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**Review**

# Exploring Phytochemistry and Pharmacology of a Rejuvenating Edible Plant: *Boerhavia diffusa* L. *(Punarnava)*

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## ABSTRACT

*Boerhavia diffusa L. (Family – Nyctaginaceae), is commonly known as Horse Purslane, Pigweed, Punarnava, Shophaghni, Kathila, Shilatika, etc. It is a small, creeping perennial herb with little pinkish flowers and found throughout in India, tropical and subtropical Asia, Africa, Australia and America. Leaves and whole plant of B. diffusa are consumed in daily diet by various ethnic communities of India. Medicinally, it is used for treatment of several diseases for example, anemia, asthma, blood impurity, body pain, cough, rheumatism, gall bladder stone, jaundice, joint pain, heart disease, enlargement of liver and spleen etc. in Ayurveda and Ethnomedicine and well-known for its rejuvenating properties. The present article provides an overview of pharmacological properties of B. diffusa such as antioxidant, anti-inflammatory, antidiabetic, hypolipidemic, hypotensive, hepatoprotective, antiproliferative, anticonvulsant, nootropic, immunomodulatory activities etc. along with its phytochemical profile which could be very useful in development of a nutraceutical from the plant.*

**KEYWORDS**: Boeravinone, β-sitosterol, Rotenoids, Antioxidant, Eupalitin

## INTRODUCTION

*Boerhavia diffusa* L. belongs to a dicot Family – Nyctaginaceae. It is known by various names for example, Red Spiderling, Horse Purslane, Hogweed, *Punarnava, Raktapunarnavaa, Shophaghni, Kathila, Varshabhu, Shilatika, Kuthillaka, Chotwa Bhaji, Santi ghass, Gadahpurana, Vishkhapra, Balavadaka, Lal sathi, Satodi, Gajpurni, Kavthali* etc.in different languages[1]. It is a perennial, creeping herb with typical diffuse branching and stout root stocks. The leaves are arranged in opposite fashion and vary from ovate to oblong in shape with smooth and wavy margins (Fig. 1). Flowers are small, pink or pale-pink and born usually from August to December in panicles of cyme[2,3]. It is an herb of pantropical distribution for example, it is found in India, tropical and subtropical Asia, Africa, West Indies, Australia, North South and Central America. It has also taken place under Invasive species list as it has invaded various countries as a weed namely, Argentina, Chile, Paraguay, Hawaii, Japan, Trinidad and Tobago, and Cambodia[4].

Leaves and whole plant of *B. diffusa* are consumed as vegetable in many states of India such as Rajasthan, Uttaranchal, Odisha, Madhya Pradesh, Jharkhand and West Bengal[1]. In fact, Sarkar[5] has recommended use of *B. diffusa* vegetable for patients of heart disease as a dietary therapy. Nutritionally, it is rich in vitamins and minerals, for example, vitamins C, E, $B_1$, $B_2$and $B_3$ and minerals such as Mg, Ca, Mn, Zn, Fe, Na, K and P. Roots and whole plant of *B. diffusa* also possess many essential and non-essential amino acids[6,7].

*B. diffusa* is considered as *'rasayana'* in Ayurveda due to its rejuvenating, anti-ageing and disease prevention properties. The root of the plant has laxative, diuretic and expectorant properties and widely used for treatment of phlegmatic asthma[3,6]. In Ayurveda, the Indian traditional system of medicine; it is mentioned for the treatment of asthma, pneumonitis, bronchitis, ascitis, cardiac disease, inflammation on feet, indigestion, menorrhagia, liver and spleen enlargement, malaria, sprue, renal diseases, pleurisy, renal and urinary calculus, spermatorrhoea, dysmenorrhoea, amenorrhoea, hemicranias, influenza, insomnia, orchitis,

**Figure 1:** *Boerhavia diffusa* L.

hypertension, rheumatism, rhinitis, earache etc.[8]. It is widely used in many commercial Ayurvedic formulations such as *Punarnavasava, Sukumara ghrita, Punarnavadyarishta, Punarnavadi mandura, Sothaghna Lepa, Kumaryasava, Punarnavamandoora, Maha Narayan Taila, Dashamoolarista, Punarnavastaka kvatha curna, Punarnava guggulu, Punarnavadi kvatha curna* and *Varunias* well as in Siddha formulation for example, Talakacenturam[6].

Besides, it is used for treatment of abscess, anemia, arthritis, asthma, blood impurity, blood dysentery, body pain, cataract, conjunctivitis, cough, diabetes, debility, diarrhea, dropsy, dysentery, eczema, gall bladder stone, epilepsy, fever, flatulence, hair fall, jaundice, joint pain, kidney problem, night blindness, pimple, scorpion bite, skin disease, snake bite, stomachache, swelling, urinary trouble, vomit, wound by various ethnic communities of India[1].

Plant-based diets have shown to reduce the risk of several diseases such as diabetes, obesity, hypertension, cancer and cardio-metabolic disorders[9,10]. In this context, use of *B. diffusa* in diet along with its multifarious health-beneficial activities could be useful. Due to its widespread use for medicinal purpose, an attempt has been made to compile the scientific studies carried out on this plant in connection with its various pharmacological properties and phyto-constituents.

## METHODOLOGY

For this purpose, the well-known electronic databases such as Scopus, Pubmed, Wiley, Google Scholar, Sci-hub, Springer Link, Research Gate and Science Direct were thoroughly searched using the keyword *Boerhavia diffusa* in combination with others such as Pharmacology, Phytochemistry, Traditional Medicine, Ethnomedicine, Chemical Constituents, Herbal medicine and Ayurveda. Information thus obtained regarding Phytochemistry and Pharmacological activities of *B. diffusa* is presented below.

## PHYTOCHEMICAL PROFILE

Several phyto-constituents belonging to various classes of secondary metabolites for example, phenolics, isoflavanoids, flavanoid glycosides, steroids, rotenoids and alkaloids have been isolated from different parts of *B. diffusa*[11] which are responsible for its multifarious medicinal properties (Table 1). Preliminary phytochemical screening of aerial parts of *B. diffusa* demonstrated the presence of alkaloids, flavonoids, steroids, terpenoids, saponins, tannins, anthraquinones, cardiac glycosides and reducing sugars[12]. Beegun and associates[13] have shown presence of alkaloids, tannins, steroids, flavonoids, saponins, phlobatannins and phenolics in different extracts of *B. diffusa.* Dhingra and Valecha[14]isolated quinoline alkaloid named as punarnavine from ethanolic extract of *B. diffusa.* Besides this various rotenoids were also isolated from roots of *B. diffusa* such as boeravinone B, D, E, F, G, H and N[15-20]. Sharma and Sahai[21] isolated various chemical constituents named as uridine triacetate, boeravinone B, quercetin 3-O-α-D-rhamnoside, eupalitin 3-O-β-Dgalactopyranoside, 3-O--D-glucopyranosyl sitosterol β, -amyrin, -Pamyrin acetate and -β sitosterol from the leaves of *B. diffusa.* Jayachitra et al.[22] demonstrated presence of alkaloids, tannins, flavonoids, terpenoids, glycosides, phenols and minerals such as sodium, potassium, calcium, manganese, iron, copper, zinc and magnesium in leaves of *B. diffusa.* Kunwar and associates[23] has shown presence of flavonoids, steroids, terpenoids, phenols, tannins, phlobatannins, saponins and cardiac glycosides in leaves of *B. diffusa.* Recently, Priya and Sharma[24] have shown saponins, phenols, alkaloids, tannins and flavonoids in its roots.

**Table 1:** Major Phytochemicals isolated from various parts of *Boerhavia diffusa* L.

| Plant part | Chemical compounds | References |
|---|---|---|
| Root | β-sitosterol, Hentriacontane | Misra and Tiwari[25] |
| | Myristic acid, myricyl alcohol, hypoxanthine 9-L-arabinose | Ojewole and Andesina[26] |
| | Punarnavoside | Jain and Khanna[27] |
| | Boeravinone A, Boeravinone B, fatty acids, Glycerides, Sterol derivatives, Heptadecyclic acid, Palmitic acid, oleic acid, stearic acid, arachidic acid, behenic acid, stigmasterol, Campesterol | Kadota *et al.* [28] |
| | Triacontanol | Suri *et al*.[29] |
| | Liriodendrin, Syringaresinol mono-β-D-glucoside | Lami *et al.* [30] |
| | Boerhavisterol, Boerhadiffusene, Diffusarotenoid, Boerhavilanostenyl benzoate | Gupta and Ali[31] |
| | 2'-O-Methyl abronisoflavone | Borrelli *et al*.[32] |
| | α-2-sitosterols, β-amyrin, β-amyrin acetate, eupalitin 3-O-β-D-galactopyranosyl-(1‴ → 2)-O-β-D-galactopyranoside , 3,3′,5-trihydroxy-7-methoxyflavone, 4′,7-dihydroxy-3′-methylflavone, 3,4-dimethoxyphenyl-1-O-β-D-apiofuranosyl-(1″ → 3′)-O-β-D-glucopyranoside, Quercetin-3 O-β-D-glucopyranoside-7- O-β-D-glucopyranoside, Eupalitin-7-O- α –rhamosyl (1→ 2) - α – rhamnosyl (1→ 6) β-D-galactopyranoside | Maurya *et al.*[33] |
| | Isomenthone, Limonene, Menthol, Phellandrene, Safranal, α-Pinene, Geranylacetone, Hexen-1-ol, trans 2-Octanal, Nonen-1-olc, eugenol, cis 4-Hexen-1-ol,Dihydroactinidiolide,camphor, β-Ionone | Pereira *et al*.[34] |
| | Alkaloids, Carbohydrates, Saponins, Glycosides, Amino acids, Phytosterol, Phenolics, Flavonoids, Terpenoids, Tannins | Baskaran *et al.*[35] |
| | N-trans-feruloyltyramine, Alkamide | Do *et al*.[36] |
| | Punarnavine | Dhingra and Valecha[14] |
| | Ferulic acid | Tacchini *et al*.[37] |
| | Boeravinone B, C, D,E, F, G, H, J, M, N, Q, R, S | Bairwa *et al*.[15]; Bairwa *et al*.[38]; Lami *et al.*[16]; Borrelli *et al.*[17]; Aviello *et al.*[18]; Bose *et al.*[19]; Ningtyas and Wulandari[20] |
| | Sitosterol 3-O-β-glucoside, ß-Ecdysone | Cao *et al*.[39] |

| | | |
|---|---|---|
| Leaves and root | 3,4-dihydroxy-5-methoxycinnamoyl-rhamnoside, Kaempferol 3-o-robinobioside, Quercetin 3-o rhamnosyl(1→6)galactoside, Kaempferol 3-o-(2″-rhamnosyl)-robinobioside, 3,5,4′-trihydroxy-6,7-dimethoxyflavone 3-o-galactosyl(1→2)glucoside, Quercetin 3-o-(2″-rhamnosyl)-robinobioside, Caffeoyl tartaric acid, Eupalitin 3-o-galactoside, Quercetin, Kaempferol | Ferreres *et al.*[40] |
| Leaves | Uridine triacetate, Boeravinone B, Quercetin 3-O-α-D-rhamnoside, Eupalitin 3-O-β-D galactopyranoside, 3-O-b-D-glucopyranosyl sitosterol, b-amyrin, b-amyrin acetate, b-sitosterol | Sharma and Sahai[21] |
| | Syringic acid, genistic acid, O-coumaric acid | Daniel[41] |
| | Myo-lnositol,4-C-methyl-1,14-Tetradecanediol, 1-pentadecyne, Phytol, 3,5-Bis(trimethylsilyl)-2,4,6-cycloheptatrien-1-one, Androstane-11, 17-dione, 3-[(trimethylisilyl)oxy]-17-[O-(phenylmethyl)oxime], (3a,5a), Vitamin E acetate | Umamenaka *et al*.[42] |
| Aerial parts | Anthraquinones, Cardiac glycosides, Reducing sugars | Apu *et al.*[12] |
| | Boeravinone P, Boeravinone Q, Rotenoid glycosides, Sesquiterpene lactone, Boerhaavic acid | Misra and Tiwari[25] |
| | Ursolic acid | Pereira *et al.*[34] |
| | Methylpyrrole, 3-Phenyl-2-(20-pyridyl)-indole, Indole, Eugenol, β-Cyclocitral, Ionone, Dihydroactinidiolide,1-β-D-glucopyranosyloxy-3,4-dimethoxybenzene,1-β-D-glucopyranosyloxy-1-phenylmethane,1-β-D-glucopyranosyloxy-2-pheny-lethane, 1-β-D-glucopyranosyloxy-2-methoxy-4-ethanoylbenzene, N-trans-feruloyl-3 Methyldopamine, (+)-zedoalactone A, Ciwujiatone,1-β-D-glucopyranosyloxy-3,5-dimethoxy-4-hydroxybenzene,Sophorophenolone, Allantoin 3-acetoxy-α-amyrin, 4, 10-dihy-droxy-8- methoxyguai-7(11)-en-8,12- olide | Do *et al.*[36] |
| | Glutinol | Thuy *et al*.[43] |
| Flowers | Betaline pigment, Phenolic acids, Arabinose L(+) | Chetty and Rao[44] |
| Seeds | Palmetic acid, Stearic acid, Palmitoleic acid, Oleic acid, Linoleic acid | Saeed *et al.* [45] |

## PHARMACOLOGICAL PROFILE

It has also shown many pharmacological properties (Fig. 2) such as antioxidant, anti-inflammatory, antimicrobial, hepatoprotective, anticonvulsant, antidiabetic, hypolipidemic, thrombolytic, cytotoxic, diuretic, nootropic etc. in various in vitro and in vivo studies[46,47]. Following is the brief detail of such activities:

*Anti-inflammatory activity*

Bhalla *et al.*[48] reported anti-inflammatory activity from ethanolic extract of leaves of *B. diffusa.* Maximum anti-inflammatory activity of 30.4, 32.2, 33.9 and 32% was demonstrated in a dose of 400mg/ml with carrageenan, serotonin, histamine and dextran induced rat paw edema models respectively. Anti-inflammatory effect of water insoluble alcoholic extract of root, stem, leaves and flowers of *B. diffusa* was demonstrated against carageenan-induced oedema in rats by Mudgal[49]. A comparative study was performed to evaluate the effect of anti-fibrinolytic agents; α-aminocaproic acid, tranexamic acid; anti-inflammatory drugs like indomethacin, ibuprofen, naproxen; and root extract of *B. difffusa* on endometrial histology of IUD-fitted menstruating monkeys and the root extract was found to be the most effective in reducing stromal edema and inflammation as well as increasing the degree of deposition of fibrin and platelets in the vessel lumen[50]. Gharate and Kasture[51] have also shown anti-inflammatory, analgesic, antipyretic and antiulcer activity of three different brands of punarnavasava. Paw edema in rats induced by carrageenan, granulomas from cotton pellets, yeast-induced hyperpyrexia, and pyloric ulcers were all greatly reduced by the formulation.

Anti-inflammatory activity was also assessed by Muthu[52] in carrageenan induced hind paw edema and cotton pellet induced granuloma in wistar rats and maximum anti-inflammatory activity was found at a dose of 400mg/kg body weight with a percent inhibition of 38.39% and 65.52% in both assays respectively. *In vivo* anti-inflammatory activity was evaluated from aqueous extract of *B. diffusa* leaves against carrageenan induced rat paw edema (acute inflammation) and cotton pellet induced granuloma model(sub acute inflammation). Significant ($p<0.001$) anti-inflammatory activity of *B. diffusa* leaves was demonstrated in a dose of 400mg/kg/bw with51.97% inhibition in carrageenan induced rat paw edema and 31.03% inhibition in cotton pellet induced granuloma by Sudhamadhuri and Kalasker[53]. *In vitro* and *in vivo* anti-inflammatory activity of ethanolic extract of *B. diffusa* leaves was evaluated using hemolytic activity of sPLA2 enzymes and sPLA2-induced mouse paw edema and maximum activity was observed in inhibition of human sPLA2[54].

*Antioxidant activity*

Satheesh and Pari[55] have shown in vivo antioxidant potential of aqueous extract of *B. diffusa* leaves in alloxan induced diabetic rats where administration of leaf extract (200 mg/kg, p.o.) significantly reduced thiobarbituric acid reactive substances and hydroperoxides with significant increase in reduced glutathione, superoxide dismutase, catalase, glutathione peroxidase and glutathione transferase after 4 weeks. Gacche and Dhole[56] have shown *in vitro* antioxidant activity of 50% ethanolic extract of whole plant of *B. diffusa* in DPPH radical scavenging assay and polyphenol oxidase inhibition with an $IC_{50}$ of 0.21 mg/ml and 0.95 mg/ml respectively. Ethanolic extract of leaves of *B. diffusa* has demonstrated DPPH scavenging capacity and a reductive potential of 78.32 ± 2.41% and 0.65 ± 0.02 mg/g ascorbic acid respectively[57]. Beegum *et al.*[58] investigated *in vitro* antioxidant activity from ethanolic, chloroform and petroleum ether extracts of *B. diffusa* and found that maximum activity was shown by ethanolic extract than other extracts. Moreover, $IC_{50}$ values of 82.12 µg/ml, 100.19µg/ml and 99.8µg/ml of ethanolic extract were found for DPPH scavenging, hydroxyl radical scavenging and superoxide radical scavenging assays respectively.

Patel *et al.*[59] also demonstrated *in vitro* antioxidant activity of hydro-alcoholic extract of *B. diffusa* with maximum inhibition of 81.91%., 69.06%, 81.65%,80%, 72.12% and 71.08% in the superoxide radical, hydroxyl radical, nitrous oxide, DPPH radical scavenging activity, reducing ability and $Fe^{+2}$ chelating ability respectively. Methanolic extract of *B. diffusa* root has also shown significant inhibition of DPPH ($IC_{50}$ 163.1±6.7 µg/ml) nitric oxide (295 µg/ml) and $H_2O_2$ (159±5.25 µg/ml) radical scavenging activity[60.] *In vitro* antioxidant activity of ethanolic extract of *B. diffusa* root has been investigated by Khalid *et al.*[61]. Results have demonstrated that maximum activity was shown by DPPH radical scavenging assay (101.29 ± 3.78) followed by nitric oxide scavengingassay (82.31 ± 2.83) and ABTS radical scavenging activity (81.73 ± 2.73 mg/ml). Ethanolic and aqueous extracts of *B. diffusa* were evaluated for antioxidant activity and results have shown significant ($p \leqslant 0.05$) antioxidant activity against DPPH (58.20%), ABTS (71.46%,), Fe2+ chelation (61.03%), FRAP (2.72 mg AAE/g)and hydroxyl radicals (66.58%) respectively[62].

*Antdiabetic activity*

Antidiabetic activity of chloroform extract of *B. diffusa* leaves has been demonstrated in streptozotocin induced non-insulin-dependent diabetic rats[63]. Similarly, Pari and Satheesh[64] have also demonstrated antidiabetic activity of aqueous extract of *B. diffua* leaves in a dose of 200 mg/kg in normal and alloxan induced diabetic rats after 4 weeks. *In vitro* antidiabetic activity of petroleum ether, chloroform, ethanolic and aqueous extracts of leaves and seeds of *B. diffusa* were assessed using α-glucosidase inhibitory activity. This study revealed potent inhibitory activity of chloroform extract of both the leaves and seeds in doses ranging from 50-250µg/ml followed by aqueous, chloroform, and petroleum ether extract[65]. Alam *et al.*[60] have evaluated *in vitro* antidiabetic activity of methanolic extract of root of *B. diffusa* against streptozotocin (STZ) induced diabetes in male wistar rats. A significant ($p<0.05$) decrease in elevated levels of blood glucose, body weight, insulin level and glycogen content was observed after 15 days administration of 200mg/kg methanolic extract.

*Hypolipidemic activity*

Ethanolic extract of *B. diffusa* roots has significantly reduced elevated levels of all plasma lipids parameters such as, Total cholesterol, Triglycerides, Very low density lipoprotein-C (VLDL-C), Low density lipoprotein-C (LDL-C), non-HDL-C and malondialdehyde (MDA) in hyperlipidemic rats[66]. Methanolic extract of *B. diffusa* leaves was assessed to investigate hypolipidemic activity against D-Galactosamine induced hepatotoxicity in male albino wistar rats. Methanolic extract was orally administered in doses of 50, 100 and 200 mg/kg body weight to animals and significant reduction in increased levels of total cholesterol, free fatty acids, triglycerides and phospholipids was observed in kidney of rats[67]. *In vitro* hypolipidemic activity of methanolic extract of *B. diffusa* root was evaluated against STZ-induced hyperlipidemia in rats[68]. Results have shown marked reduction in elevated level of plasma lipids, free fatty acids, phospholipids, HMG-CoA reductase activity, conjugated diene, lipid hydroperoxide, and MDA in all treatment groups

*Antihypertensive activity*

A clinical study conducted on 60 patients of essential hypertension to evaluate the efficacy of *B. diffusa* (BD) demonstrated that the administration of BD capsule (containing 250 mg of BD extract) in a dose of two capsules twice a day for 6 weeks effectively and significantly reduced systolic and diastolic blood pressure with improvement in subjective complaints[69].

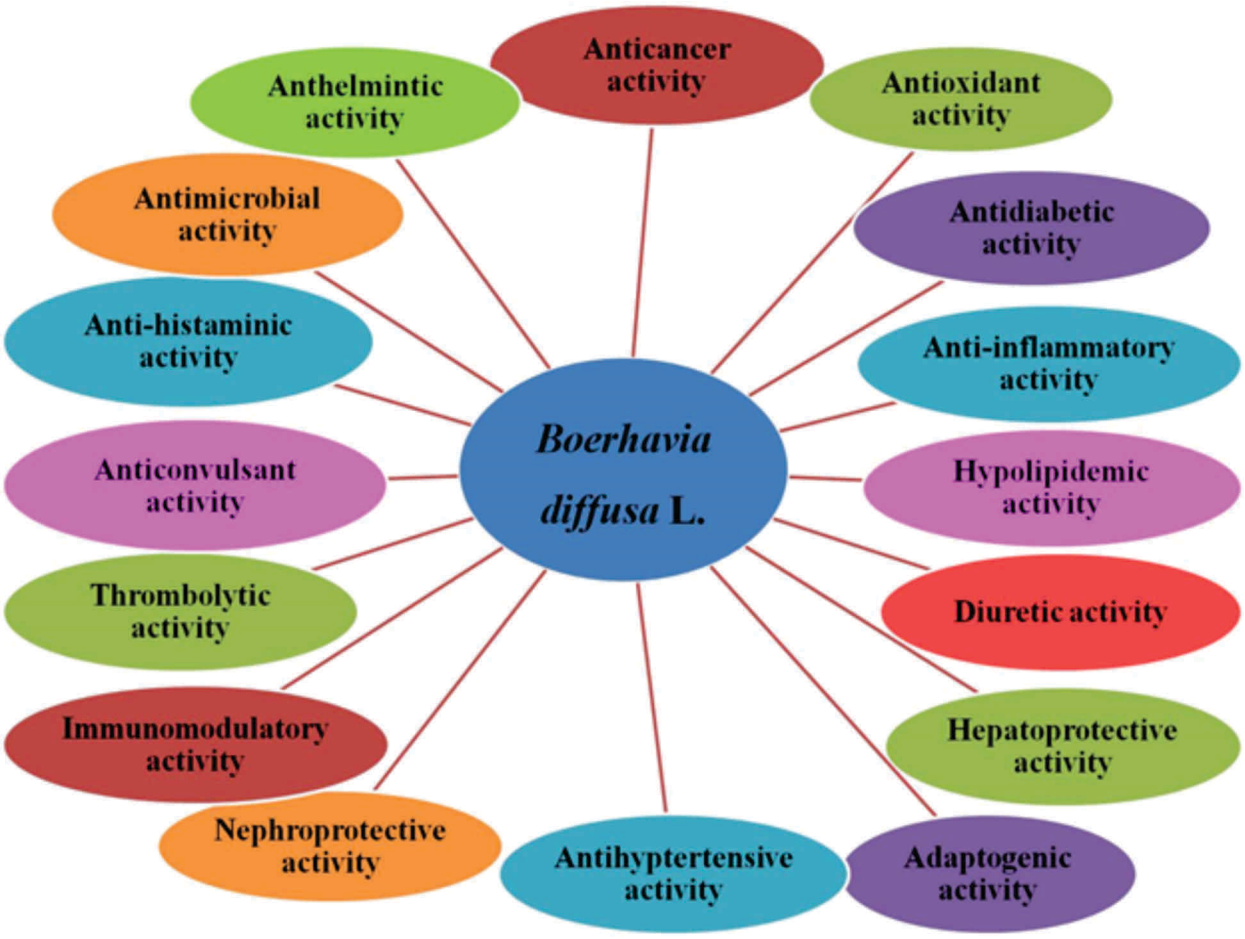


**Figure 2:** Pharmacological armor of *Boerhavia diffusa* L.

*Hepatoprotective Activity*

*In vivo* hepatoprotective activity was demonstrated in petroleum, chloroform and methanol extracts of root and aerial parts of *B. diffusa* against carbon tetrachloride (CCl4) induced hepatotoxicity in rats. A reduction in elevated levels of serum glutamate oxaloacetate (SGOT), serum pyruvate transaminase (SGPT) and serum alkaline phosphatase(ALP) was observed[70]. Chandan *et al.*[71] have also shown hepatoprotective activity of alcoholic extract of *B. diffusa* in experimentally induced carbon tetrachloride hepatotoxicity in rats and mice.

The aqueous extractof root of *B. diffusa*(2ml/kg) has shown significant hepato protective activity against thioacetamide induced hepatotoxicity and efficient protection against a majority of serum parameters like, SGOT, SGPT, ALP, and Average total acid phosphatase (ACP) but not Glutamate dehydrogenase and bilirubin[72].

Hepatoprotective action of aqueous and ethanolic extracts of *B. diffusa* leaves was evaluated using acetaminophen-induced liver damage in rats. Both the extracts reduced the increased activities of ALP, lactate dehydrogenase (LDH), alanine aminotransferase (ALT), aspartate aminotransferase (AST), and the level of bilirubin in the serum[57.] Patel and Verma[73] also demonstrated a significant ($p<0.05$) reduction in ALT, AST, ALP, ACP, LDH and γ-GT after administration of *B. diffusa* extract to swiss albino female mice induced with $CCl_4$ hepatotoxicity. Beedimani and Jeevangi[74] also demonstrated hepatoprotective potential of aqueous extract of *B. diffusa* against $CCl_4$ induced hepatotoxicity in male albino rats by ameliorating the increased levels of ALT, AST, ALP and serum bilirubinat doses of 250 and 500 mg/kg. *In vivo* hepatoprotective potential of 200 mg/kg bw dose of swaras and hima extracts of *B. diffusa* against paracetamol induced hepatotoxicity in swiss albino mice was investigated. A significant ($p< 0.01$)reduction in SGOT and ALP levels was observed after seven days[75].

*Anticancer activity*

Inhibitory effect of Aqueous-methanolic (3:7) extract of *B. diffusa* on metastases formation by B16F10 melanoma cells in C57BL/6 mice was reported by Leyon *et al.*[76]. Prophylactic administration of the extract at a dose of 0.5mg exhibited 95% inhibition of metastases formation. Crude ethanolic extract of roots of *B. diffusa* has shown 30% cell death at concentration of 200µg/ml and the alkaloid fraction and leaf extract have shown 40% cell death at 300µg/ml in both HeLa and U-87 tumor cell lines[77]. Sreeja and Sreeja[78] demonstrated antiproliferative activity in methanolic extract of *B. diffusa* against MCF-7 breast cancer cell line with a percent increase from 69.1% to 75.8%. *In vitro* cytotoxic activity of ethanolic extract of *B. diffusa* was investigated by Teepica *et al.*[79]. Maximum inhibition of 89% at 1000 µg/ml of plant extract with $IC_{50}$ value of 50µg/ml was observed. *In vitro* antiproliferative potential of crude ethanolic extract of *B. diffusa* roots was observed on growth of HeLa cells with 30% cell death in at a concentration of 300 µg/ml. Methanol:chloroform fraction (BDF 5) of the extract showed maximum cytotoxicity with 85% cell death at 300 µg $ml^{-1}$ in 72 h[80].

Kayande and Kushwah[81] have evaluated *in vivo* antitumor activity in ethanolic extract of *B. diffusa* leaves (EBD) against the Dalton's ascitic lymphoma (DAL) in Swiss albino mice. The average number of tumour volume in DAL treated group was found to be 2.68±0.11 and results have shown that after the treatment of EBD at the doses of 250 and 500 mg/kg body weight, a significant ($P<0.05$) reduction in tumour volume was observed. Moreover, viable cell count of the tumor bearing mice was significantly decreased while non-viable cell count was found to be increased in EBD treated mice. Muthulingam and Chaithanya[82] evaluated the cytotoxic effect of methanolic leaf extract of *B. diffusa* against MCF-7 cell lines by using3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT), a yellow tetrazolium assay. The results demonstrated that the methanolic extract at doses of 25, 50, 100, and 200 µg/ml have exhibited significant cytotoxic activity of 13.9%, 27.96%, 43.65%, and 52.86% respectively. Anticancer activity of the methanolic extract of aerial part of *B. diffusa* on triple-negative MDA-MB-231 breast cancer cells was determined using MTT cell viability test[83]. The methanolic extract has shown reduction in number of viable cells in all the doses after 24 and 48 hours along with $IC_{50}$ values of 582.9 µg/ml and 304.7 µg/ml.

*Adaptogenic activity*

*In vivo* adaptogenic activity of root extract of *B. diffusa* was evaluated in mice by Sumanth and Mustafa[84] which revealed the significant increase in carbon clearance which is suggestive for reticulo-endothelial system stimulation. Krupavaram et *al*.[85] demonstrated adaptogenic activity of alcoholic and chloroform extracts of *B. diffusa* roots in albino mice and rats using anoxia stress tolerance test and rats to swimming and cold restraint stress test. Results elucidated that the both extracts had significantly increased the anoxia stress tolerance time when compared to stress control and have significantly($P<0.01$) reduced the levels of biochemical parameters like glucose, cholesterol, triglycerides and blood urea nitrogen and elevated blood cells count like RBC, WBC, DLC whereas prevented weights of organs like liver, spleen and adrenal glands due to swimming and cold restraint stress.

*Nephroprotective activity*

Aqueous extract of leaves of *B. diffusa* was investigated to assess *in vivo* nephroprotective activity in male wistar albino rats against the mercuric chloride toxicity. Aqueous extract was administered orally at dose of 200mg/kg/bw for ten days and elevated levels of antioxidant enzymes such as glutathione peroxidase, reduced glutathione, vitamin C and catalase were observed in animals treated with the extract[86]. *In vitro* synergistic nephroprotective potential of *B. diffusa* and Tinospora cordifolia herbal combination was evaluated against diclofenac induced nephrotoxicity. Results have shown significant ($p < 0.05$) nephroprotective effect by decreasing renal oxidative and inflammatory stress[87].

In a recent experimental study, *B. diffusa* root extract was evaluated in CRF model in dogs and compared with standard Enalapril treatment. The study comprises of two groups of 10 each CRF dogs. Group I was given enalapril 0.5 mg/kg p.o. one daily for 90 days and group II was administered *B. diffusa* root extract 500 mg p.o. daily for 90 days. Both the treatment groups show significant ($p<0.05$) reduction in systolic and diastolic blood pressure at the end of 30 days as well as significant reduction in serum creatinine, urea nitrogen, phosphorus, urinary protein, alkaline phosphatase, glutamyl transferase by day 60. Interestingly, potassium levels were normalized by *B.*

*diffusa* root extract treatment only by day 30. The study, therefore, clearly shows that the efficacy of *B. diffusa* root extract was comparable to standard enalapril treatment chronic renal failure in dogs[88].

*Diuretic activity*

Mudgal[89] observed that *B. diffusa* root extract (water insoluble component of alcoholic extract) had a strong diuretic effect. The volume of urine in rats treated with the extract (300 mg/Kg) increased by 90.3% whereas the volume of urine in rats treated with the leaves and flower extract increased by 67.22%. *In vivo* diuretic activity of alcoholic extracts of stem and leaves of *B. diffusa* was demonstrated in male wistar albino rats. The extracts were orally administered to experimental rats in doses of 150 and 300mg/kg and furosemide was used as a standard drug. A significant increase in urine volume and the excretion of sodium was observed[90].

*Immunomodulatory activity*

Alkaloid fraction of *B. diffusa* in a dose of 25–100 mg/kg has shown *in vivo* immunomodulatory activity by significant inhibition in SRBC-induced delayed hypersensitivity reactions in mice during the post-immunization drug treatment[91]. Mehrotra *et al.*[92] evaluated the immunomodulatory properties of ethanolic extract of *B. diffusa* roots which showed *in vitro* inhibition of human NK cell cytotoxicity, production of NO in mouse macrophage cells, IL-2 and TNF-α in human peripheral blood mononuclear cells and demonstrated the immunosuppressive effect of plant extract. Immunomodulatory effect of the purified alkaloid punarnavine isolated from *B. diffusa* was observed in a dose of 40mg/kg bw in Balb/c mice. An increase in WBC count, bone marrow cellularity and number of alpha-esterase positive cells and enhanced proliferation of thymocytes, splenocytes, and bone marrow cells was observed. Punarnavine also significantly decreased the LPS induced elevated levels of proinflammatory cytokines such as TNF-α, IL-1β, and IL-6 in mice[93]. Immunostimulatory action of punarnavine alkaloid isolated from roots of *B.diffusa* was also evaluated in albino mice by observing its effects on organ weight (liver, spleen, thymus and kidney), expression of cytokines, bone marrow cellularity and alpha-esterase positive cells along with plaque forming assay, delayed type hypersensitivity, and phagocytosis activity[94].

*Thrombolytic activity*

Methanolic extract of aerial parts of *B. diffusa* have been screened for *in vitro* thrombolytic potential by Apu *et al.*[12] using streptokinase as a positive control and normal saline as a negative control. A statistically significant ($P<0.001$) percent clot lysis activity of methanolic extract (10.26%) as compared with streptokinase (40.40%) was observed. Recently, Kunwar *et al.*[23] evaluated *in vitro* thrombolytic activity of methanolic extract of *B. diffusa* leaves and results have demonstrated a significant percent clot lysis activity of 38.42±1.28 as compared to streptokinase as a positive control (44.72±0.87) and distilled water as a negative control (3.74±0.37).

*Anti-histaminic Activity*

Anti-histaminic activity of ethanolic extract of *B. diffusa* roots was evaluated in experimental animals by using isolated goat tracheal chain preparation and histamine induced bronchoconstriction in guinea pigs. Results have shown significant inhibition in contraction of goat tracheal chain produced by histamine as well as showed significant protection by prolonging preconvulsion dyspnoea time in guinea pigs in a dose-dependent manner suggesting potential role of *B. diffusa* in the treatment of asthma[95].

*Anticonvulsant activity*

A dose-dependent protection against pentylenetetrazole (PTZ) induced convulsion was observed in liriodendrin-rich fraction of *B. diffusa*[96]. Anticonvulsant activity of crude methanolic extract of roots of *B. diffusa* has shown a dose dependent protection against PTZ-induced convulsions in male swiss albino mice[97].

*Anti-fibrinolytic activity*

Anti-fibrinolytic activity of root extract of *B. diffusa* was evaluated by Barthwal and Srivastava[98] as compared to anti-fibrinolytic agents (ε-aminocaproic acid, EACA; tranexamic acid, AMCA) using menstrual cycle length (MCL), duration of menstrual flow (DMF), menstrual iron loss (MIL) and activity of uterine tissue plasminogen activator (tPA) in IUD-fitted monkeys. Result have shown significant reduction in elevated levels of DMF (124%), MIL (120.8%), and tPA activity (272%) in IUD-fitted monkeys treated with *B. diffusa* root extract as compared to anti-fibrinolytic agents.

*Anti-nociceptive activity*

Anti-nociceptive activity of fresh juice of leaves of *B. diffusa* has also been observed in the acetic acid-induced abdominal writhing in mice[99].

*Antimicrobial activity*

Several extracts (petroleum ether, chloroform, ethyl acetate and ethyl alcohol) of aerial parts and roots of *B. diffusa* were evaluated for antifungal activity(inhibition in sporulation) against dermatophytic fungi *Microsporum gypseum, M. fulvum* and *M. canis* by using broth dilution method. Results have demonstrated that the maximum activity was shown by ethyl acetate extract of root and maximum inhibition of mycelial growth was observed for *M. gypseum* (78.83%) followed by *M. fulvum* (62.33%) and *M. canis* (42.30%) at a concentration of 1000 g/ml after 24 hours of incubation[100]. *In vitro* antibacterial activity of aqueous and methanolic extracts of *B. diffusa* was demonstrated by using agar diffusion method against some human pathogenic bacteria such as *Bacillus cereus, Bacillus subtilis, Escherichia coli, Klebsiella sp., Proteus mirabilis, Pseudomonas aeruginosa, Salmonella typhi, Shigella sp., Staphylococcus aureus* and *Yersinia enterocolitica* at a concentration of 50 microlitre[101]. Ethanolic and aqueous extracts of its leaves have shown *in vitro* antibacterial activity against *B. subtilis* and *E. coli* with a minimum inhibitory concentration of 125 and 250g/ml for *B. subtilis* and *E. coli,*

respectively[102].

Umamaheswari and Shreevidya[103] investigated *in vitro* antimicrobial activity of various solvent extracts of *B. diffusa* leaves against the gram positive *(S. aureus, B. subtilis, Streptococcus faecalis and Micrococcus luteus)* and the gram-negative bacteria *(E. coli, P.aeruginosa, S. typhi, Klebsiella pneumoniae, Proteus vulgaris, Serratia marcescens, Shigella flexneri and Vibrio cholera)* and the ethanolic extract was found to be more effective against *S. aureus* and *E. coli* than the other solvent extracts. *In vitro* antibacterial activity of petroleum ether, chloroform and methanol extracts of *B. diffusa* aerial and root parts was evaluated using agar well plate method against six microorganisms namely, *E. coli* ATCC 69314, *K. pneumoniae* NCIM 2719, *P. aeruginosa* NCIM 2200, *Agrobacterium tumefaciens* NCIM 2943, *S. aureus* NCIM 2080 and *B. subtilis* MTCC 441. Among the three extracts, crude methanolic extract of aerial parts and root have shown maximum antibacterial potential[104]. Methanolic extract of *B. diffusa* roots was evaluated against eight human pathogens such as *E. coli* MTCC 43, *P. aeruginosa* MTCC 424, *S.typhimurium* MTCC 98, *S. aureus* MTCC 96, *S. flexneri* MTCC 1457, *S. pneumoniae* MTCC 655, *K. pneumoniae* MTCC 432 and a fungi *Aspergillus niger* MTCC 282 by using agar well diffusion method. Results have demonstrated that roots extract inhibited the growth of all tested microorganisms with the large inhibition zone ranging between 4.26 ± 0.12 -16.61± 0.24mm[105]. Antibacterial effects of ethanolic and aqueous extract of *B. diffusa* leaves was investigated against the selected bacterial strains such as *B. cereus, S.aureus, P.aeruginosa, E. coli* and *S. typhimurium.* Results exhibited that ethanolic extract showed better inhibitory performances (zone of inhibition: 2–12 mm) than the aqueous extract (zone of inhibition: 1–8 mm)[62].

*Radioprotective activity*

Hydroalcoholic extract of *B. diffusa* (20mg/kg)was evaluated for radioprotective potential against the gamma radiation induced damage in mice which elevated white blood cells count and reduced the elevated levels of serum liver alkaline phosphatase and liver glutamate pyruvate and lipid peroxidation levels[106].

*Antiplasmodial activity*

*In vivo* antiplasmodial activity of methanolic extract of *B. diffusa* roots was reported against *Plasmodium berghei* NK 65 (chloroquine resistant strain) by using three malaria models and the optimum activity was found at the lowest dose (125 mg/kg) of the extract in suppressive and prophylactic models and at 10$^{th}$day in the curative model. The dose of 500 mg/kg had the highest plasmodial activity at 9$^{th}$day in curative model[107].

*Anthelmintic activity*

Dried root powder of *B. diffusa* has shown curative effect in children or adults suffering from helminth infection. Oral administration of dried root powder cured the worm infection within five days[108]. Deshmukh *et al*.[109] have shown insecticidal activity in hexane and acetone extract of twigs of *B. diffusa* against *Culex p.fatigans* and *Musca domestica. In vitro* anthelmintic activity was reported in crude ethanolic extract of leaves of *B. diffusa* against Indian earthworm *Pheretima posthuma* by measuring time taken to paralyze/death of the earthworms[110]. Biva *et al*.[111] reported anthelmintic activity of *B. diffusa* in normal saline solution containing 5% Dimethyl formamide against earthworm *P. posthuma.* Results have shown a moderate anthelmintic activity at 100 mg/ml concentration measured by the time taken to paralyze or death of the earthworm.

## CONCLUSION

*Boerhavia diffusa* is a diffuse, procumbent, small herb. It has been mentioned for treatment of various ailments in both codified and non-codified systems of medicine. Interestingly, many of the medicinal claims have been scientifically proven through its numerous pharmacological activities. Some prominent activities are, antioxidant, anti-inflammatory, hypoglycemic, hypolipidemic, immunomodulatory anticancer among others. Various phenolic compounds, flavanoids, flavonoid glycosides, steroids impart the plant with such a strong armor providing protection against many diseases. Recent addition of thrombolytic activity of leaves of *B. diffusa* to its pharmacological profile indicates towards the importance of diet in prevention of several diseases. Overall, these health-beneficial pharmacological activities play a significant role in modifying various cardiovascular risk parameters such as abnormal oxidation, high lipid and blood sugar levels. Dietary addition of *'Punarnava'* as a vegetable; thus, points out towards indigenous knowledge and insight for maintaining health. It could be further explored from the view of developing nutraceutical compounds so as to be a part of daily diet.

## CONFLICT OF INTEREST:

Authors declare that there is no conflict of interest related with this article.

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## REFERENCES

1.Jain V, Jain SK: Compendium of Indian Folk Medicine and Ethnobotany (1991-2015). New Delhi: Deep Publications. 2016.

2.Tiagi YD, Aery NC: Flora of Rajasthan (South and South-east region). 2007; Himanshu Publications, Udaipur.

3.Manjunath BL (Ed.): The Wealth of India: A Dictionary of Indian Raw Materials & Industrial Products. 1948; Vol. I, p. 199, New Delhi: NISCAIR.

4.Website 1. https://www.cabi.org/isc/datasheet/9460#:~:text=Singh%2C%201988).-,B.,USDA%2DARS%2C%202015).

5.Sarkar PR: Yogic treatments and natural remedies. Kolkata: AMPS publications. 1986.

6.Mishra S, Aeri V, Gaur PK, Jachak SM. Phytochemical, therapeutic, and ethnopharmacological overview for a traditionally important herb: *Boerhavia diffusa* Linn. Biomed Res Int. 2014;2014:808302. doi: 10.1155/2014/808302.

7.Gaur PK, Rastogi S, Lata K.: Correlation between phytocompounds and pharmacological activities of *Boerhavia diffusa* Linn. with traditional-ethnopharmacological insights. Phytomedicine Plus 2022; 2:100260

8.Bhutya RK: Ayurvedic Medicinal Plants of India, Vol. 1. Jodhpur, India: Scientific Publishers. 2011.

9.Tuso PJ, Ismail MH, Ha BP, Bartolotto C: Nutritional update for physicians: plant-based diets. Perm J. 2013;17(2):61-6. doi: 10.7812/TPP/12-085

10.Kim J, Kim H, Giovannucci EL. Plant-based diet quality and the risk of total and disease-specific mortality: A population-based prospective study. Clin Nutr. 2021; 40(12):5718-5725. doi: 10.1016/j.clnu.2021.10.013

11.The Wealth of India: A Dictionary of Indian Raw Materials & Industrial Products. 2004; Vol. 1, p. 144-5, New Delhi: NISCAIR.

12.Apu AS, Liza MS, Jamaluddin ATM, Howlader MA et al: Phytochemical screening and in vitro bioactivities of the extracts of aerial part of *Boerhavia diffusa* Linn. Asian Pac J Trop Biomed. 2012; 2(9): 673-678. http://dx.doi.org/10.1016/S2221-1691(12)60208-1

13.Beegun JG, Beevy SS, Sugunan VS: Qualitative phytochemical screening and GC-MS analysis of *Boerhavia diffusa* L. Int J Emerging Technol Adv Eng. 2014; 4:318-24.

14.Dhingra D, Valecha R: Evidence for involvement of the monoaminergic system in antidepressant-like activity of an ethanol extract of *Boerhaavia diffusa* and its isolated constituent, punarnavine, in mice. Pharm Biol. 2014; 52(6):767-774. https://doi.org/10.3109/13880209.2013.870583

15.Bairwa K, Srivastava A, Jachak S M: Quantitative analysis of boeravinones in the roots of *Boerhaavia diffusa* by UPLC/PDA. Phytochem Anal. 2014; 25(5):415–420. https://doi.org/10.1002/pca.2509

16.Lami N, Kadota S, Kikuchi T: Constituents of the roots of *Boerhaavia diffusa* L. IV. Isolation and structure determination of boeravinones D, E, and F. Chem Pharm Bull.1991; 39(7):1863-1865.https://doi.org/10.1248/cpb.39.1863

17.Borrelli F, Milic N, Ascione V, Capasso R: Isolation of new rotenoids from *Boerhaavia diffusa* and evaluation of their effect on intestinal motility. Planta Med. 2005; 71(10): 928-932.https://doi.org/10.1055/s-2005-871282

18.Aviello G, Canadanovic-Brunet JM, Milic N, Capasso R: Potent antioxidant and genoprotective effects of boeravinone G, a rotenoid isolated from *Boerhaavia diffusa.* PLoS one. 2011; 6(5):e19628.https://doi.org/10.1371/journal.pone.0019628

19.Bose M, Kamra M, Mullick R, Bhattacharya S: A plant-derived dehydrorotenoid: a new inhibitor of hepatitis C virus entry. FEBS letters. 2017; 591(9):1305-1317. https://doi.org/10.1002/1873-3468.12629

20.Ningtyas F, Wulandari S: Boeravinone F, Withanolide D, and Chitranone are a potential antagonist of Angiotensin Receptor 1 In-silico for hypertension treatment. Nexus of Translational Medicine. 2017; 6(1).http://jurnal.fk.uns.ac.id/index.php/Nexus-Kedokteran-Translasional/article/view/1797

21.Sharma K, Sahai M: Chemical constituents of *Boerhavia diffusa* leaves. J Med Plants Stud. 2017; 5(4):166-169.

22.Jayachitra J, Janani B, Bharathi V, Manikandan R: Phytochemical analysis and mineral composition of methanolic extract of *Boerhavia diffusa* L. Res J Pharm Technol. 2020; 13(10):4856-4860. https://doi.org/10.5958/0974-360X.2020.00854.9

23.Kunwar B, JainV, Verma S: In vitro clot lysis activity of *Boerhavia diffusa* L. leaves. Pacific J Med Health Sci. 2021; 3:1-7.

24.Priya K, Sharma HP: Phytochemical screening and saponinn estimation of *Boerhavia diffusa.* Int J all Res Educ Sci Methods. 2021; 9(2): 1156-1160.

25.Misra AN, Tiwari HP: Constituents of roots of *Boerhaavia diffusa.* Phytochemistry. 1971; 10(12):3318-3319.

26.Ojewole JAO, Adesina SK: Isolation, identification and some cardiovascular actions of a purine nucleoside from the roots of *Boerhaavia diffusa.* Fitoterapia. 1985; 56(1): 31-36

27.Jain GK, Khanna N M: Punarnavoside: A new antifibrinolytic agent from *Boerhaavia diffusa* Linn. Ind J Chem. 1989; 28(B):163-166.

28.Kadota S, Lami N, Tezuka Y, Kikuchi T: Constituents of the roots of *Boerhaavia diffusa* L: Examination of sterols and structures of new Rotenoids, Boeravinones A and B. Chem Pharm Bull. 1989; 37(12):3214-3220.https://doi.org/10.1248/cpb.37.3214

29.Suri OP, Kant R, Jamwal RS, Suri KA et al: *Boerhaavia diffusa,* a new source of phytoecdysones. Planta Med.1982; 44(03):180-181. https://doi.org/10.1055/s-2007-971436

30.Lami N, Kadota S, Kikuchi T, MoMos EY: Constituents of the roots of *Boerhaavia diffusa* L. III. Identification of Ca2+ channel antagonistic compound from the methanol extract. Chem Pharm Bull. 1991a; 39(6):1551-1555.https://doi.org/10.1248/cpb.39.1551

31.Gupta J, Ali M: Chemical constituents of *Boerhavia diffusa* Linn. roots. Indian J Chem. 1998;37:912-917.

32.Borrelli F, Ascione V, Capasso R, Izzo AA et al: Spasmolytic effects of nonprenylated rotenoid constituents of *Boerhaavia diffusa* roots. J Nat Prod. 2006; 69(6):903-906. https://doi.org/10.1021/np060073h

33.Maurya R, Sathiamoorthy B, Deepak M: Flavonoids and phenol glycosides from *Boerhavia diffusa*. Nat Prod Res. 2007; 21(2):126-134. https://doi.org/10.1080/14786410600906194

34.Pereira DM, Faria J, Gaspar L, Valentão P et al: *Boerhaavia diffusa*: Metabolite profiling of a medicinal plant from Nyctaginaceae. Food Chem Toxicol. 2009; 47(8):2142-2149. https://doi.org/10.1016/j.fct.2009.05.033

35.Baskaran C, Sivamani P, Rathabai V: Evaluation of phytochemical and antimicrobial activities of *Boerhavia diffusa.* J Pharm Res. 2011; 4(2):434-436.

36.Do TML, Truong AV, Vo TN, Pinnock TG et al: New derivatives from the aerial parts of *Boerhaavia diffusa* L.(Nyctaginaceae). Phytochem Lett. 2013; 6(4):544-551. https://doi.org/10.1016/j.phytol.2013.07.001

37.Tacchini M, Spagnoletti A, Marieschi M, Caligiani A et al: Phytochemical profile and bioactivity of traditional ayurvedic decoctions and hydro-alcoholic macerations of *Boerhaavia diffusa* L. and *Curculigo orchioides* Gaertn. Nat Prod Res. 2015; 29(22):2071-2079. https://doi.org/10.1080/14786419.2014.1003299

38.Bairwa K, Singh IN, Roy SK, Grover J et al: Rotenoids from *Boerhaavia diffusa* as potential anti-inflammatory agents. J Nat Prod. 2013; 76(8): 1393-1398.

39.Cao H, Chai TT, Wang X, Morais-Braga MFB et al: Phytochemicals from fern species: potential for medicine applications. Phytochem Rev. 2017; 16(3):379-440. https://doi.org/10.1007/s11101-016-9488-7

40.Ferreres F, Sousa C, Justin M, Valentão P: Characterisation of the phenolic profile of *Boerhaavia diffusa* L. by HPLC-PAD-MS/MS as a tool for quality control. Phytochemical analysis: Int J Plant Chem Biochem Tech. 2005; 16(6):451-458. https://doi.org/10.1002/pca.869

41.Daniel M: Medicinal plants: Chemistry and properties. Science Publishers. 2006.

42.Umamenaka R, Vijayakumari K, Senthilkumar S: GC-MS analysis of *Boerhavia diffusa* Linn leaf extract traditional valuable plant. Int J Deccan Pharma Life Sci. 2012; 3(2):21-26.

43.Thuy TT, Thu Trang NT, Hoa PN, Trang PT et al: A New Coumaronochromone From *Boerhaavia diffusa.* Nat Prod Commun. 2019; 14(6):1934578X19856253. https://doi.org/10.1177%2F1934578X19856253

44.Chetty KM, Rao KN: Studies on phytochemical and floral features of some members of traditional Centrospermae. Indian J For. 1990; 13(1):49-52.

45.Saeed TM, Rauf A, Pasha MK, Osman SMJ: Fatty Acid Composition of Minor Seed Oils. Indian Chem. Soc. 1990; 67(6):528-529.

46.Agrawal B, Das S, Pandey A: Boerhaavia diffusaLinn.: A review on its phytochemical and pharmacological profile. Asian J App Sci. 2011; 4(7):663-684. http://dx.doi.org/10.3923/ajaps.2011.663.684

47.Kumar R, Gautam S, Singh KD, Kumar, P et al: Pharmacological properties of *Boerhavia diffusa*: A review. Int J Chem Stud.2018; SP4:72-80.

48.Bhalla TN, Gupta MB, Sheth PK, Bhargava KP: Anti-inflammatory activity of *Boerhaavia diffusa*. Indian J Physiol Pharmacol. 1968; 12:37.

49.Mudgal V: Comparative studies on the anti-inflammatory and diuretic action with different parts of the plant *Boerhaavia diffusa* Linn (Punarnava). J Res Edu Indian Med. 1974; 9: 2.

50.Barthwal M, Srivastava K: Histologic studies on endometrium of menstruating monkeys wearing IUDs: comparative evaluation of drugs. Adv Contracept. 1990; 6(2):113-124.https://doi.org/10.1007/bf01849237

51.Gharate M, Kasture V: Evaluation of anti-inflammatory, analgesic, antipyretic and antiulcer activity of Punarnavasava: an Ayurvedic formulation of *Boerhavia diffusa.* Orient Pharm Exp Med.2013;13:121-126. https://doi.org/10.1007/s13596-012-0081-3

52.Muthu S: Anti-inflammatory effect of ethanolic extract of *Boerhavia diffusa* leaves in Wistar rats. Malaya J Biosci. 2014; 1(2):76-85.

53.Sudhamadhuri A, Kalasker V: Evaluation of anti-inflammatory effect of aqueous extract of *Boerhaavia diffusa* leaves in rats. Int J Health Sci. 2014; 2:517-521.

54.Giresha AS, Pramod SN, Sathisha AD, Dharmappa KK: Neutralization of Inflammation by Inhibiting *In vitro* and *In vivo* Secretory Phospholipase A2 by Ethanol Extract of *Boerhaavia diffusa* L. Pharmacogn Res. 2017; 9(2):174.https://doi.org/10.4103%2F0974-8490.204650

55.Satheesh MA, Pari L: Antioxidant effect of *Boerhavia diffusa* L. in tissues of alloxan induced diabetic rats. Indian J Exp Bio. 2004;42(10):989- 992.

56.Gacche RN, Dhole NA: Antioxidant and possible anti-inflammatory potential of selected medicinal plants prescribed in the Indian traditional system of medicine. Pharm Biol 2006; 44(5):389-395.https://doi.org/10.1080/13880200600751691

57.Olaleye MT, Akinmoladun AC, Ogunboye AA, Akindahunsi A: Antioxidant activity and hepatoprotective property of leaf extracts of *Boerhaavia diffusa* Linn against acetaminophen-induced liver damage in rats. Food Chem Toxicol. 2010; 48(8-9):2200-2205.https://doi.org/10.1016/j.fct.2010.05.047

58.Beegum GJ, Beevy SS, Sugunan VS: Natural antioxidant activity of *Boerhavia diffusa* L. Int J Pharmacogn Phytochem Res. 2016; 8(1):8-13.

59.Patel M, Verma R, Srivastav P: Antioxidant activity of *Boerhavia diffusa* extract. Int J Pharmacogn Phytochem Res. 2014; 6(3):598-605.

60.Alam P, Shahzad N, Gupta AK, Mahfoz AM: Anti-diabetic effect of *Boerhavia diffusa* L. root extract via free radical scavenging and antioxidant mechanism. Toxicol Environ Health Sci. 2018; 10(3):220-227.http://dx.doi.org/10.1007/s13530-018-0367-z

61.Khalid M, Alqarni MH, Foudah AI, Akhtar J: Evaluation of free radical scavenging potential of different bioactive fractions present in *Boerhavia diffusa* Linn. root extract: An in-vitro approach. J. Pharm. Res. Int. 2020; 32:99-107. https://doi.org/10.9734/jpri/2020/v32i1230567

62.Adeku E, Osundahunsi OF, Malomo SA, Asasile II: Phytochemical constituents and assessment of crude extracts from *Boerhavia diffusa* L. and Lonchocarpus sericeus (Poir.) Kunth ex DC. leaves for antioxidant and antibacterial activities. Measurement: Food. 2022; 5:100018. https://doi.org/10.1016/j.meafoo.2021.100018

63.Nalamolu RK, Boini KM, Nammi S: Effect of chronic administration of *Boerhaavia diffusa* Linn. leaf extract on experimental diabetes in rats. Trop J Pharm Res. 2004; 3(1):305-309. https://doi.org/10.4314/tjpr.v3i1.14614

64.Pari L, Satheesh MA: Antidiabetic activity of *Boerhaavia diffusa* L.: Effect on hepatic key enzymes in experimental diabetes. J Ethnopharmacol. 2004; 91(1):109-113.https://doi.org/10.1016/j.jep.2003.12.013

65.Panda KC, Mishra J, Digambar B: Antidiabetic activity of leaves and seeds of *Boerhavia diffusa.* Int J Pharma Eng. 2018;6(4):846-852.

66.Khan A, Chandel AS, Ishaq F, Chettri S et al: Therapeutic impacts of tocotrienols and *Boerhaavia diffusa* on cholesterol dynamics, lipid hydroperoxidation and antioxidant status on hyperlipidemic rats: induced by oxidized cholesterol. Recent Res Sci Technol. 2011;3(11):13-21.

67.Arivu I, Muthulingam M: Hypolipidemic efficacy of *Boerhaavia diffusa* (linn.) in kidney on d-galactosamine induced fatty liver in male albino wistar rats. Int J Mod Res Rev. 2015; 3(7):721-725.

68.Akhter F, Alvi SS, Ahmad P, Iqbal D: Therapeutic efficacy of *Boerhaavia diffusa* (Linn.) root methanolic extract in attenuating streptozotocin-induced diabetes, diabetes-linked hyperlipidemia and oxidative-stress in rats. Biomed Res Ther. 2019; 6(7):3293-3306.https://doi.org/10.15419/bmrat.v6i7.556

69.Nayak S, Nayak S, Dash DP, Das B: A Clinical Study on the effect of *Boerhaavia diffusa* (Punarnava) in Essential Hypertension. Ayushdhara: 2015; 2(6):390-396.

70.Chakraborti KK, Handa SS: Antihepatotoxic investigations of *Boerhaavia diffusa* L. Indian drugs. 1989; 27:161-166.

71.Chandan BK, Sharma AK, Anand KK: *Boerhaavia diffusa:* a study of its hepatoprotective activity. J Ethnopharmacol. 1991;31(3):299-307.https://doi.org/10.1016/0378-8741(91)90015-6

72.Rawat AKS, Mehrotra S, Tripathi SC, Shome U: Hepatoprotective activity of *Boerhaavia diffusa* L. roots-a popular Indian ethnomedicine. J Ethnopharmacol. 1997; 56(1):61-66.https://doi.org/10.1016/s0378-8741(96)01507-3

73.Patel M, Verma R: Hepatoprotective activity of *Boerhavia diffusa* extract. Int J Pharma Clin Res. 2014; 6(03):233-240.

74.Beedimani RS, Jeevangi S K: Evaluation of hepatoprotective activity of *Boerhaavia diffusa* against carbon tetrachloride induced liver toxicity in albino rats.Int J Basic Clin Pharmacol. 2015; 4(1):153.

75.Kaushik A, Husain A, Awasthi H, Singh DP et al: Antioxidant and hepatoprotective potential of Swaras and Hima extracts of Tinospora cordifolia and *Boerhavia diffusa* in Swiss albino mice. Pharmacogn Mag. 2017;13(Suppl 3):658-662.https://doi.org/10.4103/pm.pm_448_16

76.Leyon PV, Lini CC, Kuttan G: Inhibitory effect of *Boerhaavia diffusa* on experimental metastasis by B16F10 melanoma in C57BL/6 mice. Life Sciences. 2005; 76(12):1339-1349.https://doi.org/10.1016/j.lfs.2004.06.031

77.Srivastava R, Saluja D, Chopra M: Isolation and screening of anticancer metabolites from *Boerhavia diffusa.* Indian J Med Res. 2005; 151(supplement 1): S19.

78.Sreeja S, Sreeja S: An in vitro study on antiproliferative and antiestrogenic effects of *Boerhaavia diffusa* L. extracts. J Ethnopharmacol. 2009; 126(2):221-225.https://doi.org/10.1016/j.jep.2009.08.041

79.Teepica PDD, Sasikumar JM, Kulandhaivel M: In vitro antioxidant and cytotoxic analysis of *Boerhaavia diffusa* Linn. Ethnobot leafl. 2009; 2009(1):34.

80.Srivastava R, Saluja D, Dwarakanath BS, Chopra M: Inhibition of human cervical cancer cell growth by ethanolic extract of *Boerhaavia diffusa* Linn.(punarnava) root. Evid. Based Complementary Altern Med. 2011; 2011:427031. https://doi.org/10.1093/ecam/nep223.

81.Kayande N, Kushwah P: *In vitro* and *in vivo* evaluation of anticancer activity of *Boerhaavia diffusa* Linn in experimental animals. PharmaTutor. 2014; 2(5):133-137.

82.Muthulingam M, Chaithanya KK: *In vitro* anticancer activity of methanolic leaf extract of *Boerhaavia diffusa* Linn., against MCF-7 cell line. Drug Invent Today. 2018; 10(2): 3107-3111.

83.Sinan KI, Akpulat U, Aldahish AA, Celik Altunoglu Y: LC-MS/HRMS analysis, anti-cancer, anti-enzymatic and anti-oxidant effects of *Boerhavia diffusa* extracts: a potential raw material for functional applications. Antioxidants. 2021; 10(12):2003. https://doi.org/10.3390/antiox10122003

84.Sumanth M, Mustafa SS: Antistress, adoptogenic and immunopotentiating activity roots of *Boerhaavia diffusa* in mice. Int J Pharmacol. 2007; 3(5):416-420.

85.Krupavaram B, Rao NV, Nandakumar K, Gowda TS: A study on adaptogenic activity of root extracts of *Boerhaavia diffusa* (Linn). Indian drugs. 2007; 44(4):264-270.

86.Indhumathi T, Shilpa K, Mohandass S: Evaluation of nephroprotective role of *Boerhaavia diffusa* leaves against mercuric chloride induced toxicity in experimental rats. J Pharma Res. 2011; 4(6):1848-1850.

87.Khan MU, Basist P, Zahiruddin S, Ibrahim M: Nephroprotective potential of *Boerhaavia diffusa* and Tinospora cordifolia herbal combination against diclofenac induced nephrotoxicity. S Afr J Bot. 2022; https://doi.org/10.1016/j.sajb.2022.01.038

88.Oburai NL, Rao VV, Bonath RB: Comparative clinical evaluation of *Boerhavia diffusa* root extract with standard Enalapril treatment in Canine chronic renal failure. J Ayurveda Integr Med. 2015;6(3):150-7. doi: 10.4103/0975-9476.166390

89.Mudgal V: Studies on medicinal properties of Convolvulus pluricaulis and *Boerhaavia diffusa.* Planta Med. 1975; 28(05):62-68.

90.Venkatesh P, Dinakar A, Senthilkumar N: Evaluation of diuretic activity of an alcoholic extracts of *Boerhaavia diffusa* and Anisochilus carnosus in rats. The Int J Drug Dev Res. 2012; 4:239-242.

91.Mungantiwar AA, Nair AM, Shinde UA, Dikshit VJ et al: Studies on the immunomodulatory effects of *Boerhaavia diffusa* alkaloidal fraction. J Ethnopharmacol. 1999; 65(2):125-131.https://doi.org/10.1016/s0378-8741(98)00153-6

92.Mehrotra S, Mishra KP, Maurya R, Srimal RC et al: Immunomodulation by ethanolic extract of *Boerhaavia diffusa* roots. Int Immunopharmacol. 2002; 2(7):987-996.https://doi.org/10.1016/s1567-5769(02)00031-0

93.Manu KA, Kuttan, G: Immunomodulatory activities of Punarnavine, an alkaloid from *Boerhaavia diffusa.* Immunopharmacol Immunotoxicol. 2009; 31(3):377-387.https://doi.org/10.1080/08923970802702036

94.Aher VD, Chattopadhyay P, Patra A: Immunomodulatory activity of punarnavine alkaloid from *Boerhaavia diffusa*. Curr Bioact Compd. 2020; 16(4):460-468. https://doi.org/10.2174/1573407214666181119122711

95.Suralkar AA, Verma AK, Kamble RD, Tayade GV: Pharmacological evaluation of anti-histaminic activity of *Boerhaavia diffusa.* Int J Adv Pharm Bio Chem.2012; 1(4):503-507.

96.Adesina SK: Anticonvulsant properties of the roots of *Boerhaavia diffusa* Linnaeus. Int J Crude Drug Res. 1979; 17(2):84-86. https://doi.org/10.3109/13880207909067455

97.Kaur M, Goel RK: Anti-convulsant activity of *Boerhaavia diffusa:* plausible role of calcium channel antagonism. Evid. Based Complementary Altern Med. 2011; 2011: 310420.https://doi.org/10.1093/ecam/nep192

98.Barthwal M, Srivastava K: Management of IUD-associated menorrhagia in female rhesus monkeys (Macaca mulatta). Adv Contracept. 1991; 7:67–76 https://doi.org/10.1007/BF01850720

99.Hiruma-Lima CA, Gracioso JS, Bighetti EJB, Robineou LG et al: The juice of fresh leaves of *Boerhaavia diffusa* L.(Nyctaginaceae) markedly reduces pain in mice. J Ethnopharmacol. 2000; 71(1-2):267-274.https://doi.org/10.1016/s0378-8741(00)00178-1

100.Agrawal A, Srivastava S, Srivastava MM: Antifungal activity of *Boerhavia diffusa* against some dermatophytic species of Microsporum. Hindustan Antibiotic Bull. 2003; 45(1-4):1-4.

101.Girish HV, Satish S: Antibacterial activity of important medicinal plants on human pathogenic bacteria-a comparative analysis. World App Sci J. 2008; 5(3):267-271.

102.Sangameswaran B, Balakrishnan N, Bhaskar VH, Jayakar B: Anti-inflammatory and anti-bacterial activity of leaves of *Boerhavia diffusa* L. Pharmacogn Mag. 2008; S65-S68.

103.Umamaheswari A, Nuni A, Shreevidya R: Evaluation of antibacterial activity of *Boerhaavia diffusa* L. leaves. Int J Green Pharm. 2010;4(2):75-78.

104.Ramachandra YL, Ashajyothi C, Rai P: In vitro antibacterial potential of *Boerhaavia diffusa.* Int J Adv Pharma, Bio Chem. 2012; 1(3):420-424.

105.Kamlekar S, Kota K, Tahashildar J, Erumalla VR: In vitro antimicrobial potential of *Boerhavia diffusa* l. Root extract on pathogenic organisms. World J Pharm Res. 2014; 3(9):442-450.

106.Manu KA, Leyon PV, Kuttan G: Studies on the protective Effects of *Boerhaavia diffusa* L. against gamma radiation—induced damage in Mice. Integr Cancer Ther. 2007; 6(4):381-388.https://doi.org/10.1177/1534735407309743

107.Adefokun DI, Iwalewa EO, Omisore NO, Obuotor E et al: The antimalarial effect and mechanism of action of methanolic root extract of *Boerhaavia diffusa* in mice. J Pharm Res Int. 2015; 8(2):1-14.http://dx.doi.org/10.9734/BJPR/2015/13606

108.Singh RH, Udupa KN: Studies on the Indian indigenous drug punarnava (*Boerhaavia diffusa* Linn.). Part IV: Preliminary controlled clinical trial in nephrotic syndrome. J Res Indian Med. 1972; 7:28-33.

109.Deshmukh PB, Chavan SR, Renapurkar DM: Study of insecticidal activity of twenty indigenous plants. Pesticides. 1982; 16:7-10.

110.Rajagopal RR: Investigation of *in-vitro* anthelmintic activity of ethanolic leaf extract of *Boerhavia diffusa* (Nyctaginaceae) including pharmacognostical and phytochemical screening. J Pharma Res. 2013; 7(8):774-780.https://doi.org/10.1016/j.jopr.2013.08.009

111.Biva MM, Chowdhury SA, Parvin MN: Pharmacological investigations of *Boerhaavia diffusa* Linn.(Family: Nyctaginaceae). American J Food Sci Health. 2016; 2(4):88-93.