

## PHYTOTHERAPEUTIC ACTIONS OF BOERHAAVIA DIFFUSA Linn. (PUNARNAVA) IN PREVENTION AND TREATMENT OF VARIOUS AILMENTS: AN OVERVIEW

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### ABSTRACT

*Punarnava (Boerhavia diffusa) is an ayurvedic herb presented by our Mother Nature. It is extensively found in India. Punarnava (Hogweed) literally means 'bring back to life' or 'renewer'. Therefore, this herb is mainly useful for renewing the body systems. Its root, stem and entire herb is used for medicinal purposes. It has long history of use in treatment of varieties of complex diseases in Ayurvedic and traditional system of medicine. This herb has ability to rejuvenate liver and to detoxify it. It clears the lungs and reduces cough, asthma etc. It rejuvenates male reproductive system and acts as an aphrodisiac. It detoxifies skin and clears it of infections. This plant cleanses the kidneys and helps to get rid of renal calculi (kidney stones). Thus, the plant Punarnava acts on all important organ systems and rejuvenate them, giving a new life. Several scientific and clinical studies conducted in past have proved the efficacy of Punarnava in treatment of various complex diseases. The pharmacological actions of this important medicinal herb might be mediated through the synergistic effects due to presence of thousands of bioactive molecules making the plant capable to modulate the biological networks modestly and thereby making it more efficient in controlling complex disease systems. Thus, more extensive multidisciplinary scientific studies on the application of the important medicinal herb "Punarnava" in the treatment of complex chronic diseases using animal models followed by clinical studies on human subjects employing modern pharmacological and molecular techniques will be of great advantage in developing useful drugs for mankind.*

**Keywords:** Boerhaavia Diffusa (Punarnava); Immunomodulator; Hepatoprotective; Antifungal; Antidiabetic; Antiviral; Anthelmintic; Diuretic and Reno Protective; Anticancer

### INTRODUCTION

Boerhaavia diffusa is herbaceous member of the family Nyctaginaceae. It is a famous diuretic, renal tonic and antibiotic of the Indian Pharmacopoeia. It is anti-stress, anti-viral and anti-bacterial<sup>[1]</sup>. It is capable of protecting both the hepatocytes and nephron cells. After long term use Punarnava has even renal, hepatic and splenic regenerative effects according to scientific and clinical studies conducted by many scientists and clinicians.

It is widely distributed in the tropics and subtropics. The species of Boerhaavia diffusa (Punarnava) have been in use for medicinal purpose in different parts of India. It has a long history of uses by indigenous and tribal people and in Ayurvedic or

natural herbal medicines. The whole plant and preferably the roots are effectively used to cure several diseases including Jaundice<sup>2</sup>. The root and aerial parts of Boerhaavia diffusa were used in Ayurveda for the treatment of diabetes. It has many ethnobotanical uses. The leaves are used as vegetable. The root juice is used to cure asthma, urinary disorders, leukorrhea, rheumatism and encephalitis. This herb is medicinally used in the traditional and Ayurvedic system of medicine since ancient time. Besides, the Boerhaavia diffusa plant is reported to possess many pharmacological, clinical, and antimicrobial properties. Punarnava is an herb, which is very useful for curing kidney

diseases.

It has English name also called spread hogweed. It is very useful in curing all type of health problems. *Boerhaavia diffusa* L. is a wild perennial herb which may be encountered in different terrestrial habitats, ranging from managed grasslands, wastelands, agro-ecosystems to large forest gaps. More robust, branches long stout glabrous, pubescent or viscous, leaves 1-2 in. ovate obtuse or acute usually cordate beneath, inflorescence chiefly axillary<sup>[2]</sup>. Herbaceous, diffuse; root large, fusiform; stems prostrate or ascending, reaching 0.6-0.9 m. long, divaricately branched, slender, cylindrical, thickened at the nodes, minutely pubescent or nearly glabrous,

often purplish. Leaves at each node in unequal pairs, the larger 2.5-3.8 cm. the smaller 1.3-2 cm. long, both nearly as broad as long. Flowers very small, shortly stalked or nearly sessile, 4-10 together. Fruit 3mm. long, clavate, rounded, broadly and bluntly 5-ribbed, and very glandular<sup>[3]</sup>. In view of beneficial activity of *Boerhaavia diffusa* in the treatment of various ailments for which our modern systems of medicine have no permanent cure, attempts have been made to review pharmacological properties of this plant and its chemical constituents which may be useful for the development of newer safe and eco- friendly drugsto provide better health care for human being.

#### BOTANICAL CLASSIFICATION<sup>[4]</sup>

<b>Kingdom:</b>	Plantae
<b>Family:</b>	Nyctaginaceae
<b>Order:</b>	Caryophyllales
<b>Genus:</b>	<i>Boerhaavia</i>
<b>Species:</b>	<i>Diffusa</i> , <i>hirsute</i>



PLANT AND ROOTS OF BOERHAAVIA DIFFUSA

#### VERNACULAR NAME OF BOERHAAVIA DIFFUSA

<b>Hindi:</b>	Punarnava
<b>English:</b>	Spreading Hog-weed
<b>Sanskrit:</b>	Bhauma, Kathillaka, Krishnakhya, Krura, Lohita, Mandalpatrica, Nava, Navya, Nila, Nilapunarnava, Nilavarashabhu, Nilini, Pravreshayani, Pravrishenya, Punarbhava, Punarnava, Raktakanda, Raktapatrika, Raktapunarnava, Raktapushpa, Raktapushpika, Raktavarshabhu, Sarini, Shilatika, Shonapatra, Shophaghni, Shothaghni, Shyma, Vaishakhi, Varshabhava, Varshabhu, Varshaketu, Vikaswara, Vishaghni, Vishakarpara <sup>[3]</sup> .
<b>Synonyms:</b>	<i>Boerhavia adscendens</i> , <i>B. caribaea</i> , <i>B. coccinea</i> , <i>B. erecta</i> , <i>B. paniculata</i> , <i>B. repens</i> , <i>B. viscosa</i>
<b>Distribution:</b>	Throughout India, Baluchistan, Ceylon, Tropical and Subtropical Asia, Africa and America.
<b>Description:</b>	More robust, branches long stout glabrous, pubescent or viscous, leaves 1-2 in. ovate obtuse or acute usually cordate beneath, inflorescence chiefly axillary <sup>[2]</sup> .

## PHYTOCHEMICAL CONSTITUENTS OF BOERHAAVIA DIFFUSA

Boerhaavia diffusa has been widely studied for its chemical constituents and therapeutic activities. Boerhaavia diffusa is a good source of nutritional supplements as reported by Miralles and Ujowundu. Miralles et al. reported 15 amino acids (6 essential) in the whole plant and 14 amino acids (7 essential) in the roots along with isopalmitate acetate, behenic acid, arachidic acid (6.3%) and saturated fatty acids (38%)<sup>[5]</sup>. Ujowundu et al.<sup>[6]</sup> accounted the presence of vitamins C, B<sub>3</sub> and B<sub>2</sub> (44.80, 97.00 mg, and 22.00 mg) along with calcium (174.09 mg) in roots. In various tribal areas, Boerhaavia diffusa roots as well as whole plant have been reported to be used as culinary ingredient. Many rotenoids have been isolated from the roots of the Boerhaavia diffusa.<sup>[7,8,9,10]</sup> Plant also includes a series of boeravinones viz., boeravinone A, boeravinone B, boeravinone C, boeravinone D, boeravinone E and boeravinone F. Punarnavoside, a phenolic glycoside, is reportedly present in roots.<sup>[11,12]</sup> C-methyl flavone also has been isolated from Boerhaavia diffusa roots<sup>[13]</sup>. Two known lignans viz., liriodendrin and syringaresinol mono-β-D-glycoside have been isolated<sup>[14]</sup>. Presence of a purine nucleoside hypoxanthine 9-L-arabinose<sup>[15]</sup>, dihydroisofuroxanthone-borhavin<sup>[16]</sup>, phytosterols<sup>[8][17]</sup> have been isolated from the plant. It contains about 0.04 % of alkaloids known as punarnavine and punarnavoside, an antifibrinolytic agent. It also contains about 6 % of potassium nitrate, an oily substance, and ursolic acid<sup>[18]</sup>. The seeds of this plant contain fatty acids and allantoin and the roots contain alkaloids<sup>[19]</sup>. The green stalk of the plant has also been reported to contain boerhavin and boerhavic acid<sup>[20]</sup>.

## TRADITIONAL USES

Punarnava has diuretic, anti-inflammatory and carminative properties. For anti-inflammatory effect, Punarnava should be used with sunthi. Punarnava is also a good Rasayana so useful in Aamavata. Punarnava Root is anticonvulsant, analgesic, expectorant, CNS depressant, laxative, diuretic, abortifacient. Punarnava has been reported to increase serum protein level and reduce urinary protein excretion in clinical trials in patients suffering with nephrotic syndrome.

Punarnava is used for local application in the form of poultice or fermentation in oedema. Punarnava leaf juice is used in the eyes for topical application. Punarnava acts as diuretic in dysuria. Punarnava roots rubbed in honey are locally applied for cataract, chronic conjunctivitis, blepharitis. Punarnava is useful in reducing swelling and foul smelling in skin disorders. Punarnava is useful in heart disease, anemia, and edema. Punarnava leaves vegetable is consumed to reduce edema.

## AYURVEDIC APPLICATIONS

White-edema, anemia, heart disease, cough, intestinal colic, kidney disorders; same uses as red. Red-nervous system, heart disease, hemorrhoids, skin diseases, kidney stones, edema, rat and snake bites; chronic alcoholism, wasting diseases, insomnia, rheumatism, eye diseases, asthma (moderate doses), induces vomiting in large doses, jaundice, ascites due to early liver and peritoneal concerns; urethritis. Leaf juice with honey, dropped into the eyes for chronic ophthalmia.

## PHARMACOLOGICAL ACTIVITIES

Boerhaavia diffusa possesses many therapeutic properties useful for prevention and treatment of varieties of diseases. Few important pharmacological activities associated with this herb are presented below:

### Immunomodulator, Adaptogen and Anti-stress Activity

Ethanol extract of roots of Boerhaavia diffusa was administered to assess protective activity, behavioral effects and toxicity of the herb. Pyelonephritis and urinary tract infection were induced experimentally in rats with a strain of Escherichia coli 06 by systemic infection (intravenous route) or locally infection. The results of the study have shown that Boerhaavia diffusa is innocuous for diuretic response. There was a definite protection against E. coli induced pyelonephritis irrespective of route of administration. The drug reduced the inflammatory changes as well as abscess formation in the kidneys after E. Coli inoculation. It also reduced the bacterial count in urine samples of the infected animals<sup>[21]</sup>. Sumanth and Mustafa studied for cellular and humoral response in mice. Oral administration of the fraction (25-100 mg/kg) of

Boerhaavia diffusa significantly inhibited SRBC induced delayed hyper sensitivity reaction in mice.<sup>[22, 23]</sup> Punarnava alcoholic extract was given p.o. in dosage of 500mg/kg once daily in albino rats of both sexes for a period of 45 days. An increase in the weight of liver and spleen was found. Histological examination of these organs of the treated animals showed marked increase in the number of liver Kupffer cells and spleen malpighian cells respectively, which count for its immunomodulatory effect<sup>[1]</sup>. It is so effective in liver conditions that it brings down abnormal liver function tests to normal within 15 days. Bioactive eupalitin 3-O-β-D-galactopyranoside (5,4'-dihydroxy 6,7-dimethoxy-flavonal-3-O-β-D-galactopyranoside) and eupalitin isolated from the alcoholic extract of *B. diffusa* leaves<sup>[24]</sup> exhibited immunosuppressive properties. Hydroethanolic extract (80%) of *Boerhaavia diffusa* (HEBD) and a polyherbal formulation (Punarnava mandur) PHF-09 containing *Boerhaavia diffusa* were compared for their anti-stress activity using cold restraint stress model. Stress was induced by subjecting animals to cold restraint. Due to cold restraint stress there was an imbalance in the levels of biochemical parameters like glucose, triglycerides, cholesterol, SGOT, SGPT which were near normalized following the administration of HEBD and PHF-09. HEBD and PHF-09 were found to have comparable anti-stress activity<sup>[25]</sup>. The ethanol extract of roots of *B. diffusa* was evaluated for anti-stress, adaptogenic activity in albino mice, by swim endurance test and cold restrains stress and the extract showed improved stress tolerance in immunomodulatory activity as shown by increased carbon clearance, indicating stimulation of the reticuloendothelial system. There was an increase in DTH response to SRBC in mice, corresponding to cell mediated immunity and indicating stimulatory effects on lymphocytes and accessory cell types<sup>[26]</sup>. Adaptogens are useful in both adrenal hyperstress as well as adrenal hypofatigue. By definition, an adaptogen implies the capability for bi-directional or normalizing effects. The most important adaptogens for the adrenals include Panax Ginseng, Siberian Ginseng, Ashwagandha, Rhodiola, *Boerhaavia diffusa*, and Holybasil Leaf Extract. *Boerhaavia diffusa* (Punarnava) has the ability to support both

adrenal over and under activation. In stressful conditions, it has demonstrated the ability to buffer the elevations of serum cortisol and prevent the suppression of the immune system that takes place with elevated cortisol. On the other hand, *Boerhaavia diffusa* has also demonstrated the ability to improve cortisol levels with end stage adrenal exhaustion<sup>[27]</sup>.

### Hepatoprotective Activity

Aqueous root extract of *Boerhaavia diffusa* (2ml/kg) possessed marked hepatoprotective activity against thioacetamide induced hepatotoxicity and marked protection against a majority of serum parameters like GOT, GPT, ACP and ALP but not GLDH and bilirubin. Study also proved that aqueous form of drug (2ml/kg) administration has more hepatoprotective activity than the powder form<sup>[28]</sup>. The effect of 50 % ethanolic extract of roots of *Boerhaavia diffusa* on country made liquor (C. M. L.) induced hepatotoxicity was studied in albino rats. *Boerhaavia diffusa* (100 mg/100 g body weight/day) protected the rats from hepatotoxic action of C. M. L. as evidenced by changes in serum alanine aminotransferase (ALT), triglycerides (TG), cholesterol and total lipid levels in both serum and tissues. Histopathological studies showed marked reduction in fat deposits in animals receiving *Boerhaavia diffusa* along with C. M. L.<sup>[29]</sup> An alcoholic extract of whole plant *Boerhaavia diffusa* given orally exhibited hepatoprotective activity against experimentally induced carbon tetrachloride hepatotoxicity in rats and mice. The extract also produced an increase in normal bile flow in rats suggesting a strong choleric activity. The extract does not show any signs of toxicity up to an oral dose of 2 g/kg in mice<sup>[30]</sup>. The hydro alcoholic extract of roots of *Boerhaavia diffusa* (HEBD) exhibited a significant protective action on liver evident by a reduction in elevated levels of serum lysosomal enzymes namely serum glutamate pyruvate transaminase (SGPT), serum glutamate oxaloacetate transaminase (SGOT), alkaline phosphate (ALP) in both CCl<sub>4</sub> and rifampicin-isoniazid induced hepatotoxicity. Hence HEBD showed a dose dependent hepatoprotective activity<sup>[31]</sup>.

### Anti-diabetic Activity

Administration of Punarnava extract decreased the serum concentration of both cortisol and glucose. Thus, it appears that the hypoglycemic activity of Punarnava is mediated through its cortisol inhibiting potency<sup>[32]</sup>. In another study, Singh et al. showed the renoprotective effect of Punarnava in diabetic nephropathy (DN) patients<sup>[33]</sup>.

### Anticancer Activity

Punarnava inhibited chemically induced skin carcinogenesis<sup>[34]</sup>, proliferation of peripheral blood mononuclear cells, growth of several cell lines e.g. human macrophage cells (U937), human monocytic cells (THP-1), human embryonic kidney cells (HEK293), human erythroleukemic cells (K562), human T cells (jurkat)<sup>[35]</sup> and reduced the metastasis formation by melanoma in mice (by about 95% in case of prophylactic administration and by 87% in simultaneously administration with tumor challenge as compared to untreated control animals)<sup>[36]</sup>. The suggested molecular mechanisms responsible for this anticancer effect are: inhibition of the melanoma cell proliferation and inhibition of the expression or activity of gelatinases A and B, which are intimately related with cell invasion and angiogenesis.

### Antifungal, Antibacterial and Antiviral Activity

Pharmacological studies have demonstrated that punarnava possesses antibacterial properties against *Neisseria gonorrhoeae*, *Bacillus*, *Pseudomonas*, *Salmonella*, *Staphylococcus*<sup>[37]</sup> and antiviral properties against phytopathogenic viruses<sup>[38]</sup>. Ethyl acetate extract of punarnava roots was found to have effective antifungal activity. The maximum inhibition of mycelial growth was observed for *Microsporum gypseum* (78.83%), followed by *Microsporum fulvum* (62.33%) and *Microsporum canis* (42.30%)<sup>[39]</sup>. Punarnava has been used in association with guduchi, daruharidra, haritaki and ginger in a multiple herb formulation for the treatment of experimental hepatic amoebiasis in hamsters. The formulation was found to be curative and to reduce the degree of infection<sup>[40]</sup>. In another study, Verma et al. studied that the root extract of *Boerhaavia diffusa* is having virus inhibitory property<sup>[41]</sup>. The combination of *Boerhaavia diffusa* extract with *Myrothamnus*

*flabellifolius* extract and *Launaea taraxacifolia* extract has been found effective in inhibition of CYP2B6 in human subjects. The results of this clinical study may have direct relevance in anti-retroviral therapy<sup>[42]</sup>.

### Diuretic and Reno protective Activity

Punarnava has been found to exhibit renal regenerative effect<sup>[43]</sup>. Punarnava has diuretic activity<sup>[44]</sup>, which is increased in combination with bhumyamalaki. The mixture of punarnava and bhumyamalaki has been found to be very effective as diuretic and renoprotector, promoting elimination of kidney stones and reduction in size of stones<sup>[45]</sup>. Some sources cited on different websites<sup>[46]</sup> claim that low dosages (10-300mg/kg) produced strong diuretic effect, while higher dosages (more than 300mg/kg) produced the opposite effect- antidiuretic effect, but further scientific studies are needed for verifying this potential antidiuretic effect.

### Spasmolytic and Anticonvulsant Activity

A methanol extract obtained from Punarnava roots exhibited a significant spasmolytic activity in the guinea pig ileum, probably through a direct effect on the smooth muscle. The compounds considered to be responsible for this effect belong to the class of rotenoids<sup>[47]</sup>. The herb has been found to be anticonvulsant also<sup>[48]</sup>.

### Angiotensin Converting Enzyme Inhibitory Activity

Punarnava has found to inhibit the angiotensin converting enzyme, effect which may contribute to its hypotensive activity<sup>[49]</sup>.

### Ca<sup>2+</sup> Channel Antagonistic Activity

A lignan (liriodendrin) isolated from punarnava root was found to exhibit a significant calcium (Ca<sup>2+</sup>) channel antagonistic effect in frog heart single cells using the whole-cell voltage clamp method<sup>[10]</sup>.

### Nitric Oxide Scavenging Activity

Punarnava extract exhibited a dose-dependent nitric oxide scavenging activity. The potency of scavenging activity was in the order: bel leaf > bhumyamalaki > Krishna tulsi > guduchi (hexane, methanol extract) > punarnava > guduchi (aqueous

extract) > katuki. These results suggest that these medicinal plants might be potent therapeutic agents for regulation of pathological condition caused by excessive generation of NO and its oxidation product, peroxynitrite (inflammation, ischemia-reperfusion, septic shock, etc)<sup>[50]</sup>.

#### **Management of IUD-associated Menorrhagia and Endometrial Changes (potent haemostatic, antifibrinolytic and anti-inflammatory agent)**

Intrauterine device (IUD) insertion in monkeys induced several changes of menstruation (premature onset of menstruation, increase in duration of menstrual flow, menstrual iron loss and activity of uterine tissue plasminogen activator (tPA) and endometrial histology (a high degree of stromal edema, heavy infiltration of inflammatory cells, tortuous endometrial glands, and thin-walled empty blood vessels). Punarnava root extract was found more effective in treating these changes than antifibrinolytic agents (epsilon-aminocaproic acid, tranexamic acid) and anti-inflammatory drugs (indomethacin, ibuprofen and naproxen). Root extract of punarnava reduced duration of menstrual flow (124%), menstrual iron loss (120.8%), activity of uterine tPA (272%), stromal edema, inflammation, tortuosity of glands and increased the degree of deposition of fibrin and platelets in the vessel lumen in IUD-fitted menstruating monkeys<sup>[51]</sup>. These studies suggest the use of Punarnava root in menorrhagia, dysmenorrhea and uterine inflammatory troubles.

#### **Anthelmintic Activity**

Dried root powder of *Boerhaavia diffusa* showed curative efficiency when administered orally for one month to children or adults suffering from worm infection. The subjects became worm-free within 5 days of treatment<sup>[52]</sup>.

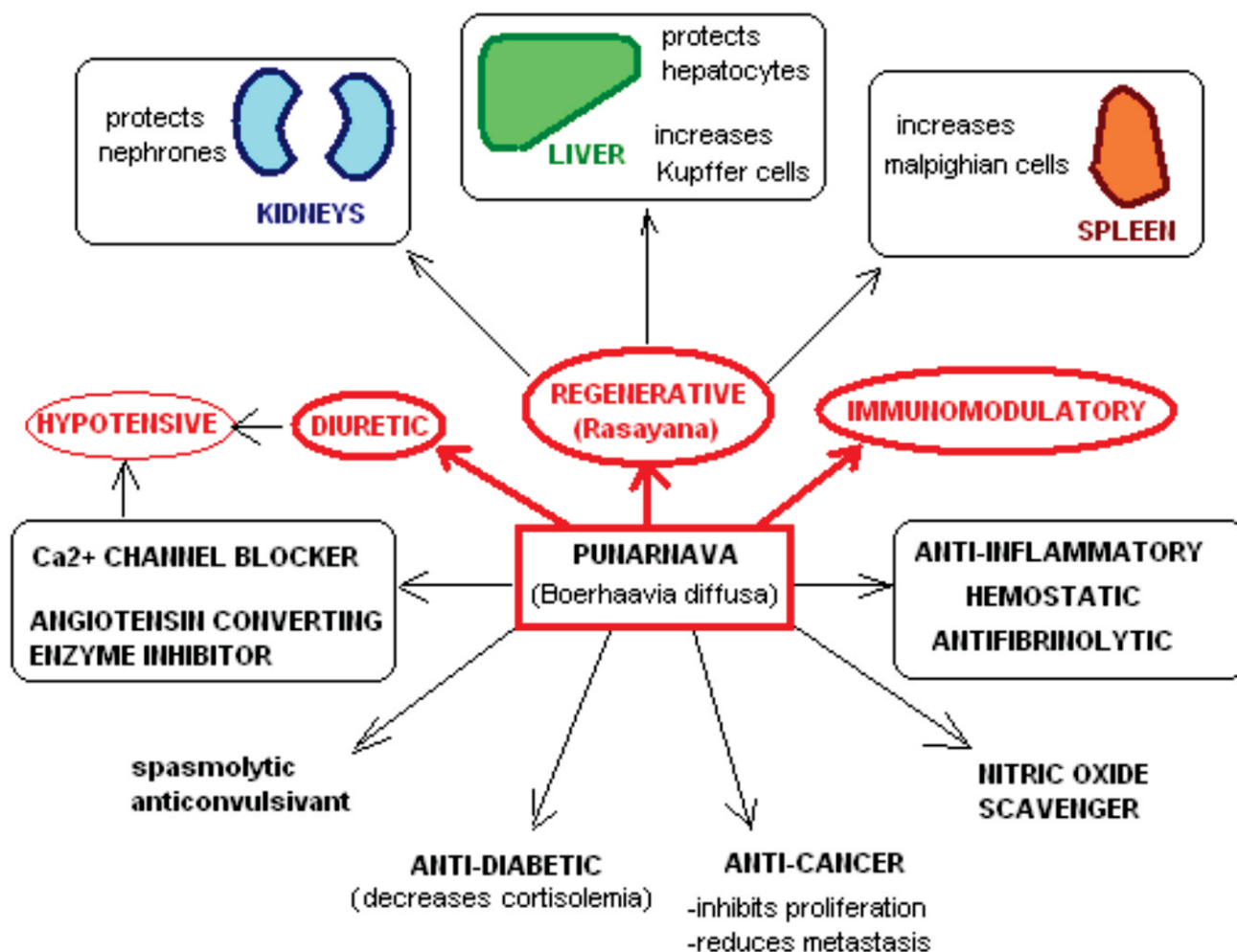
#### **Anti-edema Activity**

A study on Punarnava efficacy in the management of vrikka shotha (nephritic syndrome) in 250 patients has been conducted in various research centers of Central Council of Research in Ayurveda and Siddha and evaluated at CRU, Varanasi, India. The results of the study reported 75 cases with good response, 130 cases with fair response, and 45 cases with poor response<sup>[53]</sup>.

## **DISCUSSION**

*Boerhaavia diffusa* (Punarnava) has a long history of use in the cure of varieties of diseases since ancient time. The roots of Punarnava are employed for many disease conditions including liver, gallbladder and kidney, renal and urinary disorders. Bitter stomachic, laxative, diuretic, expectorant, rejuvenative, diaphoretic, emetic Root-purgative, anthelmintic, febrifuge, White-laxative, diaphoretic. According to Ayurveda, Punarnava is bitter, cooling, astringent to bowels, useful in biliousness, blood impurities, leucorrhoea, anaemia, inflammations, heart diseases, asthma, alternatives etc. The leaves are useful in dyspepsia, tumours, spleen enlargement and abdominal pains. According to Unani system of medicine, the leaves are appetizer, alexiteric, useful in ophthalmia, in joint pains. Seeds are tonic expectorant, carminative, useful in lumbago, scabies. The seeds are considered as promising blood purifier.

Punarnava helps maintain efficient kidney and urinary functions with its diuretic, laxative, stomachic, diaphoretic, anthelmintic, antispasmodic and anti-inflammatory action. This herb has ability to rejuvenate liver and to detoxify it. It clears the lungs and reduces cough, asthma etc. It rejuvenates male reproductive system and acts as an aphrodisiac. It detoxifies skin and clears it of infections. This plant cleanses the kidneys and helps to get rid of renal calculi (kidney stones). Thus, the plant Punarnava acts on all important organ systems and rejuvenate them, giving a new life. This herb has no side effect. Several scientific and clinical studies conducted in past have proved the efficacy of Punarnava in treatment of various complex diseases as depicted in Fig. <sup>[54]</sup>. The pharmacological actions of this important medicinal herb might be mediated through the synergistic effects due to presence of thousands of bioactive molecules like sitosterol, esters of sitosterol, punarnavine, boerhaavia acid, boeravinone, palmitic acid, ursolic acid and many other compounds making the plant capable to modulate the biological networks modestly thereby making it more efficient in controlling complex disease systems.



**Figure<sup>[54]</sup>: Pharmacological actions of punarnava (According with the present scientific evidences only)**

Due to modernization of our lifestyle human beings are prone to attack of disease throughout the world resulting into causation of dreadful diseases like kidney disease, cancer, diabetes, fungal disease, bacterial disease, viral disease, liver disease, heart disease etc. for which our Modern Systems of Medicine have no permanent cure. In the recent years ethno botanical and traditional uses of natural compounds, especially of plant origin received much attention as they are well tested for their efficacy and generally believed to be safe for human use. Thus, more extensive multidisciplinary scientific studies on the application of the important medicinal herb “Punarnava” in treatment of complex chronic diseases using animal models followed by clinical studies on human subjects employing modern pharmacological and molecular techniques will be of great advantage in developing useful drugs for mankind.

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