of pharmacologically active compounds in *Rheum* has been confirmed beyond doubt. The plant species is used both in traditional medicinal systems as well as in modern drug industry as a remedy for various disorders. The secondary metabolites of only a few species and their mechanism of action have been studied so far. Hence extensive research is required to chemically characterize other species and find out the way by which the medicinally active components act as well as their therapeutic potential to combat various diseases

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