



**CLINICAL EVALUATION OF BOERHAAVIA DIFFUSA L EXTRACT OBTAINED  
FROM DIFFERENT GEOGRAPHICAL SOURCES**

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Article Received on 20/09/2020

Article Revised on 10/10/2020

Article Accepted on 01/11/2020

**ABSTRACT**

*Boerhaavia diffusa*, a flowering plants which belong to family Nyctaginaceae. It exhibits an immense ethnopharmacological history and it is a reservoir of phytochemical stochastic therapeutic qualities. It is one of the oldest Asian medicines listed in Ayurveda as a possible cure for various diseases. The whole plant or its element (aerial components and roots) has many medicinal properties and is used for specific conditions by common and ethnic people, it is rich in glycosides, steroids, flavonoids and also contains various polyphenolic compounds. *Boerhaavia diffusa* has been studied with great interest in the field of phytochemistry and pharmacology because of its promising medicinal values, with various pre-clinical trials confirming the presence of activities like anti-inflammatory, immunostimulant, antioxidant, hepatoprotective, hypoglycemic, antifungal, anti-proliferative, antiestrogenic, analgesic, antibacterial, and other ethnopharmacological uses. Allopathic medicine is almost at the height of established research and advanced technology. Therefore, with the help of advanced research methodology, there is an urgent need to validate the principles and drugs used in the alternative medicine system, including herbal drugs. In summary, this review article provides updated information regarding the plant morphology, chemical compositions responsible for therapeutic values, traditional uses and its reported pharmacological properties, ethnopharmacological applications with a potential scope of development on *Boerhaavia diffusa*.

**KEYWORDS:** *Boerhaavia diffusa*, Chemical Constituents, Ayurveda, ethnopharmacological activities.

**1 INTRODUCTION**

It is an old phrase since Ancient times to suggest that herbal remedies are meant for natural and herbal industry. Globally more than 80,000 plant species are used in medical applications.<sup>[1]</sup>

According to the World Health Organization (WHO), about 70–80% of the developing world populations depend upon nonconventional medicines mainly of herbal sources in their healthcare.<sup>[2]</sup> Such heightened concern is attributed to rising adverse effects of allopathic medications, lack of a solution for numerous medical diseases, increasing treatment rates, microbial tolerance and emerging disorders, etc.<sup>[3]</sup>

India has a huge number of herbal drugs and traditional medicinal system, most importantly the Ayurveda traditional Indian medicinal system. “Ayurveda is a life science with universal health and personalized medicine approach. It is known to be a medical system that comprised physical, psychological, philosophical, ethical, and spiritual health”.<sup>[4]</sup>

*Boerhaavia diffusa*, a flowering plants which belong to family Nyctaginaceae. The genus *Boerhaavia* was

named after a famous Dutch physician Hermann Boerhaave, due to its typical diffuse branching, the species is named ‘*diffusa*’.<sup>[5]</sup> It is commonly known as Raktapunarnava, Shothaghni, Kathillaka, Kshudra, Varshabhu, Raktapushpa, Varshaketu, Shilatika, Spreading Hogweed, Windflower, Red Spiderling, Tarvine, Satha, Punarnava, Itcit, Kathilla.<sup>[6,7]</sup> In ancient medicine, *Boerhaavia diffusa* is commonly called as Punarnava because of its regeneration properties in the rainy season.<sup>[6]</sup>

Genus *Boerhaavia* species are distributed in humid and subtropical regions and warm climate.<sup>[8]</sup> There are 40 species in which 6 species of *Boerhaavia* are found in India namely; *Boerhaavia diffusa*, *Chinensis*, *rubicunda*, *hirsute*, *erecta* and *Boerhaavia rependa*.<sup>[1,5]</sup> It is situated at 2000m altitude in the Himalayan range in the warmest areas of India. After the rainfall in wastelands, it grows well in the region. The plant is also grown in Western Bengal.<sup>[9]</sup>

*Boerhaavia diffusa* have been known for its ethnopharmacological activity. The plant in whole or its parts (aerial parts and roots) have ample medicinal properties and are used by people of different

ethnicity.<sup>[10]</sup> There are variety of investigated and reported pharmacological and therapeutic properties of *Boerhaavia diffusa* include cardio-protective,<sup>[6,11]</sup> prostate hyperplasia,<sup>[12-14]</sup> analgesic and anti-inflammatory,<sup>[1,6,13,15-18]</sup> laxative and immunomodulatory activities,<sup>[19-22]</sup> anti-proliferative and anti-estrogenic activity,<sup>[6,13,14]</sup> inhibition of tumorigenesis, antioxidant activity,<sup>[6,12,23,24]</sup> hepatoprotective activity,<sup>[1,12,25,26]</sup> hypoglycaemic activity,<sup>[22,23,27,28]</sup> antiviral,<sup>[10,29-31][32]</sup> protective effect on GI,<sup>[33-35]</sup> antifungal, anti-fibrinolytic, antibacterial activity,<sup>[6,36-38]</sup> anticonvulsant activity,<sup>[32,39]</sup> diuretic, spasmolytic activity, anti-stress and dyspepsia.<sup>[10]</sup>

Allopathic medicine is almost at the height of established research and advanced technology, therefore, with the help of advanced research methodology, there is an urgent need to validate the principles and drugs used in the alternative medicine system, including herbal drugs.<sup>[4]</sup> As the long-term management of many chronic illnesses using prescription drugs has side-effects.<sup>[6,39]</sup> Although the use of herbs is not without risk and when they are administered together with allopathic drugs, it can lead to interactions. The result of these interactions ranges from minor to life-threatening.<sup>[40]</sup> The potential dangers associated with herb-drug interactions cannot be overlooked but should be rationally managed by several methods one being the evaluation and further research on these herbs.

Owing to the uniquely accessible chemical variety, the plant extracts have several possibilities for new lead compounds as pure compounds or as a standardized substance.<sup>[37]</sup>

## 2 MORPHOLOGY

*Boerhaavia diffusa* is a recurrent, flat or ascending herb with branches spreading up to 100cm in length or more.<sup>[41]</sup> It has a diffused branched with an orthotropic and superimposed axis. Despite its orthotropic shooting, it's flat due to the rapid propagation as the relay pole extends quickly over the main axis.<sup>[1]</sup>

The roots on the coatings are strong, pig-shaped, smooth and fusiform in colour, soft yellow and brownish-grey with timbered materials and rootlets. It is thick, highly bitter and body-like as seen in figure 2.2.<sup>[1]</sup> These roots contained 0.15% of Punarnavine alkaloids.<sup>[42]</sup> The stems are Greenish purple, inflexible, small, tube-shaped, over a meter long, inflated at nodes. Comprised of 9-12 cells and an ellipse head cortex of few parenchyma-layers, thickened walled mostly made up of thin, reclusive fibres, stele which is sometimes fastened on a ring and several large vascular bundles are stretched out.<sup>[41,43]</sup>

Fig. 2.3 shows the leaves of *Boerhaavia diffusa* which are simple, dense, and bushy distributed in uneven pairs,

generally white beneath and green above. The leaves differ in their nature; ovate-oblong, circular at the base and fluid upwards. The edges of the leaves are flat, undulate or wavy. The above and below the leaves are respectively green, shiny, rose-white and rough. Throughout the region, leaves are up to 5.5 / 3.3 cm<sup>2</sup>.<sup>[39]</sup> Flowers (Fig. 2.1) are minor, present 4-10 in tiny bracteolate umbels together, forming axillary and terminal panicles. These are hermaphrodite, pedicellate and coloured in white, brown, or orange-red<sup>[41]</sup>. Until the monsoon starts, seeds sprout and become active, bracts are deciduous.<sup>[10]</sup> In the rainy season, the plants develop and ripen seeds from between October and November.<sup>[44]</sup>



Figure 2:1 *Boerhaavia diffusa* flower.



Figure 2:2 *Boerhaavia diffusa* root.



Figure 2:3 *Boerhaavia diffusa* leaves.

**Table 1: Shows the Botanical classification of *Boerhaavia* from Kingdom to its Species.****Table 1 : Botanical classification.**

S/N		
1	Kingdom	<i>Plantae</i>
2	Subkingdom	<i>Viridiplantae</i>
3	Infrakingdom	<i>Streptophyta</i>
4	Superdivision	<i>Embryophyta</i>
5	Division	<i>Tracheophyta</i>
6	Subdivision	<i>Spermatophytina</i>
7	Class	<i>Magnoliopsida</i>
8	Superorder	<i>Caryophyllanae</i>
9	Order	<i>Caryophyllales</i>
10	Family	<i>Nyctaginaceae</i>
11	Genus	<i>Boerhavia</i> L. – spiderling
12	Species	<i>Boerhaavia diffusa</i> L. – red spiderling

### 3 Geographical distribution

*Boerhaavia* species can be found in hot, subtropical and warm areas. There are about 40 species spread across the temperate regions of the world.<sup>[5]</sup> Different species of *Boerhaavia* are found across the Northern and Southern American continent<sup>[45]</sup> the continent of Africa, in countries like Benin, Egypt, Rwanda, Senegal, Somalia, South Africa, Sudan, Zambia, Ethiopia, Ghana, Nigeria etc.<sup>[45,46]</sup> Across Asia, in countries like China and Malaysia Afghanistan, Cambodia, Kuwait, Myanmar, Nepal, Pakistan, Philippines, Saudi Arabia, India etc.<sup>[43,47]</sup>

### 4 Phytochemistry

*Boerhaavia diffusa* comprises diverse types of secondary metabolites; flavonoids, alkaloids, hormones, triterpenoids, lipids, lignins, carbohydrates, proteins, and glycoproteins. The roots and herbs have abundant proteins and fats.<sup>[48]</sup> The herb contains 15 amino acids, including 6 essential amino acids, while the root contains 14 amino acids, including 7 essential amino acids.<sup>[5]</sup> Several studies have been carried out to isolate the chemical constituent and to identify its role in the

pharmacological action of the plant. These multiple constituents may act synergistically and could hardly be separated into active parts.<sup>[49]</sup> Likewise, the chemical constituents vary depending on the harvest seasons, plant origins, drying processes and other factors.<sup>[50]</sup> Secondary metabolites like flavonoid glycoside; 3,4-Dihydroxy-5-methoxycinnamoyl rhamnoside, Quercetin 3-O-rhamnosyl (1 → 6)galactoside (quercetin 3-O-robinobioside), Eupalitin 3-O-galactosyl (1 → 2) glucoside, Kaempferol 3-O-robinobioside Eupalitin-3-O-[-D-galactopyranoside] were identified in the extract of *Boerhaavia diffusa* leaves and roots. In another article, the methanol extract of the roots of *Boerhaavia diffusa* L was separated by bioassay and 5 rotenoids compounds were isolated the known boeravinone D, boeravinone E, C5 and two new compounds named boeravinone G and boeravinone H. Boeravinone G, boeravinone E and compound 5 exhibited spasmolytic activity.<sup>[51]</sup> The distribution of chemical constituents like alkaloid is seen in different quantity throughout the herb. Two quinolizidine alkaloids identified as punarnavine-I and punarnavine-II have been isolated from the roots, stems and leaves. Figure 4.1 shows the chemical structure of main constituents isolated from *Boerhaavia diffusa*.

**Table 2 Name of compound and activity reported.**

S/N	Name of compound	Activity reported	Plant part	Reference
1	Punarnavoside	Antifibrinolytic	Roots	[52]
2	(6, 11-dihydroxy-9-10-dimethyl-4-methoxyrotenoid)	Hepatoprotective	Leaves	[25,26]
3	Flavonoids	Antibacterial	Leaves	[37]
4	Boeravinones A, B, C, D, E, F	Anticancer	Roots	[6][53]
5	Polyphenols	Antioxidant	Leaves	[27]
6	Boeravinone G, Boeravinone E, Compound 5	Antispasmodic	Roots	[51]

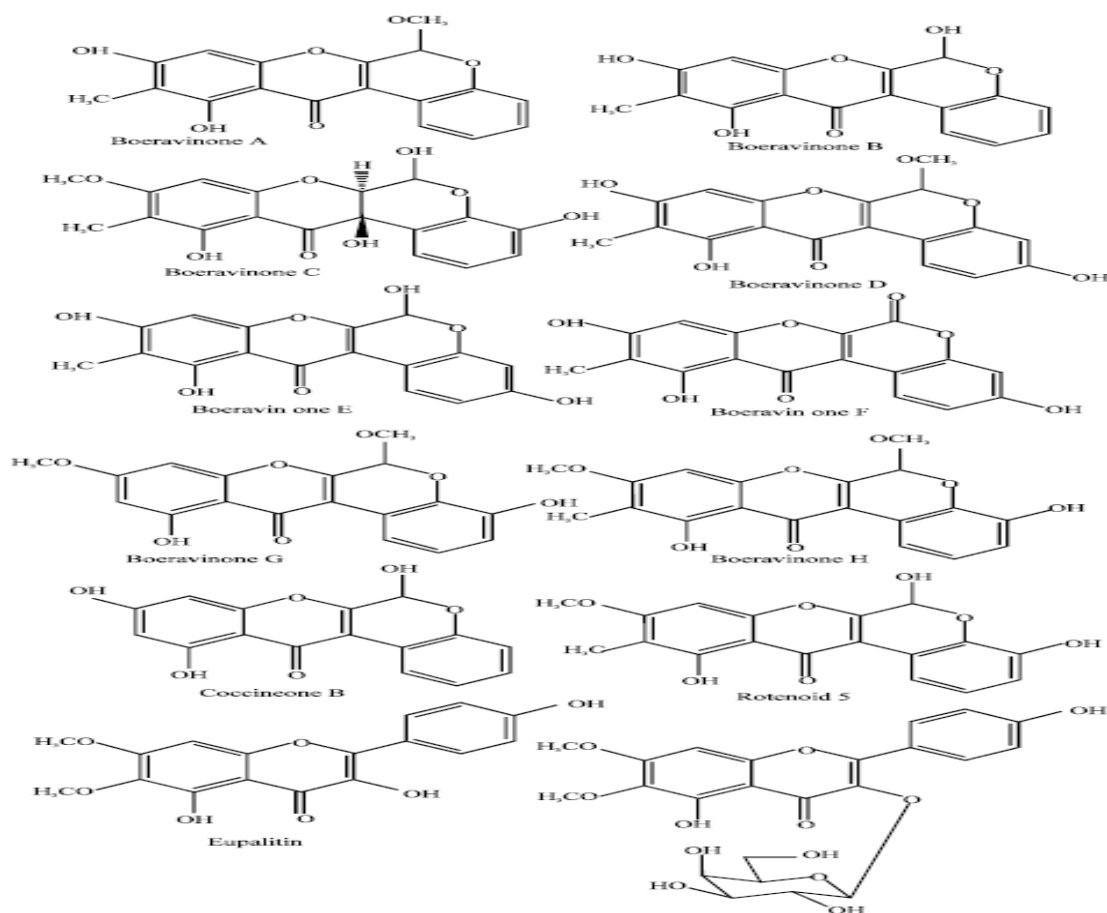


Figure 4: Chemical structure of main constituents isolated from *Boerhaavia diffusa*.<sup>(51-53)</sup>

## 5 Pharmacology and Clinical studies

*Boerhaavia diffusa* have been known for its ethnopharmacological activity, all of these uses can be verified in the light of current therapeutic studies or the compounds isolated from *Boerhaavia diffusa* L.

### 5.1 Antibacterial activity

Umamaheswari and co-workers conducted a qualitative analysis in different solvents such as ethanol, ethyl acetate, diethyl ether, methanol, chloroform and aqueous extracts of *Boerhaavia diffusa* leave to measure its activities against bacteria. The strains of bacteria used for the study were *E.coli*, *Pseudomonas aeruginosa*, *Salmonella Typhi*, *Klebsiella pneumoniae*, *Proteus Vulgaris*, *Serratia marcescens*, *Shigella flexneri*, *Vibrio cholerae*, *Staphylococcus P. Vulgaris*, *S. marcescens* and *S. flexneri*.<sup>[37]</sup> The preliminary analysis of biologically active compounds found in the plants revealed the presence or absence of various biologically active compounds qualitatively in various solvents which is responsible for its activity.<sup>[1,49]</sup> Based on the results, the *Boerhaavia diffusa* leaves have good antibacterial activity against both Gram-negative and Gram-positive bacteria that is attributed to the biologically active compounds present in the leaves according to certain studies.<sup>[2,37]</sup>

The Sahu L and colleagues experiment includes using the *Agrobacterium rhizogen* mediated transformation of *Boerhaavia diffusa* to achieve anti-microbial action against bacterial pathogens that cause urinary tract (UTI) infections. The invitro anti-microbial activity of the extracts of natural root tested against 12 pathogenic strains of UTI- causing bacteria, including two antibiotic-resistant ones. The two root extracts understudy show antimicrobial activity against selected bacterial strains under in-vitro culture. The antimicrobial activity of root extracts was compared with gentamicin, ciprofloxacin or chloramphenicol, each of which was taken as a positive control. Data shows the variable susceptibility to both forms of root extracts by the microorganisms under in vitro study.<sup>[38]</sup>

In another analysis, fungal endophytes extracted from *Boerhaavia diffusa* L were tested for the antibacterial ability. A total of 12 endophytic fungi have been isolated and classified into 7 taxa. The findings demonstrate that the development of a particular pathogen or all study pathogens substantially greater than 33 per cent of the isolated endophytic fungi was prevented by a minimum of four endophytic fungi.<sup>[54]</sup>

Studies like <sup>[37,54,55]</sup> give us an idea of how vast and effective herbs are in treating antibacterial infection, the Centres for



Disease Control and Prevention (CDC) cautioned for a post-antibiotic age, antibiotics have become less effective against a variety of infectious species<sup>[56]</sup>. The problems of drug-resistant pathogens have been reviewed and there is an urgent need for more effective antibacterial therapy<sup>[57]</sup>. Hence, natural products provide opportunities for new leads compound because of the unique availability of chemical diversity.<sup>[37]</sup>

### 5.2 Anti-diabetic activity

L. Pari and M. Amarnath Satheesh reported the effect of *Boerhaavia diffusa* leaf extract on lipids in normal and alloxan diabetic rat.<sup>[58]</sup> 30 rats (12 normal) and 18 injected with alloxan monohydrates were used 2 weeks after injection. In diabetic rats, blood glucose levels rose dramatically and plasma insulin levels dropped considerably. Blood glucose levels decreases and a major rise in plasma insulin was seen after the oral administration of *Boerhaavia diffusa* extract and Glibenclamide.<sup>[27,58]</sup> The intervention with *Boerhaavia diffusa* extract and glibenclamide has raised body weight and lowered the amount of glycosylated haemoglobin as related to diabetic rats. In rats treated with *Boerhaavia diffusa*, glibenclamide, in contrast with the diabetic population, triglycerides, cholesterol, free fatty acids and phospholipids were substantially decreased. The study indicates that the potential mechanism by *Boerhaavia diffusa* extract lowers glucose level may well be caused by potential pancreatic insulin secretion from established cells, increased blood glucose transportation to peripheral tissues or a decrease in gastrointestinal glucose absorption. Leaf extract of *Boerhaavia diffusa* is antidiabetic and has antioxidant properties.<sup>[58]</sup>

The in-vitro antioxidant activity of the *Boerhaavia diffusa* methanol extract was investigated by Alam P and Shahzad N and its protecting effects were examined in Wister rat against streptozocin induced diabetes. This research culminated in a significant decrease in plasma glucose level and a rise in insulin level, with *Boerhaavia diffusa* roots methanolic extract at 200 mg/kg. It also shows that *Boerhaavia diffusa* methanol extract culminated in a substantial drop in serum urea and creatinine concentrations, this indicated its renoprotective effects.<sup>[27]</sup>

Other studies like<sup>[23,27,59]</sup> have evaluated the Anti-diabetic Effect of *Boerhaavia diffusa* L. root extract and all show that it has potential antidiabetic and antioxidant properties.

### 5.3 Immunomodulatory activity

Immunomodulators may change the immune system's function, undermining the immune system and creating side effects is a function of chemotherapeutic agents. Immunomodulators originating from plants are used as a general adaptor and immune strengthener without harmful effects.<sup>[60]</sup>

Aher Vaibhav and colleagues reported the immunomodulatory activity of Punarnavine Alkaloid from *Boerhaavia diffusa* root. Studies have confirmed that the treatment of punarnavine could increase the humoral immune response due to antibody synthesis that in turn increases macrophages and lymphocyte subsets. Increasing numbers of  $\alpha$ -esterase positive and bone marrow cells are demonstrated by the proliferation of stem cells because of the immunomodulatory effect. Punarnavine increases multiple organ weight.<sup>[61]</sup>

Aryan Manu and colleagues investigated the immunomodulatory activities of Punarnavine. The result shows a relative weight increased of both thymus and spleen in Punarnavine treated group of animals comparing the untreated control showing statistical significance ( $p < 0.001$ ). Treated animals showed a significant ( $p < 0.001$ ) increase in bone marrow cell number as compared to normal animals. The number of  $\alpha$ -esterase positive cells also increased significantly ( $p < 0.001$ ) in punarnavine treated animals compared to untreated control. The increase in the number of bone marrow cells, the differentiation of stem cell with  $\alpha$ -esterase involvement, induced bone marrow cell proliferation with and without mitogens both in vitro and in vivo suggest that Punarnavine has an immunostimulatory impact on stem cells.<sup>[62]</sup>

Other studies on anti-stress, adaptogenic and immunopotentiating activity roots of *Boerhaavia diffusa* in mice all concluded that *Boerhaavia diffusa* could be developed as a potent immunomodulatory agent.<sup>[63-65]</sup>

### 5.4 Anti-inflammatory activity

It was reported that *Boerhaavia diffusa* has chemical constituents like Boeravinones A-J present in the root.<sup>[51,53,66,67]</sup>

In a report by Khemraj Bairwa and colleagues on the ability of *Boerhaavia diffusa* rotenoids as anti-inflammatory agents, 5 new rotenoids were isolated by phytochemical investigation of the methanol extract of *Boerhaavia diffusa* roots.<sup>[68]</sup> Using the carrageenan-induced paw oedema method, described by Winter et al.<sup>[69]</sup> the anti-inflammatory activity of the 70% ethanol extract, a rotenoid-rich fraction, and boeravinone B (6) of *Boerhaavia diffusa* was evaluated. The reference standard medication ibuprofen was given to the positive control groups at a dose level of 100 and 50 mg/kg PO. The three other classes were treated at a dose of 100 mg/kg PO with 70 % ethanol extract, 100 mg/kg PO with rotenoids section and 50 mg/kg PO with boeravinone B (6). Oedema was induced by subcutaneous injection of 100  $\mu$ L of 1% carrageenan in saline solution into the left hind paw of the rats, 1 h after test compound administration. The volume of the paw was measured immediately before (basal) and after (3 and 5 h) carrageenan injection using a plethysmometer.<sup>[68]</sup>

C.A. Hiruma and colleagues evaluated the significance of juice of fresh leaves of *Boerhaavia diffusa* L to reduce

pain in mice. The crude extracts were prepared from fresh leaves juice using only 10% water and as a 10% leaf decoction. The analgesic properties were tested by the abdominal writhing of acetic acid triggered mouse. 10% water, dipyrone, and 10% leaf decoction extract meaningfully inhibited abdominal writhing in mice (50, 100 and 47%, respectively) as compared to negative control animals. The hot-plate test was used to measure response latency, a latency period of 30 s was defined as complete analgesia. In conclusion, the study indicated the analgesic property of aqueous extracts obtained from *Boerhaavia diffusa*, mainly from the leaf juice of the plant.<sup>[70]</sup>

G.M. oladele and co-workers reported the anti-inflammatory and membrane-stabilizing effects of aqueous root extract of *Boerhaavia diffusa* Linn in rats.<sup>[17]</sup> The results show a significant ( $p < 0.05$ ) dose-dependent inhibit carrageenan-induced rat paw oedema by the extract in doses of 100-400 mg/kg. hence, concluded that the extract possesses anti-inflammatory as well as a membrane stabilizing properties.<sup>[17]</sup>

Studies by Manisha Gharate & Veena Kasture, V. Mudgal all shows the anti-inflammatory activity of the root and leaves of *Boerhaavia diffusa*.<sup>[18,71]</sup>

### 5.5 Anti-cancer activity.

Rupjyoti Bharali et al evaluated *Boerhaavia diffusa* chemopreventive action on 7, 12-dimethyl benzoanthracene (DMBA) mediated skin carcinogenesis in mice. Bodyweight of the animals was recorded at weekly intervals and also at the time of autopsy animals were divided into 4 sets. Different groups were given a different dose of *Boerhaavia diffusa* extract in acetone and some were used as control. The result indicates that tumour occurrence rates are greatly reduced by an equal amount of tumours per mouse with a tumour and papilloma per mouse with papilloma ranging from one category to other. This leads to the conclusion that the plant extract may have prevented tumorigenesis either by preventing the development of active carcinogens from their precursors or by the detoxification phase, by preventing promotional events in the skin of the mouse utilizing free radical scavenging mechanism.<sup>[72]</sup>

Sreekumar Sreeja and Sreeharshan Sreeja reported the anti-proliferative and anti-estrogenic activity of *Boerhaavia diffusa* L. Extracts of *Boerhaavia diffusa* has a significant inhibitory effect on in-vitro breast cancer cell growth and ER-mediated anti-estrogenic activity. The presence of alkaloids, flavonoids, phenols and saponins in of *Boerhaavia diffusa* extract has been demonstrated in phytochemical studies. These different compounds can be attributed to the antiestrogenic activity shown by the extract.<sup>[73]</sup>

Remia *et al.* conducted an in-vitro experiment to study the cytotoxicity of B root decoction in Michigan Cancer Foundation-7 breast. The test sample of *Boerhaavia*

*diffusa* at a concentration of 800 µg / ml demonstrated cytotoxicity of around  $65.1 \pm 1.2$  during 48 hours of incubation in the breast cell line MCF-7.<sup>[6]</sup> Kayande and Kushwah also record the anticancer activity of ethanol extract from *Boerhaavia diffusa* leave against Dalton's ascetic lymphoma in mice.<sup>[74]</sup>

### 5.6 Antifibrinolytic activity

Barthwal M, Srivastava K, has evaluated the antifibrinolytic effects on the endometrial histology of IUD-fitted menstrual monkeys by antifibrinolytic agents such as  $\alpha$ -aminocaproic acid, tranexamic acid, anti-inflammatory drugs and root extracts of *Boerhaavia diffusa*. It is effective in reducing stromal oedema, inflammation and increasing the amount of fibrin and platelet deposition in the vessel lumen.<sup>[75]</sup> Also, the mechanism of this process was evaluated and NAD-dependent 15-hydroxy prostaglandin dehydrogenase activity was discovered in the endometrium.<sup>[76]</sup>

### 5.7 GI Protective activity

The anti-inflammatory, antipyretic and antiulcer activities of Punarnavasava were evaluated by Gharate M and Kasture V, showing that *Boerhaavia diffusa* had antiacid activity, the aqueous extract significantly reduced ulcer index and improved protection in dose-dependent.<sup>[77]</sup>

Devi and Jyothi studied *Boerhaavia diffusa* pharmacodynamic interaction with omeprazole in rats(experimentally induced ulcers) and assesses *Boerhaavia diffusa* healing effect. They concluded that the administration of *Boerhaavia diffusa* alone or along with Omeprazole successfully leads to a reduction of gastric ulcer secretion in indomethacin-induced gastric ulcers, stress-induced duodenal and pylorus ligation induced gastric ulcers and gastric ulcers in rats. The healing effect of root extract of *Boerhaavia diffusa* was due to a decrease in gastric secretion and also due to reduced gastric action.<sup>[78]</sup>

Many pathways such as soothing effects, gastric secretion regulation, anti-inflammatory properties and mucus inducing effects tend to regulate *Boerhaavia diffusa's* antiulcer activities.<sup>[79]</sup>

### 5.8 Hepatoprotective activity

The hepatoprotective function of *Boerhaavia diffusa* L root was evaluated by A.K.S. Rawat and others in thioacetamide-induced toxicity in albino rats after recognition of the importance and common use of roots in the treatment of liver disorders by several ethnic groups in India.<sup>[80]</sup> It assessed the frequent levels of liver enzymes, the effect of various root types and the season in which the plants are grown. The findings indicate that aqueous form of a drug has a higher percentage of protection than in the powdered form. The increased serum Glutamic- Oxaloacetic Transaminase, Glutamic-Pyruvate Transaminase, Alanine Transaminase Acid, Phosphatase Alkaline Phosphatase concentrations were

substantially reduced by *Boerhaavia diffusa* L thin root extract (aqueous), as compared to the thick roots proposing that the drug derived from thin roots has more hepatoprotection, which may be due to the presence of more biologically active metabolites in the thin root compared to the thicker woody roots. It also shows how the activity of the majority of the serum enzymes is greater in the summer, as compared to the other seasons, signifying that this is the proper time for collection of the herb, however, no significant protection at  $P < 0.01$  was observed in the case of glutamate dehydrogenase and bilirubin.<sup>[80]</sup> In conclusion, the studies revealed that the herb possesses marked hepatoprotective activity against thioacetamide-induced hepatotoxicity and support various theories proposed for the mechanism by which thioacetamide damages the liver.<sup>[81]</sup>

In adult male albino rats of Charles Foster strain (150-200 g) and male adult Swiss mice (20-25 g), B.K Chandan and his colleagues evaluated the hepatoprotective function of *Boerhaavia diffusa* alcoholic root extract, the hepatic injury was induced with 1.5 ml/kg Carbon Tetrachloride (Ccl4) mixed to the same volume of liquid paraffin administered orally. Control group received liquid paraffin of equivalent volume.<sup>[82]</sup> The animals were divided into 3 groups (n=10), 1 group was given *Boerhaavia diffusa* (500 mg/kg) 48 h, 24 h and 2 h before and 6 h after Ccl4, administration the second group received Ccl4 only, the third group served as vehicle control. Hexobarbitone (60 mg/kg, i.p) "sleeping" time (time of lost righting reflex) was documented 18 h after Ccl4 administration.<sup>[83]</sup> The work has concluded that *Boerhaavia diffusa* will substantially shorten the "sleep" period for hexobarbitone both in rats and mice as against animals receiving Ccl4 alone and thus confirm its protection against hepatic enzymes. Evidence suggests that in the event of any liver damage the time lost reflex caused by short-acting barbiturates would be substantially increased and can be used as a measure of liver-metabolic enzymes' activity.<sup>[84,85]</sup>

Other studies suggest that the rise in the peripheral levels of certain enzymes, principally serum glutamic oxaloacetic transaminase (SGOT) and serum glutamic pyruvic transaminase (SGPT), under the influence of Ccl4 has been attributed to the disturbed/damaged structural integrity of the liver.<sup>[86]</sup> *Boerhaavia diffusa* appears to preserve the structural integrity of the hepatocyte cell membrane which is evident by a reduction in the Ccl4-induced rise of SGOT and SGPT levels. It was observed that the treatment with *Boerhaavia diffusa* extract before and after Ccl4 poisoning resulted in a substantial decrease in serum bilirubin levels, and reduced the prothrombin time (which was increased by Ccl4) indicates that the drug is effective in the maintenance of the normal functional status of the liver and capable of protecting the prothrombin synthetic activity of the liver. so it was

concluded, that the alcoholic extract of *Boerhaavia diffusa* is a potent and safe ant hepatotoxic drug.<sup>[82]</sup>

The antioxidant activity and hepatoprotective property of leaf extracts of *Boerhaavia diffusa* Linn were examined by M. Tolulope Olaleye and associates against acetaminophen-induced liver damage in rats.<sup>[87]</sup> Different groups were given doses of acetaminophen and the ethanol extract of *Boerhaavia diffusa* other were used as control groups. The results show that there were significant increases in the activities of serum AST, ALT, ALP, LDH and bilirubin in the acetaminophen treated group compared with the control and there was a decrease in the serum albumin concentration compared with the control ( $p < 0.05$ ). Administration of both aqueous and ethanolic extracts caused decreases in level and activity of serum AST, ALT, ALP bilirubin and LDH as compared with the acetaminophen treated group.<sup>[87]</sup>

Mama Sirou and colleagues studied protective Effects of *Boerhaavia diffusa* Linn on the liver of Streptozotocin-induced diabetic rats,<sup>[88]</sup> Surendra K. Pareta1 Protective Effects of *Boerhaavia diffusa* Against Acetaminophen-Induced nephrotoxicity in Rats.<sup>[89]</sup>

Debendranath Deu and colleagues study Hepatoprotective Activity of BV-7310, a Proprietary Herbal Formulation of *Phyllanthus niruri*, *Tephrosia purpurea*, *Boerhaavia diffusa*, and *Andrographis paniculata*, in Alcohol-Induced HepG2 Cells and Alcohol plus a Haloalkane, CCl4, Induced Liver Damage in Rats<sup>[26]</sup> all indicates that *Boerhaavia diffusa* has hepatoprotective activity.

### 5.9 Anti-viral activity

Lohani and colleagues suggested that *Boerhaavia diffusa* have antiviral activity against phytopathogenic viruses.<sup>[90]</sup> Further research by Babita and associates shows that the antiviral means was found to be a glycoprotein with a mass of 16-20 kDa.<sup>[91]</sup>

Awasthi and Verma experimented to isolate the virus inhibitor from the root extract of *Boerhaavia diffusa* by inducing systemic resistance in plants. The result shows that the elution profile of the inhibitor from a Sephadex G-200 column identified protein-containing fractions were responsible for virus inhibition. The inhibition ranged from fraction 24 to 30 in which protein concentration was high. Some protein was present in fractions 12-40 but all these were nonantiviral.<sup>[92]</sup> The aqueous extracts of plant material were prepared and tested in-vitro as well as in vivo against phytopathogenic viruses on their hypersensitive and systemic hosts. The botanical identity of each plant was established before the extracts were prepared. Of a large number of plants screened, *Boerhaavia diffusa* root extracts were found to have a broad spectrum and very high antiviral activity.<sup>[10]</sup>

### 5.10 Antioxidant activity

Antioxidants are compounds that forage free radicals and show importance in averting ailments caused by free radicals.<sup>[93]</sup>

The antioxidant activity of *Boerhaavia diffusa* methanol extract was examined by Dr J.Jayachitri and his colleagues.<sup>[24]</sup> 70% methanolic, an aqueous extract of the drug was prepared. The in-vitro activity was determined by, 1,1-diphenylhydrazyl (DPPH), different concentrations of plant extract (200,400,600 and 800µl/ml) were chosen for the antioxidant action. The percentage of inhibition of overall antioxidant function, 1,1-diphenylhydrazyl radical scavenging and hydroxyl radical scavenging activity varies between methanol and water extracts. The UV spectrum confirmed the presence of alcohols, alkanes, aldehyde, ketones and aromatic compounds in methanol extract of *Boerhaavia diffusa* L leaves.

*Boerhaavia diffusa* extract possesses potent antioxidative properties. The free radical scavenging effects observed in plant extract may be due to flavonoids and tannins. They are phenolic compounds and the primary antioxidants or free radical scavengers activity is ascribed to the phenolic group.<sup>[24,94]</sup>

Sawardekar SB et al. evaluated the aqueous extract of the root of *Boerhaavia diffusa* in nephrotoxicity induced by gentamicin in rats. Authors measured the levels of serum creatinine, kidney malondialdehyde (MDA), glutathione (GSH) and blood urea nitrogen (BUN), and concluded that *Boerhaavia diffusa* extract protected the nephrotoxicity (structural and functional damage) induced by gentamicin and this was possibly due to antioxidant property of extract.<sup>[95]</sup>

Oburai NL et al. compared the *Boerhaavia diffusa* extract in canine chronic renal failure in dogs with standard enalapril. Authors were measured blood pressure, serum urea, creatinine, phosphorous, sodium, and glutamyl transferase and concluded that extract was comparable with standard enalapril.<sup>[96]</sup>

The antioxidant and hepatoprotective effects of the *Boerhaavia diffusa* Linn leaf extracts were studied by M. Tolulope and partners. For ethanol extract, the cumulative amounts of phenolic, cumulative flavonoid, vitamin C and E, selenium and zinc were analyzed. It indicates the existence in the plant, significant groups of antioxidant nutrients, as confirmed by several unique bioactive compounds extracted from the plant.<sup>[87]</sup>

### 5.11 Anticonvulsant activity

The vast ethnopharmacological activity of *Boerhaavia diffusa* makes it gain importance in the field of Phytochemistry. It is widely used in Nigeria for convulsion.<sup>[97]</sup> The *Boerhaavia diffusa* methanolic root extract has been reported to display calcium channel antagonistic activity due to isolated compound 'liriodendrin'.<sup>[98]</sup>

Kaur and Goel tested the anti-convulsant activity of various root extracts of *Boerhaavia diffusa* in male swiss albino mice. The methanolic extract, the liriodendrin rich fraction, of this extract, chloroform fraction and a phenolic compound fraction (of different concentration) showed anticonvulsant activity in pentylenetetrazol (PTZ) induced seizures in mice and concluded that the calcium channel blocking activity is responsible for this since the activity was maintained only by a liriodendrin-rich fraction, additionally established by anticonvulsant activity in BAY k8644-induced seizures.<sup>[72,98]</sup>

Other Studies showed the crude methanolic extract of *Boerhaavia diffusa* and its liriodendrin-rich fraction exhibits dose-dependent protection against PTZ-induced convulsions.<sup>[99]</sup>

## 6 CONCLUSION AND FUTURE PERSPECTIVES

Phytochemical analysis and separation of indicator compounds of *Boerhaavia diffusa* have confirmed the significant bioactive chemicals such as flavonoids, retinoids, amino acids alkaloids etc.<sup>[100]</sup> The efficiency and efficacy were enhanced by analytical methods including Ultrasound Liquid Chromatography (UPLC) for boeravinones and other compounds from *Boerhaavia diffusa*. Researches had been done to ascertain the authenticity of the bioactive component of *Boerhaavia diffusa* L. especially alkaloid, flavonoids and rotenoids like boeravinone (A-G), by identification and quantification through several chromatographic techniques like rapid HPLC analysis.<sup>[101,102]</sup> The quantity of Boeravinone and other bioactive components contained in *Boerhaavia diffusa* extracts was seen to be compatible with that described in the publications.<sup>[102]</sup> The collected findings show that the bioactive components can be used as lead compounds to produce medicines that could be beneficial in many fields. Furthermore in-vitro and in vivo experiments are needed to verify these anticipated findings, more study on separation, purification, recognition of active constituents and assessment, as well as systematic research to promote acceptance and incorporation of *Boerhaavia diffusa* in conventional medicine is important. Regardless of the absence of medical evidence, the world economy is inaccessible to Ayurvedic and traditional medicines. Ayurvedic work needs to accelerate the adoption of its formulations on a global scale. There is also an immediate need to verify fresh drugs through introduction of modern techniques as ingredients and different polyherbal formulations.

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