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Review Article

THERAPEUTIC AND PHARMACOLOGICAL EFFICACY OF PLANT *BOERHAAVIA DIFFUSA*–A REVIEW

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ABSTRACT

Boerhavia diffusa (BD) is a herb of rasayana type, according to ayurvedic statements. It is considered to offer anti-aging, anti-disease, and life-strengthening qualities. Diffusa Boerhaavia Linn. Contains a wide variety of therapeutic qualities that have been demonstrated to be beneficial in the treatment of hyperglycemia, inflammation, anxiety, hepatotoxicity, jaundice, and heart problems. Here, we focus on the chemical composition and ethnomedicinal uses of B. diffusa that extend back to ancient times, as well as their future development.

B. diffusa's exceptional antioxidant, hepatoprotective, antibacterial, anti-diabetic, and anticarcinogenic capabilities have drawn pioneers in science and medicine. Additionally, this herb possesses medicinal properties, which is a result of the presence of polyphenols and flavanoids, creates it more vital for clinicians and scientists to exploit in order to obtain a better understanding of its biological and pharmacological capabilities.

Keywords: Medicinal plant, *Boerhaavia diffusa,* Therapeutic effects

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INTRODUCTION

An herb called *Boerhavia diffusa Linn. (Nyctaginaceae)* is the most often utilised in traditional Indian medicine, as well as in other countries of the world, such as South America and Africa. Its different parts, particularly the roots, were utilised for gastrointestinal, hepatoprotective, and gynecological purposes in the aforementioned countries of the globe, as well as in India. It is a prominent element in around 35 formulations of various types found in ayurvedic scriptures.

In Ayurveda, the herb B. diffusa is referred as as a "rasayana" herb, which is characterized by its ability to protect the liver and modulate the immune system, so enhancing the body's ability to withstand any adversity, in other words, hepatoprotective effect and immunomodulation [1].

The chemical components and medicinal properties of B. diffusa were widely investigated. Rotenoids, flavonoids, flavonoid glycosides, xanthones, purine nucleosides, lignans, ecdysteroids, and steroids are all isoflavonoids found in the roots. Numerous invivo studies and clinical trials have proven that the compound possesses immunomodulatory, hepatoprotective, antifibrinolytic, anticancer, antidiabetic, anti-inflammatory, and diuretic activities. The traditional applications, chemical ingredients, and documented pharmacological effects of this plant have been reviewed in this article to demonstrate its chemical and medicinal potential. Additionally, this paper presents an ethnopharmacological assessment of a significant therapeutic herb.

The genus *Boerhavia* contains forty tropical and subtropical species. During rainy seasons, it grows as a weed in the Indian, Northern, and Southern American continents, as well as in South-Eastern Africa. Boerhavia was given its name in honour of Hermann Boerhaave, a well-known 18th-century Dutch physician, while the species was called for its characteristic scattered branching.

Boerhavia diffusa seems to have a long tradition of use in the treatment of a number of diseases, including wounds, inflammations, and hypertension [2]. Decoction of roots for the removal of kidney stones [3] The roots have traditionally been used to treat dyspepsia, jaundice, spleen enlargement, and stomach pain [4]. Boerhavia diffusa roots are used as diuretics, laxatives, and stomachics, while the leaves have been used as an appetiser [5]. Boerhavia diffusa Linn. Stimulates the liver and alleviates viral jaundice. This herb possesses diuretic, anti-inflammatory, and anti-arthritic qualities, and it also has spasmodic and antimicrobial characteristics. As a painkiller, laxative, diuretic, and abortifacient in the treatment of conjunctivitis, the roots of the plant have long been employed [6]. It is supposed to aid in the improvement and protection of vision. The plant is diuretic in nature and is utilised by diabetics to help them control their blood glucose levels. The root has been used as a diuretic in the treatment of jaundice, an enlarged spleen, gonorrhoea, as well as other inner inflammations. Aside from being an expectorant, it is also used as an expectorant, anthelmintic, cardiotonic, hepatoprotective, and anthelmintic. A paste of the roots is applied directly to the skin to treat abscesses and ulcers. [7]. Fig. 1 shows the *Boerhavia diffusa*

Fig. 1: *Boerhavia diffusa*

Chemistry

According to Miralles and Ujowundu, B. diffusa is an excellent source of dietary nutrients. There are 15 amino acids in the total plant (six of which are essential), 14 in the roots (seven of which are essential), and isopalmitate acetate, behenic acid, arachidic acid (6.3 percent) and saturated fatty acids, according to Miralles *et al.* research. 's (38 percent). Ujowundu *et al.* [8] determined the presence of vitamins C, B3, and B2 (44.80, 97.00, and 22.00 mg, respectively) in roots, as well

as calcium (174.09 mg). B. diffusa roots and the entire plant have been recorded to be utilised as a culinary component in a variety of tribal locations. Based on the aforementioned investigations, its application can be considered validated.

Pharmacological activities

B. diffusa has different pharamacological action. Fig. 2 explain the different pharmacological action of *B. diffusa*

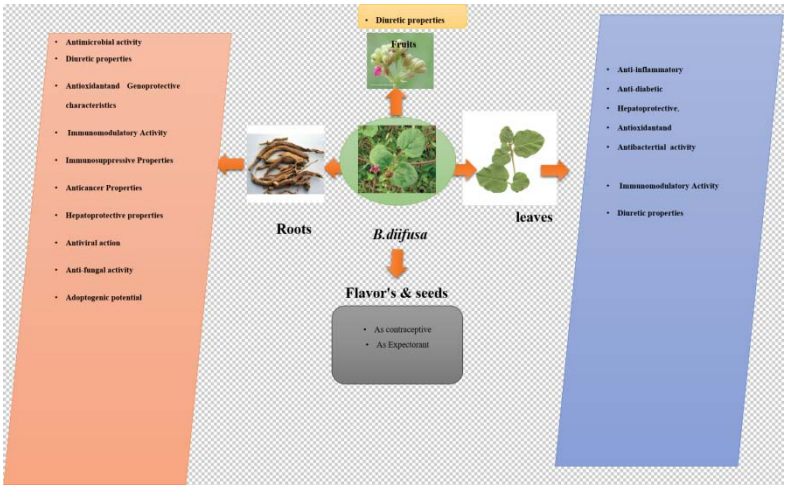

Fig. 2: *B. diffusa* pharmacological activities

Antimicrobial action

Roots of Boerhavia diffusa L. were tested for their antibacterial action against a variety of pathogens. The observed inhibitory zones ranged in size from 4.26 0.12 mm to 16.61-0.24 mm. Every single bacterium examined was inhibited by the roots extract with wide inhibition zones. An inhibitory zone of 10.40 0.26-24.80 0.37 mm was seen at a 30g/ml concentration for chloramphenicol and miconazole nitrate, two commonly used antibiotics [9].

Crude extracts of B. diffusa showed enhanced antibacterial action for the tested pathogen at higher doses, as per an antibacterial study. Extracts of B. diffusa demonstrated strong antifungal property that might be attributed due to anthraquinones' presence [10]. Gram-negative and Gram-positive bacteria were more effectively treated by ethanol extracts of B. diffusa leaves, except for V. cholerae (e. g. E. coli, zone of diameter 9 mm). The results established that B. diffusa L. extract of leaves possessed antimicrobial possess antimicrobial action against a variety of human pathogenic pathogens [11].

Diuretic properties

A water extract of B. diffusa's roots was tested for diuretic impacts on albino rats and the findings were compared to the standard diuretic furosemide. Boerhavia diffusa extract exhibits a "diuretic dose-response relationship" that reportedly reaches its peak at 300 mg/kg (oral). In addition, the sample drug showed an optimal rise in urine volume and excretion of electrolytes [12]. When Boerhavia diffusa Linn. Stimulated diuresis and accelerated crystallization dissolution, it boosted the clearance of nitrogenous waste products and reduced oxalate excretion, most likely by affecting metabolism. Antiurolithiatic action of Boerhavia diffusa Linn is enhanced by each one of these effects [13].

Antioxidant and genoprotective characteristics

Several disorders, including diabetes, cancer, and cardiovascular disease, can be attributed to the excessive production of free radicals known as oxidative stress. Numerous antioxidants or phytochemicals found in plants have been shown to mitigate the diverse effects of oxidative stress [14]. Boeravinone G, a rotenoid found in B. diffusa was demonstrated to be a potent antioxidant and genoprotectant [15]. Rotenoids have anti-oxidant and anti-aging qualities that help prevent diseases caused by free radicals, cancer, and ageing. There are numerous pathological conditions that could benefit from boeravinone G's remarkable antioxidant properties, including those induced by reactive oxygen species (ROS).

Immunomodulatory action

Using an E. coli-induced abdominal sepsis stress paradigm, Mungantiwar and colleagues studied the immunomodulatory effects of B. diffusa (water-extract, 50–200 mg/Kg/day orally) and found a 50% reduction in mortality in treated mice. Reversal of stress-induced changes to SGPT and BUN as well as sugar and lipid levels was also observed in rats treated with the extract [16]. Reversing immune system dysfunction and regulating plasma cortisol levels in rats were achieved by using the alkaloidal portion. B. diffusa and ashwagandha both increased floating time in mice fed an alcohol extract of both, according to Sumanth and his colleagues. Total WBC count, sugar levels, and corticosterone level were all significantly lowered by the extract. It had phagocytic activity similar to that of the drug levamisole in macrophages [17]. It was found that oral treatment of the alkaloidal portion (25–100 mg/kg p. o.) by Mungantiwar and colleagues significantly reduced early and late hypersensitive symptoms in rats. When an alkaloid is metabolised into its active form, the author claims, it stimulated the immune system [18].

Although *B. diffusa* has been suggested to have adaptogenic properties, the term "adaptogen" encompasses a wide variety of actions. The word refers to an overall improvement in an organism's tolerance to any sort of stress, whether physical, chemical, or biological. This phrase is roughly tied to Ayurveda's rasayana notion. Immunomodulation is a significant rasayana herb action. Mungantiwar and Sumantha investigated immunomodulatory activity, but the effect was attributed to a crude or semipurified alkaloidal extract. Two more compounds, besides quercetin, have only been found in the roots of the plant that is the authoritative version of the drug "punarnava."

Immunosuppressive properties

Mehrotra and colleagues investigated the immunomodulatory effects of an ethanolic extract of B. diffusa roots at concentrations of 100 and 500 g/ml on NK cell cytotoxic effects, LPS-induced NO generation, and messenger RNA measurement. Cellular cytotoxicity was prevented by the extract (MIC 10g/ml), which also reduced NO generation in mouse macrophage cells and IL-2 and TNF-production by PBMCs (MIC 10 ng/ml), *in vitro*. The author speculated that the beneficial immunosuppressive qualities could be due to the alkaloid/lignan [19]. Furthermore, Pandey and colleagues investigated hexane, chloroform, and ethanol extracts of B. diffusa leaves and discovered that chloroform and ethanol extracts (5–

500g/ml) suppressed PHA-induced PBMC proliferation, two-way MLR, NK cell cytotoxicity, and LPS-stimulated NO generation by RAW 264 [20].

Both of the above data imply that B. diffusa suppresses the immune system; however, the two reports are from distinct plant sections. Two immunostimulants have been isolated from the roots: syringaresinol mono-D glucoside (eleutheroside E1 and acanthoside B) and punarnavine. Additionally, Pandey and colleagues discovered eupalitin-3-O—D-galactopyranoside and attributed it with immunosuppressive activity. Additionally, this chemical has been shown to exhibit antiosteoporotic action [21]. Osteoporosis is a condition associated with inflammation and age, and it has been discovered that it also has an immunological component. Apart from their role in immune response, cytokines are required for the formation and activation of osteoclasts. B. diffusa has quite a long tradition of usage in conventional and ethnopharmacological medication used in the therapy of rheumatism, a wide term that refers to a multitude of medical diseases impacting the bones and connective tissues. The occurrence of antiosteoporotic, immunosuppressive, and anti-inflammatory compounds substantiates B. diffusa's use in rheumatic diseases, for which it could be utilised since prehistoric times.

Anticancer properties

In vitro, Srivastava and colleagues found that B. diffusa root and leaf extracts had a dose-dependent cytotoxic effect on HeLa and U-87 cancer cell lines. The root and leaf crude ethanolic extracts (200g/ml and 300g/ml, respectively) showed 30% and 40% cell death; however, the alkaloidal fraction (300g/ml, plus methotrexate (200 nM) revealed 40% cell death [22].

Human PBMC were stimulated with the T cell mitogens PHA, Con-A, and PPD antigens and then treated with a 95 percent ethanolic root extract, as part of a study by Mehrotra and colleagues. It reduced proliferation of PBMCs generated by all of the aforementioned stimulators and human mixed lymphocyte culture. The extract inhibited a variety of cell lines (mouse and human), with particular emphasis on lymphoma and leukemic cells [23].

Ahmed-Belkacem and colleagues extracted two rotenoids (boeravinones G and H) from roots as well as identified those as promising tumour resistance protein efflux inhibitors (ABCG2). Additionally, the authors postulated a link between the structure and function of drugs that inhibit BCRP [24].

An ethanolic extract of root was fractionated by Chopra's team, and they found 30% cell death in HeLa cells (300g/ml) after bioassay supervision. At a dosage of 300g/ml, a more powerful fraction was obtained after purification through column chromatography, killing 85 percent and 55 percent of cells in 72 and 24 h, respectively [25].

Experimenting with 320g/ml methanol extraction of the whole plant, Sreeja and colleagues found a 46% reduction of cell viability after 48 h at 320g/ml in the MCF-7 cell line [26]. Additionally, the extract reduced the proliferation of cells stimulated by oestrogen. MCF-7 cells treated with extracts at various concentrations (20–320g/ml) demonstrated G0-G1 arrest, with the population of cells in the G0-G1 phase increasing from 69.1 to 75.8 percent.

The effect of an aqueous methanol (3: 7) extract of the whole plant on C57BL/6 mice bearing a B16F10 melanoma model was studied by Leyon and colleagues. At 0.5 mg/dose, the extract inhibited metastasis by 87% and 95%, respectively. Additionally, the chance of survival of mice was boosted to 157 percent. The extract was administered prophylactically and resulted in an 85 percent decrease in serum indicators associated with metastasis [27]. It also contained punarnavine, which showed antibody-dependent cytotoxicity and complement activation, in addition to a rise in the activity of natural killer cells. Punarnavine boosted IL-2 and IFN-production [28]. Punarnavine treatment dramatically decreased the levels of GM-CSF and proinflammatory cytokines such as IL-1, IL-6, and TNF-. Punarnavine (40 mg/kg) can also be used to prevent and treat lung metastases by up to 95.25–93.9 percent, according to the author for ten days following tumour inoculation [28].

An extract of the entire herb (20 mg/kg, i. p.) was found to protect mice bone marrow and the intestines from the effects of a 70 percent aqueous methanolic extract (600 rads administered sublethally in a single dosage). Comparing the experimental group to the control group saw a 46.66 percent decrease in the total WBC count following exposure to radiation on day 9. There was a 46% drop in bone marrow cellular proliferation in the presence of BD extract, as compared to a 68% reduction in cell viability in the absence of BD extract, demonstrating radiation's impact on bone marrow cellularity. A fascinating discovery was that on the eleventh day, the number of bone marrow cellular proliferation increased by 9.2 percent over the starting number. Extraction treatment restored normal LAP, GPT, and lipid peroxidation levels in the serum and liver after radiation exposure [29].

Abdominal tumours are a vital determinant of BD in folk medicine. Numerous reports (*in vitro* and *in vivo*) reveal that a variety of extracts derived from several plant components contain anticancer and discovered that it possesses antimetastatic activity [30]. Another study discovered that boeravinones G and H may prevent medication efflux caused by breast tumor resistance protein (ABCG2) [24].

Radiotherapy is crucial in cancer treatment, despite the considerable negative impacts of myelosuppression or immunosuppression, which can also lead to higher infectivity throughout anticancer therapy. Numerous strategies exist for preserving a cancer patient's immune system in order to improve his or her overall state. Herbal preparations containing immunomodulators produced from plants may be a viable option in this area. In cancer therapy, B. diffusa provides a multitarget regimen. It possesses antitumor, immunomodulatory, and radioprotective properties. Thus, it may be established that it is a valuable supplement in cancer treatment.

Hypoglycemic and anti-diabetic effect

Chude and colleagues demonstrated that an aqueous extract of B. diffusa leaf decreased blood sugar levels in alloxan-treated diabetic animals in a drug concentration manner. After administering 200 mg/kg extract, they found a 51.95% decrease in blood sugar levels [31]. Satheesh and colleagues analysed the aqueous leaf extract of the leaves (200 mg/kg) to glibenclamide (600 mg/kg) in treated rat's diabetic animals in another study. The extract raises plasma insulin concentration from 4.92U/ml to 10.4U/ml, whereas glibenclamide achieves a peak insulin concentration of 9.74U/ml. In 120 min, the extract entirely replenishes the early glucose level, but glibenclamide causes a nearly 10% increase in glucose [32].

Using a chloroform extract of B. diffusa leaves, we found that in diabetic rats, it caused dose-dependent hypoglycemia. Both B. diffusa leaf extract and libenclamide (25g/kg) decreased glucose levels by 59.01 and 38.63 percent, separately, in the 4th week of treatment. Excessive activity may be a result of cell renewal or some other extrapancreatic function, according to the author [33].

Gulati and coworkers accounted for the ethanolic extract's (1.72g/ml)-glucosidase inhibitory action ex vivo [34]. The author discovered no conventional or ethno-botanical accounts of B. diffusa's antidiabetic action or formulations incorporating B. diffusa as an ingredient; nonetheless, the aforementioned research clearly suggest B. diffusa's antihyperglycemic potential. In the therapy of diabetes, only one patented product from the Unani-Tibb system (Glucostop) was noted.

Anti-inflammatory activity

An anti-inflammatory effect of BD's water-soluble alcohol extract was studied in rats by Mudgal. In rats, the anti-inflammatory effect of the leaf and flower extracts was only 55.78% effective in lowering the edoema. Both the juice and lyophilized decoction of the leaves (both 1000 mg/kg; p. o.) were more effective than dipyrone sodium (200 mg/kg) in reducing abdominal writhing in mice. Additionally, the juice increased the delay in mice when compared to morphine in the hot plate test. Also of note, naloxone (at a dose of 5 mg/kg, i. p.) pretreatment abolished the juice's action excluding the decoction. As a result, the author proposed an antinociception mechanism

involving opioids. Asadulla found rats with a 61.29 percent edoema after extracting sitosterol from BD roots [35].

Inflammation is a significant application of B. diffusa. Additionally, this plant is referred to as sothaghni, which means "one who alleviates inflammation. Many studies have shown that the leaves, either whole or in a powdered form, have been used to treat scorpion and snake bites and to promote wound healing.

Hepatoprotective properties

B. diffusa has a long history of usage as a hepatoprotective medication. Several preparations of this plant's aerial portion and roots shown hepatoprotective activity against CCl4 country liquor, thioacetamide, and acetaminophen-induced hepatotoxicity in rats and obtained significant results [36]. Chakraborti and Handa37 demonstrated hepatoprotective efficacy in *in vitro* models of CCl4 intoxication [37].

Antiviral action against viruses that infect plants

Extracts from B. diffusa L. roots had demonstrated a prospective preventive role against potato virus X infection in oversensitive and systemic animals. The inhibition elicited by the extract was systemic and actinomycin D-sensitive. B. diffusa aqueous root extract reduced the mungbean yellow mosaic disease (Vigna radiata), which is caused by the mungbean yellow mosaic virus. Six sprays of B. diffusa root extract were shown to be the most beneficial, significantly delaying symptom onset, reducing symptom severity, and reducing disease incidence by 80–90%. Aside from that, the treatment increased root nodulation, plant height, primary and secondary branch growth, pod formation, and yield of grains [38]. Purified B. diffusa glycoproteins (70–80% protein, 8%–13% carbohydrates, 16–20 kDa) showed significant antibacterial activity against RNA bacteriophages. One of the most important sources of this protein is the root of the B. diffusa plant, which is used to develop systemic resistance in a wide range of crops that are particularly susceptible to virus infection.

Anti-fungal activity

Antifungal activity was determined for several extracts of aerial and root portions of B. diffusa against the dermatophytic fungus Microsporum gypseum, Microsporum fulvum, and Microsporum canis [39]. Extracts of aerial organs lacked detectable antifungal action. The extract of the plant's roots in ethyl acetate was shown to be the most efficient against the target fungus species. M. gypseum (78.83 percent inhibition of mycelial growth), M. fulvum (62.33 percent inhibition of mycelial growth), and M. canis (42.30 percent inhibition of mycelial growth) were observed after 24 h of incubation with ethyl acetate at a test concentration of 1000 g/ml [40].

Adoptogenic potential

Adrenal hyper stress and hypofatigue appear to benefit from the use of adaptogens. To be an adaptogen, a substance must be able to work in both directions at once. A study by Mungantiwar *et al.* [41] examined the adaptogenic potential of B. diffusa root powder by assessing its effects on Escherichia coli-induced abdominal necrosis, macrophage phagocytosis, and cold and forced swimming anxiety in rats. Taking 200 mg/kg of plant extract daily for 15 d before an E. coli challenge in mice led to significant leucocytosis and a decrease in macrophage phagocytic activity. The plant extract significantly decreased glucose, cholesterol, serum glutamate pyruvate transaminase, and triglycerides, all of which were previously raised due to stress. The plant's alkaloid component demonstrated restorative efficacy against variations in plasma and adrenal cortisol levels caused by stress. Additionally, when stressed rats were compared to control rats, it greatly increased antibody production [42].

Effect on the morphology of the sperm and testes

Adenubi *et al.* examine the impact of oral delivery of an aqueous extract of B. diffusa leaves (50, 100, and 150 mg/kg) on semen and testicular morphology in male Wistar rats over a 60-day period. Researchers measured the concentrations of testosterone in the blood, as well as measurements of the weights of the testes, epididymes, and seminal vesicles and histology of these structures as well as the spermatozoa found in the cauda epididymis of the groups. Between treatment and control rats, no significant difference in serum testosterone levels was observed. A significant reduction (P0.5) in rats given 100 and 150 mg/kg of the extract compared to the control. The testes of treated rats showed significant degradation of germinal epithelia with spermiostasis. This data indicates that the aqueous extract of B. diffusa had a detrimental effect on the rats' sperm and testicular morphology.

CONCLUSION

The herb B. diffusa is widely used in folk and ethnopharmacological medicinal systems around the world. It contains a variety of chemical substances that have been proven to have medicinal properties, including diuresis, anticancer, anti-inflammatory, hepatoprotective, and immunomodulatory properties. Even though the herbal market is mostly untapped, it has yet to gain traction there. B. diffusa could prove to be a viable and cost-effective commodity for hepatoprotection, diuresis, and immunomodulation in the current plant-based pharmaceutical market. These compounds may also indicate that new semisynthetic chemicals can be developed for new applications, given that the rotenoid compounds are structurally distinct.

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AUTHORS CONTRIBUTIONS

All the authors have contributed equally.

CONFLICT OF INTERESTS

Declared none

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