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RHEUM EMODI: PHYTOCHEMISTRY, BIOACTIVE COMPOUNDS AND THEIR BIOLOGICAL ACTIVITY

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ABSTRACT

Phytochemical investigation of methanolic extract of *Rheum emodi* reveals the presence of diverse groups of phytoconstituents. A number of anthraquinone derivatives including emodin, aloe-emodin, physcion, chrysophanol, rhein, emodin glycoside and chrysophanol glycoside, sulfemodin,8-O-b-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, anti-proliferative, immune -enhancing, antiviral and antioxidant activities.

Key words: Antifungal, Anti-microbial, Anti-Parkinson's, Anti-proliferative, Immune –enhancing.

INTRODUCTION

Over recent decades, a substantial body of the evidence has demonstrated a wide range of pharmacological activities for a number of medicinal plants. The investigation of crude plant extracts through ethno-pharmacological evaluation of plants with medicinal value, showed that a number of plants exit medicinal properties which may include anti-oxidant, anti-inflammatory and antitumorractivities, (Borgiat *et al*.,1981; Heras *et al*., 1998). The presence of various compounds like flavonoids, polyphenolics, tannins and steroids have been implicated in a no. of medicinal properties of the plants (Mc Clure *et al*., 1975; Harbone *et al*., 1999; Hertog *et al*., 1998).

Rheum emodi Linn (Polygonaceae) locally known as''Pambchallan'' (Kashmir) is a leafy perennial herb distributed in altitudes ranging from 2800 to 3800 m in the temperate and subtropical regions of Himalayas from Kashmir to Sikkim in India (Nautiyal *et al*., 2003).

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The herb has been traditionally used to treat pathological ailments like fevers, ulcers, bacterial infections, fungal infections, jaundice and liver disorders (Agarwal *et al*., 2000; Babu *et al*., 2003; Borgia *et al*., 1981). Rhubarbs, the rhizomes of Rheum species are used in remedies of blood stagnation syndrome, which includes diabetes, atherosclerosis, ischemia, and inflammation in Japanese and Chinese traditional medicine (Matsuda *et al*., 2001). R. emodi constitutes an important food source in various different forms for the people of Kashmir particularly in the rural and high altitude locations of the valley. The rhizomes are cut into short pieces, threaded on a string and dried in the sun or by artificial heat. These dried pieces are then stored and cooked during winters. The leaves locally known as ''Pambhaak'' are also cooked as a vegetable and the leaf stalks are eaten raw or boiled sprinkled with salt and pepper by the locals. The flowers are also edible (Wealth of India, 2003). *R. emodi* is also used for making pies that are used as antipyretic,antihelminthic, laxative, atonic indigestion, constipation, jau ndice and liver disorder (Alam *et al*., 2005). The present investigation was to carried out to establish phytochemistry, phytoconstituents and therapeautic uses of *Rheum emodi*, the study will greatly

help in quality assurance of finished products containing this herbal drug as component.

PHYTOCHEMICAL SCREENING OF CRUDE EXTRACTS OF PETROLEUM ETHER, AND METHANOL FROM *RHEUM EMODI* L

Phytochemical screening of the extracts was carried out according to the standard procedures (Trease *et al*., 1989) The Petroleum ether, Chloroform and methanolic extracts were subjected to preliminary phytochemical screening to identify the various phyto-constituents present in them i.e. Alkaloids, Terpinoids, Glycosides, Steroids, Triterpenoids, Flavonoids, Carbohydrates, Saponins and Tannins.

Test for carbohydrates
Molish test

Treat the test solution with few drops of alcoholic alpha-napthol. Add 0.2ml of Conc. Sulfuric acid slowly through the sides of the test tube, a purple to violet color ring appears at the junction.

Test for alkaloids
Mayer's test

Crude extract was mixed with Mayer's reagent (Potassium mercuric iodide solution) Cream color ppt. was formed showing the presence of alkaloids

Hager's Test

To the 2-3 ml of filtrate, Hager's reagent was added. Yellow precipitate was formed showing the presence of alkaloids

Test for Terpenoids
Salkowski Test

To 2 ml of extract, 2 ml of chloroform and 2 ml of conc. H_2SO_4 were added. The solution was shaken well. A reddish brown coloration of the interference indicated the presence of terpenoids.

Teat for flavonoid
Shinoda test

Crude extract was mixed with few fragments of magnesium ribbons and conc. hydrochloric acid was added drop wise. Pink scarlet color appears after Zinc hydrochloride test To the test solution, add a mixture of Zinc dust and conc. Hydrochloric acid. It gives red color after few minutes.

Test for triterpenes
To the extract, chloroform and conc. H_2SO_4 was added. Appearance of red color indicated the presence of triterpenes.

Test for tannins
$FeCl_3$ Solution Test

On addition of 5% $FeCl_3$ solution to the crude extract, deep blue black color appeared, indicated the presence of tannins

Test for saponins
About 2 g of the powdered sample was boiled in 20 ml of distilled water in a water bath and filtered. 10ml of the filtrate was mixed with 5 ml of distilled water and shaken vigorously. Persistent froth indicated the presence of saponins.

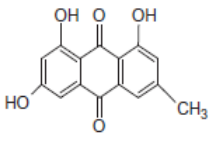
Teat for Amino acids
Ninhydrin test

To the 3ml of crude sample, 3 drops 5% ninhydrin was mixed and heated for 10min in boiling water bath. Purple or bluish color indicated presence of amino acids (Table No. 6).

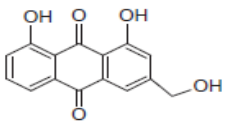
Glycosides
To 2 ml extract glacial acetic acid ,few drops of 5% fecl3 and conc.H2SO4 were added reddish brown colour junction of the two liquid layers and upper layer appears bluish green indicates the presence of glycosides(Trease and Evans,1989)

BIOACTIVECOMPOUNDS REPORTED FROM *RHEUM EMODI* LINN

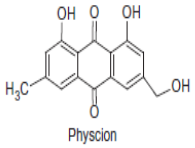
Indian Rhubarb, which is official in the Indian Pharmacopoeia consists of the dried rhizomes of *Rheum emodi* Linn (Singh *et al*., 2005). The major phytoconstituents reported to have been isolated from the rhizomes are: free anthraquinones and their glycosides. The anthraquinones, both with and without carboxyl groups are found in *Rheum emodi* Linn. Anthraquinones with carboxyl group include rhein, while those without carboxyl group include chrysophanol, aloeemodin, emodin, physcion (emodinmonomethylether), 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).



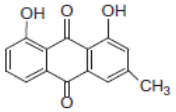
Emodin



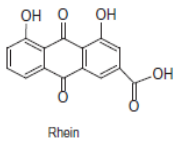
Aloe emodin



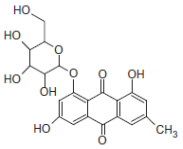
Physcion



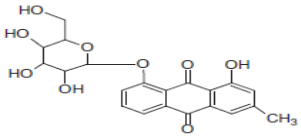
Chrysophanol



Rhein

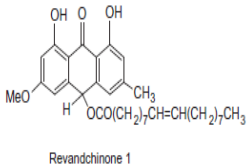


Emodin glucoside

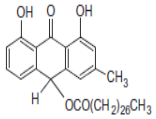


Chrysophanol glucoside

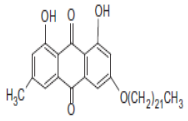
Another chemical group which has been isolated from *Rheum emodi* Linn is anthrone C-glucosides. These anthrones occur in the form of 10- hydroxycascaroside C, 10-hydroxycascaroside D, 10R-chrysaloin 1-O-b-D-glucopyranoside, cascaroside C, cascaroside D and cassialoin (Krenn *et al*., 2004). Different 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).



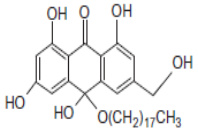
Revandchinone 1



Revandchinone 2

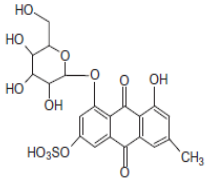


Revandchinone 3

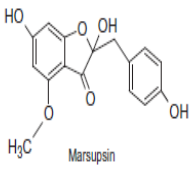


Revandchinone 4

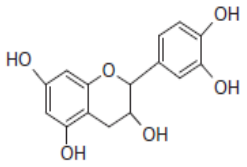
Other compounds, namely, naphthoquinones, rutin, rheinal, rhein 11-O-b-D-glucoside, torachrysone 8-O-b-D-glucoside, epicatechin, auronols (carpusin and maesopsin), the sulfated anthraquinone glycoside sulfemodin 8-O-b-D-glucoside (Krenn *et al*., 2003), b-asarone (Singh *et al*., 2005) and some stilbene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



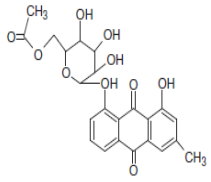
Sulfemodin 8 *O* Glucoside



Marsupsin



Epicatechin



Glucopyranosylchrysophanol

Tannins are also present in rhubarb which includes hydrolysable tannins, containing ester or glycosidic bonds composed of gallic acid, glucose and other monosaccharides and condensed tannins, derived primarily from the flavone derivatives catechin and Leucocyanidin (Roux *et al*., 1982; Haslam *et al*., 1982; Shah *et al*., 1991)

BIOLOGICAL ACTIVITY OF ISOLATED BIOACTIVE COMPOUNDS OF *RHEUM EMODI*

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 *et al*., 2004).

Treatment of Severe Acute Respiratory Syndrome (SARS)

After screening 312 Chinese medicinal herbs, emodin, one of themain 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-pseudo typed 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 (H *et al*., 2007).

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-a, IL-12 and a decrease in IL-10 by RAW 264.7 in macrophage cell lines in the presence of extract alone (Kounsar *et al*., 2011).

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 *et al*., 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 *et al*., 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 *et al*., 2002). The extract from the rhizomes of R. emodi has shown significant hepatoprotective activity against CCl4-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 utilization of glucose, by correcting impaired liver and kidney glycolysis and by limiting its gluconeogenic process, similar to insulin (Radhika *et al*., 2010).

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 *et al*., 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 *et al*., 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 (S1, S2 and S3) 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 S2 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 *et al*., 2005

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 *et al*., 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 *et al*., 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 *et al*., 2002).

DISCUSSION

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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