

Boerhavia Diffusa Linn: Unravelling the Medicinal Tapestry from Ayurvedic Traditions to Modern Science

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ABSTRACT

Boerhavia diffusa Linn., categorized as a Rasayana in Ayurveda and belonging to the *Nyctaginaceae* family, exhibits a diverse range of medicinal properties. These include the treatment of conditions such as diabetes, inflammation, stress, hepatotoxicity, jaundice, and heart failure. *B. diffusa* has garnered attention for its notable antioxidant, hepatoprotective, antibiotic, antidiabetic, and anticancer qualities among pioneers in the fields of science and medicine. This review on *B. diffusa* explores its chemical compositions and ethnomedicinal uses, tracing its historical significance to the present and contemplating potential avenues for future development. Additionally, the review provides a recent update on the mechanistic approaches of *B. diffusa*, offering valuable insights for researchers in this field. Due to the plant's therapeutic value, which is ascribed to its abundance of flavonoids and polyphenols, medical professionals and researchers should thoroughly investigate the biological and pharmacological aspects of this plant.

Keywords: *B. diffusa*; Ayurveda; Anticancer; Medical Importance; Ethnomedicinal Uses

Introduction

The *Nyctaginaceae* family of medicinal plants, *Boerhavia diffusa* Linn., is well-known in Indian traditional medicine for its therapeutic qualities. It is also acknowledged in other areas of the world and in certain countries of South America. In the context of Indian traditional medicine, it goes by several names such as Punarnava, Shothaghni, Kathillaka, Varshabhu, Raktapushpa and Varshaketu [1]. Within the context of Indian Ayurveda, *Boerhavia diffusa* is designated as a "rasayana" herb, believed to possess diverse qualities including anti-aging effects, enhancement of life and memory power, and disease prevention. These attributes suggest that the herb fortifies the body's resis-

ience against external threats, essentially offering hepatoprotection and immunomodulation [2]. In specific areas, the entire plant serves as a vegetable. For instance, in regions like Assam and West Bengal in India, local communities cook the leaves as a culinary delicacy [3]. Different types of the *Boerhavia* genus can be located across tropical, subtropical, and temperate regions worldwide, spanning Australia, Asia, the United States, and Africa. Within the Indian subcontinent, *B. diffusa* is prevalent in warmer regions of the country, reaching altitudes of up to 2000 m in the Himalayan region [4]. Six of the forty species in this genus—*B. diffusa*, *B. erecta*, *B. rependa*, and *B. rubicunda*—can be identified in the Indian subcontinent. In particular, *B. diffusa* has been the subject of a great deal of research because of its

chemical makeup and medicinal qualities.

The roots of *B. diffusa* are the source of a distinct group of isoflavonoids known as rotenoids, along with flavonoids, xanthenes, purine nucleosides, lignans, and steroids. Numerous studies and trials have confirmed its diverse activities, including immunomodulation, anti-cancer effects, antidiabetic properties, antioxidants, and anti-inflammatory attributes. During diverse studies conducted on the *B. diffusa* plant, preliminary examinations have detected the existence of β -sitosterol [5], and alkaloids [6]. The root of this plant has been traditionally used by several tribes to alleviate liver disorders. Specifically in South Garhwal, the tribal community has applied the roots for the treatment of various diseases such as liver enlargement [7]. Moreover, tribes have been using the plant's roots of 'Punarnava' (*Boerhavia diffusa*) to treat jaundice in the eastern parts of Rajasthan and Gujarat state [8,9]. Besides, *B. diffusa* roots are recommended in some parts of Madhya Pradesh to treat kidney and liver problems [10]. This review offers a condensed overview of the bioactive components and documented pharmacological effects, presenting an ethnopharmacological evaluation of the said plant.

Geographical Distribution

The *Boerhavia* genus, consisting of 40 species, is distributed across tropical, subtropical, and temperate zones worldwide. *Boerhavia diffusa*, or *B. diffusa*, is a plant that was originally native to Brazil and India but is now found in tropical, subtropical, and temperate countries with elevations of up to 1200 metres above sea level. It is found in many places, such as Mexico, Asia, Africa, the Indian and Pacific oceans, Egypt, and Sudan [11,12]. In India, six out of the 40 species within this genus can be found, namely *B. diffusa*, *Boerhavia chinensis*, *Boerhavia erecta*, *Boerhavia repanda*, and *Boerhavia rubicunda*. *B. diffusa*, specifically, is indigenous to India and flourishes in wastelands and fields after the rainy season. Furthermore, there is a limited cultivation of this plant in West Bengal [13].

Traditional Uses

As noted earlier, *B. diffusa* holds significant importance as a primary herbal ingredient in a variety of Ayurvedic medicinal formulations. Its incorporation in different preparations is effective in managing conditions like inflammation, jaundice, asthma, nephrological disorders, anaemia, and gynaecological issues. Table 1 categorizes several traditional formulations where *B. diffusa* plays a central role as a key component [14].

Table 1: Traditional formulations containing *B. diffusa* act as a major ingredient.

Name of formulation	Traditional Uses	Reference
Punarnavadyarishta	Cardiovascular conditions, inflammation, enlarged spleen, dizziness, severe jaundice, abdominal mass, persistent cough, asthma, malabsorption syndrome, and skin disorders are among the health issues discussed.	(Bhaisajyaratnavali, Sotharogadhikara: 192-196)
Varuni	Pain	[14]
Punarnavasava	Indigestion, a lump in the abdomen, abdominal diseases/enlargement,	(Bhaisajyaratnavali, Sotharogadhikara: 197-201)

Phytochemistry

Several studies on *Boerhavia diffusa* species have revealed a variety of important phytochemicals across different regions, taking into account ethnopharmacological applications and advancements in technologies like mass spectroscopy, liquid chromatography-mass

spectroscopy (LC-MS), Electrospray ionisation mass spectrometry (ESI-MS) etc. These investigations have unveiled significant phytochemicals in various parts of *Boerhavia* species, as detailed in Table 2. The conventional method for isolating compounds typically includes extraction, partitioning in different solvents, and bioactivity-guided fractionation using silica gel chromatography [15-21].

Table 2: List of chemical compounds isolated from *Boerhavia diffusa*.

Chemical category	Chemical compound	Parts used	Reference
Alkaloids	Punarnavine	Root	[15]
	Isobetanin, Neobetanin	Stem bark	[16]
Phenolics	Eupalitin	Whole plant	[17]
Terpenes	Boerhavisterol	Roots	[18]
	Camphor, Isomenthone, Limonene, Menthol, Phellandrene, Safranal, α -Pinene, Geranylacetone, cis 4-Hexen-1-ol, trans 2-Octanal, 2-Nonen-1-ol, Methylpyrrole, Eugenol	Roots, leaves	[19]

Pharmacological Activities in *Boerhavia diffusa* Linn

The plant *Boerhavia diffusa* has become significantly important in the field of phytochemistry due to its diverse pharmacological and biological activities. Various parts of *B. diffusa* are used in different parts of India to cure a variety of ailments. The whole plant, aerial parts, leaves, or root of *B. diffusa* are used in Ayurvedic herbal med-

icine for treating a range of medical conditions. Various pharmacological studies have shown that the plant roots of *B. diffusa* possess a broad spectrum of properties, including anti-inflammatory, diuretic, anticonvulsant, antifibrinolytic, antibacterial, anthelmintic, antileprotic, antiasthmatic and antistress activities (Figure 1). Table 3 compiles the available information on *Boerhavia diffusa* species from recent data published in the last 5-6 years [22-26].

Table 3: Various pharmacological activities and parts used of *Boerhavia diffusa*.

Pharmacological Activity	Parts use	Results/Outcomes	References
Antioxidant	leaves	<i>B. erecta</i> demonstrated enzymatic antioxidant capabilities, including activities like superoxide dismutase (SOD), catalase (CAT), and peroxidase (POD).	[22]
Anticancer	Aerial part	The rotenoids isolated from the ethyl acetate extract demonstrated notable cytotoxic effects on HeLa (human epithelial carcinoma) and MCF-7 (human breast cancer) cell lines.	[23]
Anti-inflammatory	Whole plant	Throughout all stages of edema development, the entire plant exhibited an anti-edematous effect, indicating a potential reduction in both the early and delayed phases of inflammation induced by carrageenan, possibly through the release of histamine or nitric oxide.	[24]
Hepatoprotective	Roots	The roots extract of <i>B. erecta</i> demonstrated the ability to replenish serum bilirubin, total protein, albumin, and serum enzymes in male Wistar rats with CCl ₄ -induced hepatotoxicity. Notably, the efficacy of the roots extract surpassed that of <i>B. rependa</i> .	[25]
Cytotoxicity	Leaves	The cytotoxicity exhibited by the leaves against MCF-7 was significantly lower than that of the standard drug Doxorubicin.	[26]

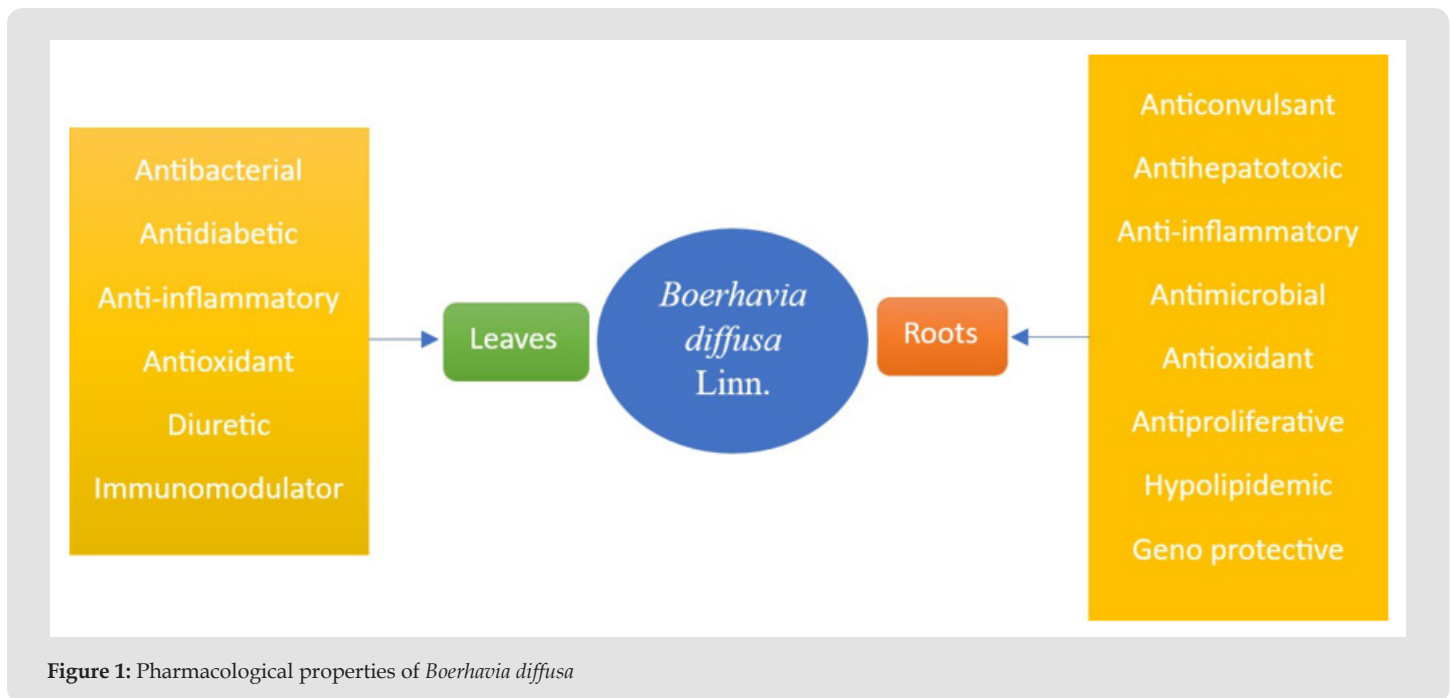


Figure 1: Pharmacological properties of *Boerhavia diffusa*

Antioxidant Activity

Due to its high content of tannins, phenols, and flavonoids, *B. diffusa* has been the subject of numerous studies examining its antioxidant potential [27-29]. The ethanolic extract of *B. diffusa* demonstrated the ability to scavenge 1,1-diphenyl-2-picrylhydrazyl (DPPH) radicals [28]. A fractionation guided by electron spin resonance of the

methanolic extract led to the identification of *boeravinone D*, *boeravinone G*, and *boeravinone H*, all exhibiting significant radical-scavenging activity, with *boeravinone G* displaying superior antioxidant properties when compared to the other two compounds [30]. This investigation also revealed the involvement of MAP kinase and NF-κB pathways in the antioxidant effects of *boeravinone G*, suggesting its

potential utility in injuries mediated by reactive oxygen species (ROS) [30]. In the realm of African traditional medicine, the preference for the redder stems of *B. erecta* prompted a study on the antioxidant potential of the redder stem bark, establishing that betacyanin's possess greater antioxidant activity than the phenolic compounds present in the stem [31]. Similarly, the antioxidant potential of *B. procumbens* was attributed to its concentration of polyphenols, as demonstrated by various antioxidant assays [32]. Furthermore, *B. diffusa* was identified as having the capability to protect tissues from hydroxyl radical-induced DNA damage [33].

Antidiabetic Activity

B. diffusa and ethanolic extracts demonstrate notable antihyperglycemic effects in rats with alloxan-induced and streptozotocin-induced hyperglycaemia. Additionally, they show potential for improving diabetes-related conditions, as evidenced by changes in parameters such as body weight, serum cholesterol, and triglyceride levels. In recent research, the impact of streptozotocin treatment on the pancreas of diabetic control rats, along with cell regeneration facilitated by glibenclamide, was examined. Additionally, comparable regenerative effects were demonstrated through the methanolic extracts of *B. diffusa* [34]. An investigation was carried out on the effects of a daily oral administration of an aqueous solution containing *B. diffusa* L. leaf extract on the levels of hepatic enzymes and blood glucose in both normal and alloxan-induced diabetic rats over a period of four weeks. When *B. diffusa* L. was administered to both normal and diabetic rats, the results showed a notable decrease in blood glucose levels and a considerable increase in plasma insulin levels [35]. In rats with streptozotocin-induced noninsulin-dependent diabetic mellitus (NIDDM), the chloroform extracts from *B. diffusa* leaves demonstrated dose-dependent reductions in blood glucose levels. This effect was comparable to the impact of glibenclamide. These results imply that the extract's capacity to decrease blood glucose may be linked to the regeneration of pancreatic beta cells or actions extending beyond the pancreas [36].

Anticancer Activity

The *B. diffusa* root and leaf extract's *in vitro* cytotoxic effects show a dose-dependent response. Both the root and the leaf's crude ethanolic extract caused 30% and 40% of the cells to die, respectively [37]. An investigation was conducted into the effect of a root extract in 95% ethanol on the growth of human peripheral blood mononuclear cells (PBMC) activated by T cell mitogen PHA and PPD antigen. The extract showed that it inhibited the proliferation of PBMCs in a human mixed lymphocyte culture as well as that induced by these stimulators. Moreover, the extract demonstrated inhibitory actions on multiple cell lines, emphasising its efficacy in experimental settings against lymphoma and leukemic cells [38]. The 95% ethanolic extract of *B. diffusa* root was subjected to bioassay-guided fractionation, resulting in a 30% observed cell death in the HeLa cell line. Subsequent purification through column chromatography led to the isolation of a more potent fraction. [39]. In *in vivo* experiments, the extract demonstrated

inhibitions of 87% and 95% against metastasis both prophylactically and overall. Additionally, the survival rate of the experimental model increased by 157%. When the extract was given as a preventative intervention, serum markers linked to metastasis were reduced by 85% [40]. Furthermore, Punarnava was isolated by the author from the extract, exhibiting its capacity to trigger cytotoxicity mediated by complement and antibodies, in addition to augmenting the function of natural killer cells [41]. Numerous investigations, both *in vitro* and *in vivo*, show that a variety of plant extracts sourced from distinct plant sections may include chemicals with anticancer potential. Punarnava, an alkaloid isolated from the roots was identified and reported to possess antimetastatic properties [42].

Anti-Inflammatory Activity

The alcoholic extract of *B. diffusa*, which is insoluble in water, demonstrates anti-inflammatory effects in rats. Leaf and floral extracts have significant anti-inflammatory properties [43]. BD leaf extracts were tested for toxicity and for their analgesic-anti-inflammatory qualities in both juice and lyophilized decoction form. The lyophilized decoction and juice both showed about 50% reduction in abdominal writhing in mice when compared to dipyron sodium. When compared to morphine, the juice treatment increased the mice's latency in the hot plate test. Another noteworthy finding was the reversal of the juice's effects following pretreatment with naloxone, except in the case of the decoction. As a result, the author suggested that the antinociceptive mechanism of the juice may be related to opioids [44]. found that BD roots contained β -sitosterol, which significantly induced swelling in mice [45]. It is commonly known that BD has anti-inflammatory qualities and is also called sothaghni, a term that denotes its ability to reduce inflammation. Most of the ayurvedic formulations mentioned in Table 1 serve purposes related to inflammation. Numerous accounts highlight the utilization of leaves, whether in their whole form, incorporated into an oral preparation, or applied topically, particularly in instances of scorpion and snake bites or for wound healing.

Antiviral Activity

Promising protective activities against potato virus X infection in both hypersensitive and systemic hosts have been observed for compounds isolated from *B. diffusa* L. root, *Cuscuta reflexa* Roxb. stem, and *Euphorbia hirta* L. leaves. It was found that these extracts had a systemic inhibitory effect that was actinomycin D-responsive [46]. Notable control results were obtained with the mungbean yellow mosaic illness caused by the mungbean yellow mosaic virus, which was efficiently handled by the aqueous root extract of *B. diffusa*. Six application sprays of *B. diffusa* root extract proved to be particularly efficacious, significantly delaying the onset of symptoms, mitigating symptom intensity, and reducing disease occurrence by 80-90%. In addition, enhancements in pod formation and grain output were encouraged by this treatment, along with increases in plant height, root nodulation, and primary and secondary branches [47].

Hepatoprotective Activity

Chloroform and ethyl acetate extracts were made using *Bacillus cereus*, an endophyte that is present in *B. diffusa* roots. These extracts' hepatoprotective effects were studied in rats, with an emphasis on assessing how well they scavenged free radicals. The extract of ethyl acetate demonstrated a significant IC50 value, prompting its selection for subsequent *in vivo* studies [48]. The administration of endophytic bacteria extracts resulted in a normalization of the heightened levels of the aforementioned biochemicals. The findings consistently indicate that extracts derived from the endophytic bacteria of *B. diffusa* demonstrate antioxidant and hepatoprotective properties, ultimately leading to the conclusion. Tuberculosis presents a significant health challenge, and the primary treatment involves rifampicin therapy. While rifampicin effectively addresses tuberculosis, it is associated with liver damage. Methanolic extracts from *B. diffusa* leaves were investigated in the search for a natural cure. Rats were given rifampicin to induce hepatotoxicity, which resulted in a significant rise in aspartate aminotransferase, alkaline phosphatase, and alanine aminotransferase levels. In comparison to the control group, there was a concurrent decrease in serum protein levels. Studies offer proof that extracts from *B. diffusa* possess the ability to alleviate liver issues, attributed to the presence of flavonoids in the plant, known for their antihepatotoxic properties [49].

Anti-Arthritic Activity

Numerous research use arthritic rats to test the antiarthritic effects of extracts made from *B. diffusa* roots, including petroleum ether, methanol, chloroform, and water extracts. Arthritis impacted hematological factors by elevating total white blood cell counts, raising erythrocyte sedimentation rates, and diminishing red blood cell count and hemoglobin levels. Rats given extracts from *B. diffusa* had smaller paws and heavier bodies as a result. The recovery of red blood cells and haemoglobin, as well as the normalisation of the total white blood cell count and erythrocyte sedimentation rate, were among the several haematological indicators that were brought back to baseline [50].

Antibacterial Activity

With regard to the possible presence of phytochemicals, *B. diffusa* leaves have strong antibacterial qualities against both gram-positive and gram-negative bacteria. All gram-negative bacteria as well as gram-positive bacteria like *S. aureus*, *S. faecalis*, and *M. luteus* are inhibited by the ethanol extract. All gram-positive bacteria are inhibited by the methanol extract, with the exception of *M. luteus* and gram-negative bacteria. *B. diffusa* leaf extracts work well against *E. Coli*, *S. aureus*, and *P. aeruginosa* in both aqueous and ethanolic forms at various concentrations, indicating the presence of active compounds with broad antibacterial capabilities. Overall, extracts from *B. diffusa* demonstrate significant antibacterial effects against a range of bacteria [51,52].

Anticonvulsant Activity

In the context of Nigerian traditional medicine, *B. diffusa* has a historical connection to the treatment of epilepsy. As a result, studies have been undertaken to investigate its effectiveness in managing convulsions. The crude methanolic extract of *B. diffusa*, specifically its liriodendron-rich component, demonstrated a dose-dependent protective effect against PTZ- induced convulsions. The observed ability to prevent convulsions was attributed to the calcium channel antagonistic properties of the liriodendron-rich fraction [53].

Adaptogenic/Immunomodulatory Activity

The study assessed the antistress and adaptogenic effects of ethanol extracts from *B. diffusa* roots in albino mice using swim endurance and cold restraint stress tests. The extracts demonstrated enhanced stress tolerance and immunomodulatory activity, as demonstrated by enhanced carbon clearance, which suggests reticuloendothelial system activation. Furthermore, mice's reaction to sheep red blood cells (SRBC) was elevated in terms of delayed-type hypersensitivity (DTH), indicating a stimulatory effect on lymphocytes and accessory cell types involved in cell-mediated immunity [54].

Toxicological Studies

Nausea has been linked to the ingestion of higher doses of Punarava, according to research. The primary emphasis of the pharmaceutical industry is directed toward creating and advancing innovative and indigenous plant-based drugs by exploring leads from traditional medicinal systems. Toxicological studies on *B. diffusa* have verified the lack of teratogenic and mutagenic effects, with the consumption of larger doses being associated with vomiting [54].

Conclusion

In recent years, the pharmaceutical industry has significantly directed its efforts toward designing and developing novel plant-based drugs through the exploration of leads from traditional medicine systems. The ethno-botanical and traditional applications of natural compounds, particularly those of plant origin, have garnered considerable attention due to their proven efficacy and perceived safety for human consumption. The review above suggests that the utilization of *B. diffusa* is deeply rooted in tradition and has been prevalent worldwide across various clinical and pathological conditions. While the scientific basis for many of its pharmacological properties has been established, ongoing research is still underway. Consequently, further comprehensive studies are encouraged to explore the potential of this plant.

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