GSC Biological and Pharmaceutical Sciences
eISSN: 2581-3250 CODEN (USA): GBPSC2
Cross Ref DOI: 10.30574/gscbps
Journal homepage: https://gsconlinepress.com/journals/gscbps/

(REVIEW ARTICLE)

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Multi-functional therapeutic effect of *Boerhaavia diffusa*: A contemporary review

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GSC Biological and Pharmaceutical Sciences, 2022, 20(03), 299–306

Publication history: Received on 15 July 2022; revised on 13 September 2022; accepted on 15 September 2022

Article DOI: https://doi.org/10.30574/gscbps.2022.20.3.0299

Abstract

Today's world is full of different diseases due to our hasty schedule and to cure diseases huge numbers of medicines are consumed every day to control/cure those diseases. Thus, willingly or unwillingly we are forced to store great amount of chemicals which are toxic/harmful in our body. Thus, these stored chemicals create another disease in our body and to cure it another medicine is needed which adds up more toxic chemicals which were already stored. Hence, the uses of natural /herbal medicines are increasing day by day due to their bio-degradable nature. In this context a number of bio-products are in use in India, but the use of *Boerhaavia diffusa* was not so common in previous decades. Later on numbers of researches had been conducted to examine its therapeutic efficacy as a natural medicine. The chemical present in the plant which makes it as exceptionally useful plant is now been traced out. Now it is regarded as anti-inflammatory, anti-oxidant, anti-aging, anti-cancerous, anti-apoptotic, anti diabetic compound. In this review, we will try to discuss the multi-functional application of the plant and also we will try to summarize the futuristic research on this plant

Keywords: *Boerhaavia diffusa*; Function; Plant; Therapeutic effect

1. Introduction

It is been recorded in history that Medicinal herbs have been used as form of therapy for the relief of pain. The exploration of the chemical constituents from plants, pharmacological and phytochemical screening would provide the basis for developing the new lead molecules in strategic favour of natural product drug discovery. The aim and subject of many researchers is the discovery and development of isolating a new efficient, active and less toxic molecule for systemic activities. The biologically active agents from natural sources have always been of great interest to working on various diseases [1]. Tribal communities are using their traditional knowledge system to cure different diseases. They use plant as a source of drug through trial and error method and the process is experienced over hundreds of years, which says that the medicinal plants have been in the focus as lifesaving drugs right from the beginning of the human civilization. The medicinal plants have been the object of research in both systematic and advanced areas of plant sciences [2]. The traditional knowledge of these herbal recipes is popular among the indigenous and local communities. Even today the tribal communities are solely dependent on plants for their medication; hence they are using them against different. They have preserved the wealth of traditional knowledge as a part of their belief and customs. They are practicing these methods generation after generation successfully [3]. Apart from medicinal uses phytochemical components which are environment friendly, economical and effectively shows anti-corrosive properties [4, 5] and also phyto-compounds are used as bio-fuels [6- 8].

Boerhaavia diffusa L. is a herbaceous member of the family Nyctaginaceae. It is widely distributed in the tropics and subtropics. It has a long history of uses by indigenous and tribal people and in Ayurvedic or natural herbal medicines *Boerhaavia diffusa* L. is a wild perennial herb which may be encountered in different terrestrial habitats, ranging from

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managed grass lands, waste lands, agro-eco systems to large forest gaps. The species of *Boerhaavia* ('Punarnava') have been in use for medicinal purpose in different parts of India. The whole plant and preferably the roots are effectively used to cure several diseases including Jaundice [9]. The root and aerial parts of *Boerhaavia diffusa* were used in Ayurveda for the treatment of diabetes. It has many ethno-botanical uses (the leaves are used as vegetable; the root juice is used to cure asthma, urinary disorders, leukorrhea, rheumatism, and encephalitis), and is medicinally used in the traditional, Ayurvedic system. Besides, the *B. diffusa* plant is reported to posses many pharmacological, clinical, and antimicrobial properties.

2. Taxonomic Position of *Boerhaavia diffusa*

- Phylum: Plantae
- Division: Magnoliophyta
- Class: Magnoliopsida
- Order: Caryophyllales
- Family: Nyctaginaceae
- Genus: *Boerhaavia*
- Species: *diffusa*

3. Distribution

The genus *Boerhaavia* has 40 species, and is distributed in the tropical, subtropical, and temperate regions of the world. It is found in Australia, China, Egypt, Pakistan, Sudan, Sri Lanka, South Africa, USA and in several countries of the Middle East. Out of the 40 species of this genus, 6 species are found in India – *B. diffusa, B.chinensis, B. erecta, B. repens, B. rependa*, and *B.rubicunda*. *Boerhaavia diffusa* is also indigenous to India .it is found throughout the warmer parts of the country up to an altitude of 2000 m in the Himalayan region. It grows well on wastelands and in fields after the rainy season. The plant is also cultivated to some extent in West-Bengal [10].

4. Description

4.1. Macroscopic characters of Punarnava

4.1.1. Stem

Greenish purple, stiff, slender, cylindrical, swollen at nodes, minutely pubescent or nearly glabrous, prostrate divaricately branched, branches from common stalk, often more than a meter long.

4.1.2. Root

Well developed, fairly long, somewhat tortuous, cylindrical, 0.2-1.5 cm in diameter, yellowish brown to brown coloured, surface soft to touch but rough due to minute longitudinal striations and root scars, fracture, short, no distinct odour, taste, slightly bitter, sweet, pungent .

4.1.3. Leaves

Opposite in unequal pairs, larger ones 25-37 mm long and smaller ones 12-18 mm long ovate-oblong or suborbicular, apex rounded or slightly pointed, base sub-cordate or rounded, green and glabrous above, whitish below, margin entire or sub-undulate, dorsal side pinkish in certain cases, thick in texture, petioles nearly as long as the blade, slender.

4.1.4. Flowers

Very small, pink coloured, nearly sessile or shortly stalked, 10-25 cm, in small umbells, arranged on slender long stalks, 4-10 corymb, axillary and in terminal panicles, bracteoles, small, acute, perianth tube constricted above the ovary, lower part greenish, ovoid, ribbed, upper part pink, funnel-shaped, 3 mm long, tube 5 lobed, stamen 2-3.

4.1.5. Fruit

One seeded nut, 6 mm long clavate, rounded, broadly and bluntly 5 ribbed, viscidly glandular.

4.2. Microscopic structures of punarnava

4.2.1. Stem

Transverse section of stem shows epidermal layer containing multi cellular, uniseriate glandular trichomes consisting of 9-12 stalked cells and an ellipsoidal head, 150-220 µm long, cortex consists of 1-2 layers of parenchyma, endodermis indistinct, pericycle 1-2 layered, thick-walled often containing scattered isolated fibres, stele consisting of many small vascular bundles often joined together in a ring and many big vascular bundles scattered in the ground tissue, intra fascicular cambium present [11].

4.2.2. Root

Transverse section of mature root shows a cork composed of thin-walled tangentially elongated cells with brown walls in the outer few layers, cork cambium of 1-2 layers of thin walled cells secondary cortex consists of 2-3 layers of parenchymatous cells followed by cortex composed of 5-12 layers of thin-walled, oval to polygonal cells, several concentric bands of xylem tissue alternating with wide zone of parenchymatous tissue present below cortical regions, number of bands vary according to thickness of root and composed of vessels, tracheids and fibres, vessels mostly found in groups of 2-8 in radial rows, having simple pits and reticulate thickening, tracheids, small, thick walled with simple pits, fibre saseptate, elongated, thick-walled, spindle shaped with pointed ends, phloem occurs as hemispherical or crescentic patches outside each group of xylem vessels and composed of sieve elements and parenchyma, broad zone of parenchymatous tissue, in between two successive rings of xylem elements composed of thin-walled more or less rectangular cells arranged in radial rows, central regions of root occupied by primary vascular bundles, numerous raphides of calcium oxalate, in single or in group present in cortical region and parenchymatous tissue in between xylem tissue, starch grains simple and compound having 2-4 components found in abundance in most of cells of cortex, xylem elements in parenchymatous tissue between xylem elements, simple starch grains mostly rounded in shape and measure 2.75-11 µm in diameter [11].

4.2.3. Leaves

Transverse section of leaf shows anomocytic stomata on both sides, numerous, a few short hairs, 3-4 celled, present on the margin and on veins, palisade one layered, spongy parenchyma 2-4 layered with small air spaces, idioblasts containing raphides, occasionally cluster crystal of calcium oxalate and orange-red resinous matter present in mesophyll. Palisade ratio 3.5-6.5, stomatal index 11-16, and vein islet number 9-15 [11].

5. Chemical Constituents

The *Boerha aviadiffusa* plant contains a large number of compounds such as flavonoids, alkaloids, steroids, triterpenoids, lipids, lignins, carbohydrates, proteins, and glycoproteins. Punarnavine ($C_{17}H_{22}N_2O$; m.p. 236ºC–237°C) 9- 11, boeravinone A-F, hypoxanthine, Larabinofuranoside, ursolic acid, punarnavoside, liirodendrin, and a glycoprotein having a molecularweight of 16– 20 kDa have been isolated and studied in detail for their biological activity. Punarnava also contains β-Sitosterol, α-2-sitosterol, palmitic acid, ester of β-sitosterol, tetracosanoic, hexacosonoic, stearic, arachidic acid, urosilic acid, Hentriacontane, β- Ecdysone, triacontanoletc. Generally whole plant consists the following phytochemical constitiutents, those are punarnavine (*Alkaloids)*, B-sitosterol (Phytosterols), Liriodendrin (lignans), Punarnavoside (Rotenoids), Boerhavine (Xanthones) and Potassium nitrate (Salts). The roots contain the rotenoidsboeravinones AI, BI, C2, D, E and F besides the new dihydroisofurenoxanthin, Alanine, Arachidic Acid, Aspartic Acid, Behenic Acid, Beta- Sitosterol, Boeravinone A - F, Boerhaavic Acid, Borhavine, Borhavone, Campesterol, Daucosterol, Beta-Ecdysone, Flavone,5-7-dihydroxy-3'-4'- dimetho, Xy-6-8-dimethyl, Galactose, Glutamic Acid, Glutamine, Glycerol, Glycine, Hentriacontane N, Heptadecyclic Acid, Histidine, Hypoxanthine-9-l-arabinofuranoside, Leucine, Liriodendrin, Methionine, Oleaic Acid, Oxalic Acid, Palmitic Acid, Proline, Proline, hydroxy, Serine, Sitosterol Oleate, Sitosterol Palmitate, Stearic Acid, Stigmasterol, Syringaresinol-mono-beta-d-glucoside, Threonine, Triacontan-1-OL, Tyrosine, Ursolic Acid, Valine, Xylose, triacontanolhentriacontane, ß-sitosterol, ursolic acid, 5,7-dihydroxy-3,4-dimethyoxy-6,8-dimethyl flavone, and an unidentified ketone (m.p. 86°C). The roots contain the rotenoid boeravinones AI, BI, C2, D, E and F besides the new dihydroisofurenoxanthin and an anti-fibrinolytic agent. Twolignans, liriodendrin and syringaresinol mono-ß-D-glucoside, have also been reported in the roots. Many rotenoids have been isolated from the roots of the *Boerhaavia diffusa*. Plant also includes a series of boeravinones *viz.*, boeravinone A, boeravinone B, boeravinone C, boeravinone D, boeravinone E and boeravinone F. Punarnavoside, a phenolic glycoside, is reportedly present in roots. C-methyl flavone also has been isolated from *Boerhaavia diffusa* roots. Two known lignans *viz*., liriodendrin and syringaresinol mono-β-D-glycoside have been isolated. Presence of a purine nucleoside hypoxanthine 9-L-arabinose, dihydroisofuroxanthone-borhavine, phytosterols have been isolated from the plant. It contains about 0.04 % of alkaloids known as punarnavine and punernavoside, an anti-fibrinolytic agent. It also contains about 6 % of

potassium nitrate, an oily substance and ursolic acid. The seeds of this plant contain fatty acids and allantoin and the roots contain alkaloids. The green stalk of the plant has also been reported to contain boerhavin and boerhavic acid. [12-21].

6. Pharmacological and Biological Activity

The plant has gained lot of importance in the field of phytochemistry because of its various pharmacological and biological activities such as immunomodulatory effects, immunosuppressive activity, anti-metastatic activity, anti-oxidant activity, anti-diabetic activity

anti-proliferative and anti-estrogenic activity, analgesic and anti-inflammatory activity, anti-bacterial activity, anti-stress and adoptogenic activity, anti-lymphoproliferative activity, nitric oxide scavenging activity, hepatoprotective activity, anti-viral activity, bronchial asthma, anti -fibrinolytic activity, chemopreventive action, genetic diversity analysis, anti-convulsant activity.

6.1. Anti-diabetic Activity

The study indicates that *Boerhaavia diffusa* and ethanolic extracts exhibit significant anti-hyperglycemic activities in alloxan induced as well as streptazotocin induced hyperglycemic rats. They can also improve the condition of diabetes as indicated by parameters like body weight along with serum cholesterol and triglyceride levels. The number of functionally intact _-cells in the islet organ is of decisive importance for the development course and outcome of diabetes. The renewal of β-cells in diabetes has been studied in several animal models. The total _-cell mass reflects the balance between the renewal and loss of these cells. It was also suggested that regeneration of islet β -cells following destruction by alloxan may be the primary cause of the recovery of alloxan-injected guinea pigs from the effects of the drug. In alloxan-induced diabetes, (-) Epicatechin and *Vinca rosea* extracts has also been shown to act by β-ells regeneration. regeneration of β-cells by glibenclamide was observed. The comparable regeneration was also shown by methanolic extracts of *Boerhavia diffusa* [22].

6.2. Anti-bacterial activity

A Potent antibacterial activity against gram positive and gram negative bacteria shown by the leaves of *B. diffusa* might be due to the phytochemicals present in the leaves. Ethanol extract showed inhibitory an effect on gram-positive bacteria like *S. aureus, B.subtilis, S. faecalis, M. luteus* and all gram-negative bacteria selected for the study. Methanol extract showed inhibitory effect against all gram-positive bacteria selected for that study except *M. luteus* and gram-negative bacteria like *K. pneumoniae, P. vulgaris, S. marcescens* and *S. flexneri* [23]. The antibacterial activity of the various extracts of the stem bark of *Prosopis cineraria* (Linn.) Druce, was evaluated by the agar well diffusion method [24].

6.3. Anti-stress Activity

Hydroethanolic extract (80%) *of Boerhaavia diffusa* (HEBD) and a polyherbal formulation (Punarnava mandur) PHF-09 containing *Boerhaavia diffusa* were compared for their anti-stress activity using cold restraint stress model. Stress was induced by subjecting animals to cold restraint. Due to cold restraint stress there was an imbalance in the levels of biochemical parameters like glucose, triglycerides, cholesterol, SGOT, SGPT which were near normalized following the administration of HEBD and PHF-09. HEBD and PHF-09 were found to have comparable anti-stress activity as reported in other study [25].

6.4. Adaptogenic / Immunomodulatory Activity:

The ethanol extracts of roots of *B. diffusa* was evaluated for antistress, adoptogenic activity in albino mice, by swim endurance test and cold restrains stress and the extract showed improved stress tolerance in immunomodulatory activity was shown by increased carbon clearance, indicating stimulation of the reticuloendothelial system. There was an increase in DTH response to SRBC in mice, corresponding to cell mediated immunity and indicating stimulatory effects on lymphocytes and accessory cell types [26].

6.5. Hepatoprotective Activity

The hepatoprotective activity of roots of different diameters were collected in three seasons, rainy, summer and winter, and examined in thioacetamide intoxicated rats. The results showed that an aqueous extract (2 ml/kg) of roots of diameter 1-3 cm, collected in the month of May (summer), exhibited marked protection of a majority of serum parameters, i.e., GOT, GPT, ACP and ALP, but not GLDH and bilirubin, thereby suggesting the proper size and time of collection of *B. diffusa* L. roots for the most desirable results. Further, the studies also proved that the aqueous form of

drug (2 ml/kg) administration has more hepatoprotective activity than the powder form; this is probably due to the better absorbtion of the liquid form through the intestinal tract. The hepatoprotective activity of *Boerhaavia diffusa* L. roots showed marked protection of serum parameters in thioacetamide toxicity in rats. Furthermore, the aqueous extract of thin roots collected in the summer has more activity suggesting the proper time and type of root collection for the most desirable result. The investigation also validates the use of *B. diffusa* L. roots in hepatic ailments by the several tribes in India [27].

6.6. Analgesic / Anti-Inflammatory Activity

The Decoction (DE) or Juice (JE) of the leaves of *Boerhaavia diffusa* were used to study the anti-nociceptive effect in chemical (acetic acid) and thermal (hot Plate) models of hyperalgesia in Mice. The DE, raised the pain thresholds during the first period (30 min) of observation. In the acetic acid-induced abdominal writhing in mic+e, pre-treatment of the animals with naloxone (5 g/kg, i.p.) significantly reversed the analgesic effect of morphine and JE but not that of DE. The study proves that the active antinociceptive principle of *B. diffusa* is present mainly in the juice of fresh leaves and has a significant antinociceptive effect when assessed in these pain models [28].

6.7. Antitumor Activity

Cancer chemo preventive property of *B. diffusa* was evaluated on 7,12-dimethyl benz(a)anthracene (DMBA) induced skin papillomagenesis in male Swiss albino mice (6-7 weeks old). The cancer chemopreventive efficacy was assessed by its ability to modulate the activities of enzymes associated with drug metabolism and bifunctional modulators reduced the availability of ultimate carcinogen metabolites in the epithelial stage. A significant increase in the activities of hepatic phase I, phase II system enzymes and antioxidant enzymes (glutathione peroxidase, glutathione reductase, superoxide dismutase, catalase and glutathione level) were observed when mice were fed by oral gavage with *Boerhaavia diffusa* extract at a dose level of 125 mg and 250 mg/kg body weight for a period of 14 day. This lead to an assumption that the inhibition of tumorigenesis by the plant extract might have been executed either by preventing the formation of active carcinogens from their precursors or by augmenting detoxification process, preventing promotional events in the mouse skin through free radical scavenging mechanism [29].

6.8. Anti-convulsant activity

Anticonvulsant activity of methanolic extract and its different fractions, that is, liriodendrin-rich fraction and phenolic compound fraction were studied in pentylenetetrazol (PTZ)- induced seizures. The crude methanolic extract of *B. diffusa* and only its liriodendrin-rich fraction showed a dose-dependent protection against PTZ-induced convulsions. The liriodendrinrich fraction showed significant protection against seizures induced by BAY k-8644. These findings reiterated the anticonvulsant activity of methanolic extract of *B. diffusa* roots and also it can be concluded that the observed anticonvulsant activity was due to its calcium channel antagonistic action as this activity was retained only in the liodendrin-rich fraction, which has additionally been confirmed by significant anti-convulsant activity of liriodendrin-rich fraction in BAY k-8644- induced seizures [30].

6.9. Anti-proliferative and Anti-estrogenic Activity

Anti-proliferative and anti-estrogenic properties of methanol extract of *Boerhaavia diffusa* (BME) in MCF-7 breast cancer cell lines. *Boerhaavia diffusa* extracts exhibited a strong inhibitory effect on the proliferation of human breast cancer cells in vitro and the antiestrogenic effects are mediated by ER. Phytochemical studies have revealed the presence of alkaloids, flavonoids, phenols and saponins in BME. The antiestrogenic activity shown by the extract may be attributed to these diverse compounds [31].

6.10. Cytological Activity

The extract of *B. diffusa* exhibited a strong depressive effect on the mitosis of C. jagus roots. The study was conducted using *B. diffusa* extract, the mitotic index of the control experiment was found to be 5.27. There was a negative correlation between the concentrations of the treatment extracts and the mitotic indices obtained from their action. This points to an inhibition of mitosis by this extract. Inhibition of the mitotic index increased significantly with an increase in the concentration of treatment solution of *B. diffusa*. This again shows a very negative correlation between the concentration of the extract and the mitotic indices produced by the observed action. Owing to the ability of the root extracts of *B. diffusa* to accumulate metaphase and hence inhibit mitosis, it is possible to use these extracts as an alternative to the rather expensive colchicine for cytological studies [32].

6.11. Anti Fibrinolytic Activity

A study evaluated the effect of antifibrinolytic agents; Alpha-aminocaproic acid (α-ACA), tranexamic acid (AMCA); anti-inflammatory drugs (indomethacin, ibuprofen, naproxen); and plant extract (root extract of *Boerhaavia diffusa*) on endometrial histology of IUD-fitted menstruating monkeys. It is effective in reducing stromal edema, inflammation, and tortuosity of glands, and in increasing the degree of deposition of fibrin and platelets in the vessel lumen [33].

6.12. Antioxidant Activity

The evaluation of the antioxidant potential of ethanolic extract of *Andrographis echioides* and *Boerhavia diffusa* was carried out by determining the levels of enzymatic and non-enzymatic antioxidants. The results showed that both the plant extracts possessed significant levels of enzymatic and non-enzymatic antioxidants. The results of the enzymatic and non-enzymatic antioxidants in *Andrographis echioides* and *Boerhavia diffusa* exhibits that they possess. In DPPH radial scavenging activity, the ethanol extract showed 81.94% inhibition and the chloroform extract showed 42.58% inhibition at 1000 µg/ml compared with 88.02 % inhibition by Quercetin. The above results suggest that roots of *Boerhaavia diffusa* were found to reveal antioxidant potential which supports the use of this plant in traditional medicine 62.

6.13. Antiviral Activity

Boerhaavia diffusa has many ethno ethno-botanical uses (the leaves are used as vegetable; the root juice is used to cure asthma, urinary disorders, leucorrhoea, rheumatism, and encephalitis), and is medicinally used in the traditional, Ayurvedic system. Besides, the *Boerhaavia diffusa* plant is reported to possess many pharmacological, clinical, and antimicrobial properties. Recently, the authors observed potent antiviral efficacy of this plant against phytopathogenic viruses. The antiviral agent isolated from this plant was found to be a glycoprotein with a molecular weight of 16-20 kDa. Administered by foliar spraying in the field, this anti-viral agent could protect some economically important crops against natural infection by plant viruses [34].

7. Conclusion

From the above review we may suggest that the use of *B. diffusa* is very traditional and ancient throughout the world under different clinical/pathological conditions. Now the scientific basis of those pharmacological has come out and however, some of them are still under way. Thus, more in depth studies are solicited considering this plant.

Compliance with ethical standards

Acknowledgments

Financial support ton SG by Council of Scientific and Industrial Research (CSIR), New Delhi, India is gratefully acknowledged.

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