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Review Article

GENERAL OVERVIEW OF PHYTOCHEMISTRY AND PHARMACOLOGICAL POTENTIAL OF *RHEUM PALMATUM* (CHINESE *RHUBARB*)

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ABSTRACT

Recent probe of medicinal plants incorporated in traditional systems for curing infection and sustaining holistic health, has exposed good sum of therapeutic efficiency against deleterious infections and chronic illnesses. *Rheum palmatum* (Chinese *Rhubarb*, family Polygonaceae) is a significant medicinal herb, which finds an extensive use in Unani (Traditional) system of medicine. It has been traditionally employed as antiseptic, liver stimulant, diuretic, diabetes, stomachic, purgative/cathartic, anticholesterolemic, antitumor, Alzheimer's, Parkinson's, tonic, antidiabetic, and wound healer. The most vital components from *Rheum palmatum* are the phenolics, flavonoids, terpenoids, saponins, and anthraquinone derivatives such as aloe-emodin, chrysophanol, physcion, rhein, emodin and its glucorhein, and glycoside. Rhubarb also contains tannins which include hydrolysable-tannins, containing glycosidic or ester bonds composed of glucose, gallic acid, and other monosaccharide's and condensed tannins, resulting principally from the flavone derivatives leukocyanidin and catechin. In recent years, new components such asrevandchinone-1, revandchinone-2, revandchinone-3, revandchinone-4, sulfemodin8-O-b-Dglucoside, and 6-methyl-rhein and aloe-emodin have been reported from the same class. It also encompasses some macro and micro mineral elements such as Ca, K, Mn, Fe, Co, Zn, Na, Cu, and Li. Anthraquinone derivatives demonstrate evidence of anti-microbial, antifungal, anti-proliferative, anti-Parkinson's, immune enhancing, anticancer, antiulcer, antioxidant, and antiviral activities. This review article covers published study on therapeutic uses of different constituents from rhubarb.

Key words: Flavonoids, Antimicrobial, Rhubarb, Anthraquinone, Therapeutic uses, Tannins, Anticancer, Antioxidant, Minerals.

INTRODUCTION

The dilemmatic rate of surge in drug-resistance to present antibiotic has compelled the researcher to explore new gate to treat contagious diseases [1]. Medicinal plants have been the subject of man's interest since old time and assume a key job in human wellbeing. Some noteworthy varieties in phyto-pharmaceutical items have been accounted for which can be affected by hereditary assorted variety (both chromosomal and hereditary), ecological variables, plant part utilized, season of collection, developmental stage of plant and cultivation practices, etc. Numerous natural mixes utilized today having drug properties and have complex structure [2]. Traditional Chinese Medicine (TCM) has created over centuries in China and has applied its impact on restorative culture in Asia for in excess of a thousand years [3]. The worldwide about 80% population relies on traditional medicines for essential medical issues [4].

The genre *Rheum palmatum* commonly called as Gilgiti rhubarb, Indian rhubarb, Small Himalayan rhubarb, Turkey rhubarb, belongs to family *Polygonaceae* is addressed by 60 species and is generally coursed in mountains and desert regions in Asia and Europe [5]. Rhubarbs belong to plant medicines known as far back as 2700 BC. Rhubarb root was used by earlier Chinese practitioner for medical purposes to induce bile production, stimulate appetite and intestinal atony, flatulence, and treat hepatitis [6]. In China, *Rheum* plant is adored as it cures such a significant number of ailments and it is called as *Dahuang* in China. The *Rheum* plant is an edible plant. It very well may be taken as a nourishment advertisement it tends to be additionally cooked [7]. Of the various herbs renowned for their medicinal advantages in early civilizations, Chinese rhubarb stays one of few still utilized today in both "traditional and herbal medicine." The absolute first records are found in old Chinese works, going back to 2700 B.C. An investigation of Chinese history demonstrates that it was known, even in those days, for its purging effects, just as its capacity to overcome feverish conditions (Foster): It was taken by a ruler in the Liang dynasty (557–579) for fever, utilized as blessing bearing intends to a sovereign of the Tang dynasty (618–907), used to battle the plague in the years which the Song dynasty ruled (960-1127). With an assortment of medicinal uses, it was not well before this potent plant started advancing toward the different corner of the world. In fact, it became one of the most prominent items traded alongside the Silk Road. Some of the commonplace names associated with *Rheum palmatum*: "*Turkey rhubarb*," *"Russian rhubarb,"* and "*Indian rhubarb*," are legitimately associated with the trade routes for Rhubarb from China [8].

The acknowledgment of traditional medicine as an alternative form of human healthcare and the advancement of microbial resistance to the accessible antioxidants has driven researchers to explore the antimicrobial activity of medicinal plants. In like manner, the utilization of artificial antioxidants is suspected to cause or nourish negative well-being impacts on health, subsequently more grounded limitations are being put on their application and a pattern to substitute them with naturally occurring antioxidants is creating. The role of medicinal plants to counter disease or manipulate has been attributed to antioxidant properties in their constituents [9].

Different bioactivities have been credited to this genus such as anticholesterolemic, antiseptic, antitumor, [10], anti-oxidant [11], anti-angiogenic, and antitumor [12]. Its pharmacologically active constituents include emodin, physcion, aloe-emodin, rhein chrysophanol, chrysophanol glycosides, emodin glycoside, and anthraquinones [13]. 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 can cause the swelling of breathing canal [5]. Studies have demonstrated that aloe-emodin holds numerous properties consisting of antiviral, laxative, and hepatoprotective impacts. Perceptions on neutroectodermal tumors found that aloe-emodin had an anticancer activity [14].

Today, *Rhubarb* celebrations endure in territories "everywhere throughout the U.S., Canada, England, and Australia, these "social occasions" claim to the two explorers and *"rhubarb buffs"* all around the globe. For example, the 1st International Convention on *Rhubarb* was held

in China in 1990 [Foster]. Its goal was to confirm the scientific data and treatment of Chinese *Rhubarb* utilized by Chinese Pharmacopeias [15].

Taxonomical Description

Despite the fact that the species in Palmata family can be effectively distinguish from those in different segments by the palmate lobed leaves, the distinctions among types of Palmata family are questionable and for the most part dependent on the profundity of leaf division, that is, the leaves of *Rheum officinale* are lobed and that of *Rheum palmatum* are half-separated, while, that of *Rheum tanguticum* and *Rheum laciniatum* are separated and direct, individually. It is outstanding that morphological characters are impacted by ecological factors and may shift during various developmental phases of plants. During our field review, *Rheum palmatum* and *Rheum tanguticum* were observed harder to be distinguished than *Rheum palmatum* and *Rheum officinale*. Many middle of the road characters among parted and half parted leaves can be seen with the expansion of populaces. In fact, *Rheum Tanguticum* is at first distributed by Regel as an assortment of *Rheum palmatum* [20].

Chinese *Rhubarb* can deliver as high as a "six to ten-foot jointed stalk," with inexactly spread groups of blossoms along the tips that develop red in color from their regularly white or yellow blooms. Its leaves are fairly "huge, spiked, and hand – molded," developing in width of at any rate a few feet. It is important to understand that only those types of *Rheum* with lobed leaves are certified for their medicinal use. Therefore, garden rhubarb, *R. Rhubarbarum*, just as some other assortment of species with either "undulating or 'wavy' leaves" are not founded for any medicinal reason. Moreover, one can decode Chinese *rhubarb* by its somewhat thick, deep roots while the perennial garden plant is composed overwhelmingly of "flashy buds and rhizome."

Phytochemistry

Plants contain a variety of secondary metabolites such as tannins, terpenoids, alkaloids, flavonoids, phenols, steroids, glycosides, saponins, and anthraquinones which confer them a wide variety of pharmacological properties. It is, therefore, essential to identify the phytochemical constituents from medicinal plants employed in the traditional system for the treatment of various ailments. Moreover, examinations concerning antimicrobial exercises of medicinal plants can result in the alternate assets of therapeutic agents [21].

Medicinal plants are currently in extensive significance view because of their unique attributes as a big supply of healing phytochemicals that could result in the improvement of novel drugs. The vast majority of the phytochemicals from plant sources, for example, flavonoids and phenolics have been accounted for to have positive effect on health and cancer prevention. Modern Mediterranean and DASH (Dietary Approaches to Stop Hypertension) integrate a wealthy diet of phytochemicals from fruit and vegetable sources as the plant-based diet proved to extend the lifespan in Okinawan people, which has the largest number of centenarians. High content material of flavonoids and phenolics in medicinal plants has been related with their antioxidant exercises that play a role in the prevention of the development of age-related disease, especially cause by oxidative pressure. With respect to the gainful phytochemicals in medicinal plants, the research on medicinal plants especially is as significant as the exploration on ordinary medications [22].

Significant phytoconstituents of the plant include anthraquinones (aloe-emodin, physcion, emodin, chrysophanol, and rhein) and stilbenes (resveratrol and piceatannol) which holding anti-cancerous activities against prostate cancer, breast cancer, colon cancer, lymphoma, and leukemia. It is reported that phytoconstituents, oxanthrone esters (revandchinone-1, revandchinone-2, revandchinone-3, and revandchinone-4) demonstrated noteworthy antimicrobial activity against different microorganisms, namely, *Staphylococcus aureus, Bacillus subtilis* (Gram positive), *Klebsiella aerogenes, Chromobacterium violaceum*, *Pseudomonas aeruginosa*, (Gram negative), *Rhizopus oryzae*, and *Aspergillus niger*. Ethanolic extracts of the rhizome display antidiabetic and gastroprotective activities [23].

Anthraquinone is the most important class of phytochemicals, which is accountable for its pharmacological activities. These constituents are fundamentally present in rhizomes and roots. The predominant members of anthraquinone class consist of aloe-emodin, chrysophanol, emodin, rhein, and physcion, which might be proved as anticancer agents [24].

Rheum palmatum contains 5–10% tannins (gallotannin, catechin, and procyanidin). Tannins are phenolic compound discovered in numerous herbs and normal nourishments, for example, tea and sorrel. Tannins are astringent and are traditionally utilized for assortment of oozing or wet skin conditions. Therapeutically, tannins have been employed to deal with inflamed mucus membranes and diarrhea [25].

Pharmacological properties

Many plant species belonging to different families have been reported to have aptitudinal traditional medicinal usage by different communities of peoples across globe. However, nowadays, we have new and different medicines for these diseases, which unfortunately are accompanied by various side effects. Subsequently, there is a dire need to have the active principals of natural origin which can be utilized for the treatment and additionally counteractive action of illnesses/infections with no side effects. Thus, there has been an increasing interest for characteristic plant items as these are increasingly good and safe to the human body with practically no harmful symptoms [26].

Antioxidant activity

Natural constituents such as polyphenols, phenolics, tannins, flavonoids, and terpenes possess antioxidant property to scavenge "free radicals" [27]. Antioxidant ability of phenolic compound is usually due to their reducing properties. Study regarding medicinal plants and vegetables revealed that plants are the great source of anti-oxidant properties. In biological systems, these plants are capable of applying against several oxidative stresses [28]. Since oxidative-stress is one of the reasons for the progression and development of certain lethal disorders and life-threatening diseases such as atherosclerosis, cancer, diabetes, neuronal degeneration, hepatotoxicity, and hyperlipidemia. Antioxidants from plant basis might be valuable in disease anticipation and treatment. Rather than commonly applied antioxidants such as butylated hydroxyl toluene (BHT) and butylated hydroxyl anisole (BHA) which have been limited, because of their toxicity and DNA harm induction-potential. Aqueous and methanolic root extracts of *Rheum* plant are reported to have anticancer and antioxidant potential [29]. In Chinese medicine, *Rheum palmatum* is utilized in the treatment of malignant growth and liver infirmities. The compounds such as maesopsin and marsupsin acquired from the root/rhizome extracts of *Rheum* are found to have antioxidant activity [11]. According to research based study, it has been reported that anthraquinone derivatives, for example, emodin, aloe-emodin, chrysophanol, rhein, and physcion have anti-angiogenic activity, by averting blood vessel development in zebrafish embryos [30].

Nephroprotective activity

The impacts of toxic-metals on the kidney have been recognized for a long time. Nephrotoxicity may happen because of therapeutic or occupational exposure to these toxic metals. Heavy metals will in general collect in kidneys where they may create a wide range of functional and morphological impacts [31]. The nephroprotective activity of both the portions (water-insoluble and water-soluble) of alcoholic root extract of *Rheum* has been built up. The defensive impact of water-dissolvable extract is articulated on every one of the sections (S-1, S-2, and S-3) of the proximal tubule of kidney against mercury chloride, cadmium chloride, and potassium dichromate-induced nephrotoxicity in rodents. The water-insoluble part was found to have defensive impact on S-2 section only. The impact has been proposed due to the tannins present in the portion [32].

Antibacterial activity

Antibacterial activity of a crude-extract from *Rheum palmatum* and its chief bioactive compounds (emodin, aloe-emodin, rhein, physcion, and

chrysophanol) were assessed against *Aeromonas hydrophila* (Gram-negative, and pole formed bacterium). The antibacterial activity was emphatically associated with the anthraquinone content [33]. In another investigation with respect to numerous species of similar variety, the crude ethanol extracts acquired from the roots of *Rheum palmatum*, *Rheum rhaponticum,* and *Rheum undulatum* demonstrated a higher activity against strains of Gram-positive bacteria (*Staphylococcus spp*.) than against Gram-negative microbes (*E. coli, P. mirabilis,* and *K. pneumoniae*). The most grounded inhibitory impact against *Staphylococcus spp.* was applied by *Rheum undulatum* extract (MIC = 125–250 μg/mL) and it was discovered that the active constituents were anthraquinones derivatives, including emodin, aloe-emodin, and rhein. The moderate *in vitro* antibacterial activity of *Rheum undulatum* proposed that this plant could be utilized in the treatment of superficial infections brought about by *Staphylococcus epidermidis* and *Staphylococcus aureus* [34].

Chronic kidney disease

Chronic kidney disease is a world-wide general medical health problem with high cost and poor outcomes. Various sorts of incessant renal disease usually experience a dynamic procedure to create renal interstitial fibrosis, in the end inducing kidney-failure in some [35]. To comprehend the mechanisms of *Rheum palmatum* (*rhubarb*), a chain of experiments was done in 5 of 6 nephrectomized rodents. It was discovered that rhubarb brings down the serum creatinine-level, expands inulin-clearance, diminishes urinary protein discharge, constricts lipid derangement's, and also diminishes oxygen utilization and the hypertrophy of the remnant-kidney but does not impact the degree of blood pressure. In cultured rodent mesangial cells, emodin, among fundamental components of *Rheum palmatum's*, could smother lipopolysaccharide-induced cell expansion through hindrance of c-myc oncogene articulation and blocks interleukin-6 formation. It, additionally, had an inhibitory effect on LPS-stimulated interleukin-1 secretion in human macrophages and repressed the activity of Na-K-adenosine triphosphatase and Ca-adenosine triphosphatase (ATP) in renal tubular epithelial cells [36].

It has been reported that rhein, another constituent of *Rheum palmatum*, had similar impacts like emodin in enhancing kidney function and histological damage in diabetic rodents, as well as in cultured-renal cells. It enhances cell metabolism through glucose transporter-1 and declines cell hypertrophy. These outcomes show that there are various active-components even in a single herbal medicine engaged with the different healing impacts of *Rheum palmatum* in chronic kidney disease (CKD) [37].

Antifungal activity

The phytochemical analysis of *Rheum palmatum* roots extracts showed that certain phytoconstituents such as flavonoids and phenolics are present in it. Plant metabolites have been known to have antimicrobial potential. Hence, antimicrobial properties of the medicinal plants might be ascribed due to the presence of these secondary metabolites [38]. Since numerous bacterial and fungal strains are observed to be resistant against a wide assortment of antibiotics, medicinal plants have been read for their potential to have antimicrobial and anti-fungal properties. Rhein, physcion, chrysophanol, and aloe-emodin separated from *Rheum palmatum* roots showed anti-fungal activity against *T. mentagrophytes*, *C. albicans,* and *A. fumigatus* (MIC 25–250 μg/ml) using *ketoconazole* as a control [39]. The compounds separated from the roots of *Rheum palmatum* (revandchinone-1, revandchinone-3, and revandchinone-4) showed potent anti-fungal activity against *Rhizopus oryzae* and*Aspergillus niger,* with diameters of inhibition zone (DIZ) of 9 mm and 11 mm for the 150 g/ml test concentrations, respectively [26].

Anti-inflammatory activity

Inflammation is a host barrier mechanism of the body and it is a fundamental resistant reaction of the body to survival during damage

Table 1: Taxonomical classification and different names of Rheum palmatum

Biological grouping	Scientific Names	Languages	Common Names
Kingdom	Plantae	English	Chinese Rhubarb [16]
Subkingdom	Viridiplantae	Unani	Ravand Chini [17]
Division	Tracheophyta	Urdu	Ravand Chini [17]
Class	Magnoliopsida	Arabic	Revand [17]
Family	Polygonaceae	Persian	Ravand Chini [18]
Genus	Rheum	French	Rhubarbe de Chine [19]
Species	*Rheum palmatum*	Chinese	Da Huang [7]

Fig. 1: *Rheum palmatum* plant and its different parts [15].

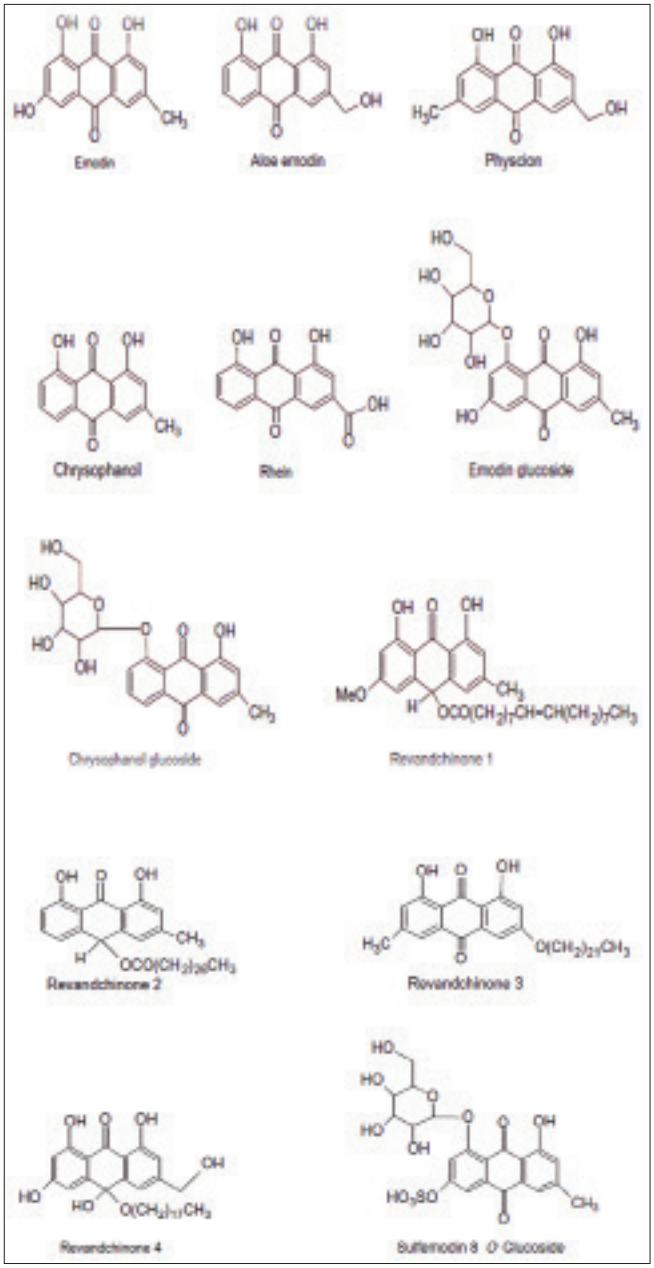

Fig. 2: Structure of bioactive components of *Rheum palmatum* [10].

or contamination and keeps up tissue homeostasis in poisonous conditions [40]. It has been reported that Rhein (20 μM) almost restrained intersegmental blood vessel development at both 48 and 72 h after fertilization (hpf) and absolutely stopped sub intestinal vessel plexus formation at 72 (hpf) in wild sort zebra-fish embryos. Rhein influenced different molecular goals related to angiogenesis, especially *TIE2* and *ANGPT2*[41]. Another research showed that tannins in rhubarb *(Rheum palmatum)* have also some anti-inflammatory actions [42].

Antidiabetic effect

Herbal drugs play an essential role in health-care services programs around the world, and there is a resurgence of enthusiasm for natural medicines for the treatment of different ailments including diabetes and hepatopathy. It has been reported that *Rheum palmatum* roots extract showed antidiabetic activity by improving the peripheral consumption of glucose, by redressing kidney glycolysis, impaired liver, and by restraining its gluconeogenic procedure, similar to insulin [43].

Another research reported that, in diabetic-rats, declines in GFR (glomerular filtration rate) and renal hypertrophy were reduced in those given *Rheum palmatum* extracts [44]. The rodents which had fractional nephrectomy, those provided dose of *Rheum palmatum* root extracts (150 mg/day) in their drinking water had specifically less severe glomerulosclerosis and less proteinuria than untreated rodents; hypertension and renal function were almost equal in the two groups. Among rodents with adenine induced renal failure, *Rheum palmatum's* ingredient tannins notably enhanced BUN (blood urea nitrogen), glomerular filtration rate, renal blood stream, and creatinine renal plasma stream [45,46].

Treatment of Severe Acute Respiratory Syndrome (SARS)

Emodin is one of the fundamental phytoconstituents of *Rheum palmatum* in *Polygonaceae* family has been located to restrain the ACE-2 connection and SARS-CoV S-protein. Emodin has been found to block both the binding of SARS-CoV S-protein to ACE-2 and the infectivity of S protein-pseudotyped retrovirus to Vero E-6 cells. These findings proposed that emodin was a novel anti SARS-CoV compound and is probably considered as a capacity lead therapeutic agent in the treatment of Severe acute respiratory syndrome (SARS) [47].

Antiulcer activity

Ulcer is a typical gastrointestinal issue which has been seen among numerous individuals. Basically, it is an aroused break in the skin or the bodily fluid layer coating the alimentary tract [48]. It has been recently reported that chrysophanol and its rich extract of medicinal plants fundamentally ensures protection against gastrointestinal impacts of cold-resistant ulcer, aspirin, alcohol, and pyloric ligation-induced ulcer in rodents. Chrysophanol productively decreased the aggregate and free acids by repressing the H+/K+-ATPase activity *in-vitro* at IC50 estimation of 187.13 μg/mL. However, it displayed much less activity than emodin [49]. Anti-ulcer effect of ethanolic extract of roots of *Rheum palmatum* was examined on pyloric ligation-induced ulcers in rodents by (Amandeep *et al*. 2013). It was found that there is reduction in ulcer index together with the decrease in volume and overall acidity, and an expansion in the pH of gastric liquid [26].

Prevention and treatment of Parkinson's disease

Around 17 phytochemicals were inspected for inhibitory activity of monoamine oxidase (MAO) A and B on rodent brain mitochondria. Emodin has been found to repress MAO-B and in this way can be utilized as a lead for the counteractive action and treatment of Parkinson's malady [50].

Anti-viral effect

The anti-viral activities of emodin (one of the significant Phytoconstituents of *Rheum palmatum*) against RSV and CVB-5 infections, in a try to discover new antiviral dealers for virus infection were tested. Emodin could diminish the mRNA articulation of IFN-α, however, decorate TNF-γ expression substantially in comparison to the viral controls *in vitro*. Our study gives a molecular basis for advancement of emodin as a safe and novel anti-viral gent for human enterovirus and respiratory infection contamination in the clinical treatment [15].

CONCLUSIONS

Rheum Palmatum is an essential medicinal plant of enormous importance and difficult to cover its all medicinal aspects in just a single article. Despite having the close look of above-mentioned pharmacological activities, it has been used as a supreme constituent of numerous herbal formulations, which are employed for the therapy of several ailments, specifically the smooth regulation of blood pressure, hepatitis, fever, cancer, and fat. However, still detail is in infancy. Plant needs further skillful gaze to be well exploited and isolate several bioactive constituent liable for its activity.

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