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ANTI DIABETIC ACTIVITY OF A TRADITIONAL HERB BOERHAVIA DIFFUSA- AN OVERVIEW

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ABSTRACT
There are many different ailments in the world today, due to our lifestyle and schedules, and in order to treat them, many people take numerous medications daily. Thus, whether voluntarily or involuntarily, we are compelled to store large quantities of dangerous or damaging compounds in our bodies. As a result, our bodies develop a new sickness as a result of these stored chemicals, and in order to treat it, we must take a new medication that contains additional hazardous chemicals that were already present. As a result of their biodegradable nature, natural and herbal treatments are being used more and more frequently. In this context, India uses a variety of bio-products, but Boerhaavia diffusa utilization was less widespread in previous decades. Numerous studies were undertaken in the future. This review focused on the micro and macroscopical characteristics anti diabetic studies by various researchers, toxicity studies. This study provides essential information for further research on Antidiabetic activity of Boerhavia diffusa.

KEYWORDS: Boerhaavia diffusa, macroscopical, Antidiabetic.

INTRODUCTION
Several kinds of herbs can be used to prevent illnesses that can affect different organs in both humans and animals. The development of bioactive compounds begins with the use of herbs of medications and their advancements.[1] Herbs have the characteristic of not only containing hazardous ingredients but also damaging ingredients.[2] Because they are plants that naturally occur, indigenous plants are the natural residents.[3] Because native species have frequently developed to adapt to particular conditions and circumstances, it is crucial to preserve them. Indigenous animals have been discovered to have specific qualities that have been utilized to create customized medications to save lives.[4] it is evident that many essential herbal medicines have been created for the treatment of illnesses based on traditional healers from long ago. Moreover, plants are the first line of treatment for a number of diseases.[5,6]

Presently, traditional herbal medicines are getting noteworthy attention in global health debate.[7]Traditional medicines are the knowledgeable tool for the various practices as well as skills.[8] These are based on the various theories, principles several benefits as well as their experiences related to their culture that is used for the health maintains as well as cure, diagnosis treatment, improvement, and also used for the treatment of physical and mental problems.[9-14]

The medicine that is traditional has been accepted by the population for the term is alternative medicine.[15] The examples of the herbal medicines are the herbal preparations as well as herbal materials or finished products that are the part of the active portion of the plants.[16-19]

A member of the Nyctaginaceae family of herbaceous plants, Boerhavia diffusa. This review focused on anti diabetic activity and the different methods used in various researches for the same. Boerhavia diffusa is distributed in different Continents like Asia, Africa, North America, Caribbean, South America, South Pacific the common names for Boerhavia diffusa are Tarvine, Punarnava, and Red Spiderling.[20]

Six of these Boerhaavia species B. diffusa, B. chinensis, B. erecta, B. repens, B. rependa, and B. rubicunda are said to exist in India. In the Atharvaveda, B. diffusa L. was referred to as Punarnava, which is Sanskrit for "one that rejuvenates the old body."Major compounds isolated from this plant are Boerhavia acid, isoflavonoids (retenoids), Punarnavine, sitosterol, Boeravinone, palmitic acid, steroids (ecdysteroid), lignan glycosides, and esters of sitosterol. B. diffusa helps in the treatment of dropsy, characterized by retention of excessive fluids in tissue and body cavities. The fluids could be discharged with the help of the plant extract.[21]

Different parts of Boerhaavia diffusa (a) roots; (b) leaves; (c) the whole plants; (d) flowers22.

(a)

(b)

(c)

(d)

Table 1: Punarnava-Names in different languages.[23]

Sanskrit :	**Kahtilla, Sophaghni, Sothaghni,**
Assamese :	**Ranga Punarnabha**
Bengali:	**Rakta punarnava**
English:	**Horse Purslene, Hog Weed**
Gujrati:	**Dholisaturdi, Motosatodo**
Hindi:	**Gadapurna, Lalpunarnava**
Kannada:	**Kommeberu, Komma**
Kashmiri:	**Vanjula Punarnava**
Malayalam:	**Chuvanna Tazhutawa**
Marathi:	**Ghetuli, Vasuchimuli, Satodimula,**
Oriya:	**Lalapuiruni, Nalipuruni**
Punjabi:	**Khattan**
Tamil:	**Mukurattai (Shihappu)**
Telugu:	**Atikamamidi, Erra galijeru**

MACROSCOPIC CHARACTERS

B. diffusa L. is a perennial creeping plant with spreading branches that can grow up to 1 m long or longer. With a woody root stock, the roots are thick and fusiform. The prostrate stem is cylindrical, woody or succulent, hairy, frequently purple, and thickened at the nodes. Simple, thick, fleshy, and hairy leaves are grouped in uneven pairs, are ovate-oblong in shape, round or subcordate at the base, and have smooth, wavy, or undulating margins. They can measure up to 5.5 3.3 cm2 in size. Hermaphrodite, pedicellate, tiny, subcapitate, and present 4–10 combined in small bracteolate umbels, creating terminal panicles and axillary panicles; Bracts are involucrate and deciduous; The perianth, which has a tubular shape and is short and narrow at the base and funnel-shaped at the top and constricted above the ovary, replaces the calyx and corolla. There are five tiny, sharp lobes in all. There are one to three stamens, which are present and somewhat extended. There is peltate stigma. The fruit, an achene, has five ribs and glands, is anthocarpous, detachable, ovate, oblong, pubescent, viscid on the ribs, and is pubescent.[24]

MICROSCOPIC CHARACTERS

Stem: Boerhaavia diffusa stem's transverse section shows an epidermal layer with uniseriate glandular trichomes and a multicellular structure with an ellipsoidal head and 9–12 stalked cells, measuring 150–220 m.Long cortex with 1-2 layers of parenchyma, indistinct endodermis, 1-2-layered, thick-walled

pericycle with scattered isolated fibres, stele made up of various small vascular bundles that are frequently joined simultaneously in a ring and various large vascular bundles dispersed throughout the ground tissue, and intrafascicular cambium.

Root: Transverse section of *boerhaavia diffusa* linn root illustrates a cork com posed of thin-walled agilely elongated cells with brown walls in the outer few layers and 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 and several concentric bands of xylem tissue alternating with wide zone of parenchymatous tissue present below cortical regions and number of bands vary according to the thickness of root of *Boerhaavia diffusa* and composed of vessels, tracheids, and fibers. Vessels generally originate in clusters of 2–8 in radial rows, containing reticulate thickening, small, thick walled, tracheids and simple pits. Fiber saseptate, thick-walled, spindle shaped and elongated with pointed ends. Phloem takes place as hemispherical outer surface each group of xylem vessels and created of sieve elements and parenchyma, broad zone of parenchymatous tissue. Two successive rings of xylem elements arranged of thin-walled additional or fewer rectangular cells organized in radial rows, central areas of root of *Boerhaavia diffusa* occupied by main vascular bundles, many raphides of calcium oxalate in single or in group present in cortical section. Parenchymatous tissue in between xylem tissue and simple starch grains, compound containing 2–4 components originate in abundance in most of cells of cortex.

Leaves: A transverse section of a Boerhaavia diffusa leaf shows anomocytic stomata on both sides, numerous, with a few short hairs, 3-4 celled, on the border and on veins, a one-layered palisade, and spongy parenchyma 2-4 layered between microscopic air holes. Idioblasts with raphides sporadically group calcium oxalate crystals and an orange-red resinous material found in mesophyll. Stomatal index 11–16, palisade ratio 3.5–6.5, and vein islet numbers 9–15.[25-29]

Table 2: Name of compound and activity reported.[30]

S/N	Name of compound	Activity reported	Plant part	Reference
1	Flavonoids	Antibacterial	Leaves	**(Umamaheswari et al., 2010)**
2	Boeravinones A, B, C, D, E, F	Anticancer	Roots	**(Kaur, 2019)(Kadota et al., 1988)**
3	Polyphenols	Antioxidant	Leaves	**(Alam & Shahzad, 2018)**
4	Boeravinone G, Boeravinone E, Compound 5	Antispasmodic	Roots	**(Borrelli et al., 2005)**
5	Punarnavoside	Antifbrinolytic	Roots	**(Jain & Khanna, 1989)**
6	(6,11-dihydroxy-9-10-dimethyl-4-methoxyrotenoid)	Hepatoprotective	Leaves	**(Dey et al., 2020; Khaliq et al., n.d.)**

Table 3: **Taxonomical classification[30]**

Taxonomical classification
Kingdom: Plantae
Class: Dicotyledons
Order: Thymilae
Family: Nyctaginaceae
Genus: Boerhaavia
Species: diffusa

Table 4: Characteristics of Boerhavia diffusa.[31]

Parts of Plant	**Boerhavia diffusa**
Plant	A perennial herb from a fusiform root
Fruit	Ovoid or sub-ellipsoid, rounded above, slightly cuneate,below, broadly and bluntly 5-ribbed, very glandular throughout
Flowers	In pendunculate, glomerulate clusters arranged in slender, long stalked, axillary or terminal corymbs
Flowering & Fruiting	Throughout the year in Indian conditions
Stem	Prostrate, decumbent or ascending, 4-10 cm long, rather slender, divaricately branched
Leaves	Opposite or sub-opposite, two of a node unequal, broadlyovate or sub-orbicular, obtuse to rounded or sub-cordate at the base.

STUDY ON ANTIDIABETIC ACTIVITY

Diabetes mellitus, which is on the rise, and the complications it causes are posing a severe threat to human health. Chemical or biochemical agents are principally responsible for its regulation and therapy. Herbal alternative therapies have a promising future in the treatment of diabetes mellitus and its consequences. They provide good clinical potential. B. diffusa possesses strong anti-diabetic properties. Its leaf extracts in various solvents shown hypoglycemic efficacy in normal animals and antihyperglycemic activity in models of diabetes caused by alloxan, streptozotocin, or dexamethasone. Aqueous B. diffusa leaf extracts were administered orally daily for 4 weeks at a rate of 200 mg/kg, and there is a significant changes in blood glucose levels and the activity of the liver's gluconeogenic enzymes (increased hexokinase activity & decreased glucose-6-phosphate and fructose-1, 6-bisphosphatase).[32]

Bhatia V et al., according to them, Boerhaavia diffusa and ethanolic extracts had strong antihyperglycemic effects in both alloxan-induced and hyperglycemic rats caused by streptazocin. Indicators of the status of diabetes, such as body weight, serum cholesterol, and triglyceride levels, can also be improved by them. For the course and result of diabetes, the number of functionally healthy cells in the islet organ is crucial. In numerous animal models, the regeneration of -cells in diabetes has been investigated. The balance between cell loss and renewal is reflected in the total mass of cells. Also, it was proposed that alloxan-injected guinea pigs' recovery from the effects of the drug may have been primarily caused by the regeneration of islet cells after the drug had destroyed them.[33]

Pari et al., has conducted a research study to find out the daily oral administration of Boerhaavia diffusa L. leaf extract (BLEt) (200 mg/kg) for four weeks affected blood sugar levels. Concentration and hepatic enzymes in diabetic and non-diabetic rats treated with alloxan. In normal and diabetic rats treated with BLEt, a considerable drop in blood glucose and a significant rise in plasma insulin levels were seen.[34]

Nalamolu et al., noticed that the Chloroform extract of B. diffusa leaf produced dose-dependent reduction in blood glucose in streptozotocin-induced NIDDM rats comparable to that of glibenclamide. The results indicate that the reduction in blood glucose produced by the extract is probably through rejuvenation of pancreatic beta-cells or through extra pancreatic action.[35]

E A. Newsholmeet et al., has compared the antidiabetic activity of glibenclamide with BLEt.The gluconeogenic pathway's regulating enzymes include fructose-1,6-bisphosphatase and glucose-6-phosphatase. Given that BLEt dramatically reduced blood glucose levels in rats given glucose, it may improve glucose utilization. It seems to imply that BLEt might work via a similar mechanism to sulphonylurea. This can be because intestinal glucose absorption has been inhibited or because the delayed insulin response has been restored. The same groups were also subjected to an oral glucose tolerance test (OGTT), in which the rats receiving BLEt showed a notable improvement in their ability to tolerate glucose. The effects of BLEt and the anti-diabetic medication glibenclamide (600µg/kg) were compared. When contrasted with glibenclamide, the effect of BLEt was more noticeable. This study clearly demonstrates the substantial potential of this herb.[36]

Alam et al., has observed the impact of B. diffusa leaf extract on lipids in normal and alloxan diabetic rats. 30 rats were utilized in the investigation (12 normal, and 18 were given alloxan monohydrate injections for two weeks). In diabetic rats, plasma insulin levels considerably dropped while blood glucose levels significantly rose. Plasma insulin levels significantly increased after oral treatment of B. diffusa extract and glibenclamide, and blood glucose levels.[37]

Shahzad et al., study reveals the effect of BTLt on levels of cholesterol when compared to diabetic rats, Rats given B. diffusa extract showed considerably lower levels of cholesterol, free fatty acids, triglycerides, and phospholipids as compared to the diabetic group. The study found that improved blood glucose transfer to peripheral tissues, a decrease in gastrointestinal glucose absorption, or a potential pancreatic insulin secretion from established cells may be the potential mechanisms by which B. diffusa extract commences its antihyperglycemic effects. B. diffusa leaf extract exhibited anti-diabetic and antioxidant effects.[38]

Md. Sheena Mini et al., compared the antidiabetic effect in Boerhaavia diffusa The plant's dried roots were ground into a rough powder. The plants 500 gm of dried root powder were macerated and extracted with 80% v/v methanol. In a sealed container, the coarsely ground plant material was soaked in methanol and let to stand for about a week while being sometimes stirred. The extract was filtered and the solvent was distilled out following the successful completion of the extraction. To create a dry residue, the extract was concentrated. With reference to air-dried powder, the extract's percentage yield was computed. For this investigation, Wistar albino rats (150–200 gm) of either sex were employed. Prior to the trial, the animals had a one-week acclimatization period. They were done right housed in polypropylene cages with a standard dry pellet meal and unlimited access to water under standard laboratory conditions (12/12 h light/dark cycle at 25–50 ºC). The animals were split into 6 groups after acclimation, with 6 rats of either sex in each group. Prior to the trial, animals were given an overnight fast with free access to water. Dexamethasone is administered subcutaneously to the animal for 10 days at a dose of 5 mg/kg body weight. In dexamethasone-induced diabetic rat models, the study conclusively demonstrates the hypoglycemic effect of

methanolic extract of Boerhaavia diffusa and their combination.[39]

Krishna Murti et al., illustrated a method to evaluate the antidiabetic activity on the roots of *Boerhaavia diffusa* and carried out the macroscopic and microscopic properties evaluation. The roots that had been shade-dried were ground into a coarse granule. Using a Soxhlet device, 250 g of dry powder were continuously heated percolated with 90% ethanol. Under lower pressure, the resulting dark-brown extract was concentrated up to 100 ml on Rota vapor. The investigation used the lyophilized, powdered, concentrated crude extracts. We utilized male Wistar rats weighing 180–200 g. Boerhaavia diffusa ethanolic extracts were administered orally to the animals in six distinct groups at concentrations of 100, 200, and 400 mg/kg body weight. The plant extract raises the possibility of strong anti-diabetic active ingredients, which in diabetic rats reduced hyperglycemia.[40]

Rao K. Nalamolu et al., studied the anti-diabetic effect in fresh leaves of *B. diffusa* were shade dried for about two weeks Three kilogram's of dry leaf powder were extracted with chloroform in a Soxhlet apparatus for twenty-four hours, and the extract was dried under vacuum in a vacuum desiccators. (268g). The study employed adult male Sprague-Dawley rats weighing 250–300 g. Six groups of six people each received a regular pellet diet and unlimited access to water. Prior to the experiment, all rats spent at least 10 days becoming used to the lab environment. They were also kept in an animal home with a 12-hour light/dark cycle that was well-ventilated. Injecting the animal with streptozotocin (65 mg/kg, intravenous; dissolved in 0.1 M citrate buffer; pH 4.5). It is clear from the findings that long-term treatment of B. diffusa extract to Blood glucose levels dropped in streptozotocin-induced NIDDM rats in a dose-dependent manner. The findings of this investigation are well congruent with diabetes in rats caused by alloxan.[41]

Panda K.C et al., examined the antidiabetic effect in the collection of leaves and seeds of *Boerhavia diffusa plant* with order to eliminate extra water; they are first washed with tap water, spread out over filter paper, and allowed to air dry at room temperature. Fresh plant material was macerated into fine powder using a mortar and pestle, then measured out 35 gm of each into thimbles for sequential extraction with a Soxhlet device. Petroleum ether, chloroform, ethanol, and water were the four main solvent systems used in the sequential extraction, ranging in polarity from low to high. Out of the four distinct extracts, the ethanolic extracts of Boerhavia diffusa of -glycosidase shown the greatest anti-diabetic effect, according to the study.[42]

Satheesh M.A. et al., Approximately 500 gms of B. diffusa leaves were minced, extracted with 1,500 ml of water using the continuous hot extraction method at 60°C for six hours, and then evaporated. The result was a dark semisolid (greenish-black) substance. (22.5 g). Until it was utilized, it was kept at 4°C. The residual extract was employed in this study when necessary, suspended in distilled water. 30 rats in total 18 diabetes survivors and 12 control rats were employed in the experiment. After the rats were given alloxan to induce diabetes, they were split into five groups. In the experiment, groups 1 through 5 each contained six rats. The rats received injections of dissolved alloxan monohydrate. 140 mg/kg of body weight in sterile normal saline was administered intraperitoneally. Higher levels of cholesterol, triglycerides, and phospholipids have been noticed in diabetic liver and kidney; oral administration of B. Diffusa leaf extract to diabetic rats corrected these alterations. Following the administration of B. Diffusa leaf extract, the diabetic condition improved, resulting in an improvement in glucose utilization and a decrease in the mobilization of lipids.[42]

Mama Sirou Amidou Ibrahima et al., stated that the stem leaves of *Boerhavia diffusa* Linn have the property of anti diabetic effect The material was collected, dried for two weeks at 22°C in the lab, and then processed into a fine powder using an electric grinder. (Excella mixer grinder). Boerhavia diffusa barks were successfully extracted into 250 g of dry powder by macerating with methanol for 72 hours while stirring. Rotating evaporators were used to dry the extract. The methanol extract was kept at 4 °C until it was required. The study employed adult male Wistar rats that were 2-3 months old and weighed 250–300g. Prior to the experiment, for two weeks, a constant temperature of 22 °C with a cycle of 12 hours of light and 12 hours of darkness was maintained. Granulated feed and unlimited water are given to them continuously in feeding bottles. After blood tests, the rats divided into two groups of six rats to guarantee batch uniformity. Rats were put under an eighteen-hour fast before being given an intraperitoneal (i.p.) injection of streptozotocin (40 mg/kg body weight) in a citrate buffer solution (0.1 M, pH 4.5) to induce diabetes. The results demonstrate that oral administration of a methanol extract of Boerhavia diffusa stem leaves exerted anti-diabetic effects via modulation of the activity of enzymes involved in the metabolism of carbohydrates, as well as anti-inflammatory and antioxidant enzymes in experimental diabetes.[43]

Firoz Akhter et al., studied the roots of *B. Diffusa* (Linn.). About 25 g of freshly shade-dried plant roots were ground into a powder, wrapped in muslin fabric, and extracted using the Soxhlet method with 0.25 L of different solvents, including water, methanol (CH3OH), and ethanol (CH3CH2OH). (H2O). The extraction was filtered, allowed to cool, allowed to dry, and then stored at 4°C for later use after the percolation procedure was repeated until the solvent became colorless. We utilized male albino rats that ranged in weight from 175 g to 220 g. The rats received free access to water and pelleted rat food. 30 overnight-fasted rats received intraperitoneal injections of STZ (freshly dissolved in 10 mM citrate

buffer, pH 4.5, 60 mg/kg b.w. t.) to cause experimental diabetes. The extracts are analysed using TLC, DPPH test, and HPLC. This study demonstrates the potent targeting FBG, HbA1c, plasma lipid and lipoprotein content, HMG-R activity, and systemic lipoperoxidative events, the methanolic extract of B. diffusa root (D-MTs) and its partially purified fraction (D-BT) have antidiabetic-cum hypolipidemic potential.[44]

M. Amarnath Satheesh et al., analyzed that the leaf extracts *B. Diffusa* having antidiabetic *effect.* The leaf of *B. Diffusa* was prepared by chopping 500 g of *B. diffusa* leaves into small pieces and subsequently extracting the chopped leaves with 1500 ml water (by continuous hot extraction at 60°C for 6 h). The resulting extract was evaporated to dryness in a rotavapor at 40 to 50°C under reduced pressure. The resulting semisolid material (22.5 g) was stored at 0-4°C until used. The residual extract was dissolved in water and used in this study. Albino rats (male) 160 to 200 g were used as experimental test animals. Before and during the experiment, rats were fed with a normal laboratory pellet diet and water *ad libitum*. The animals were grouped into 1to 5.Diabetes was induced in the rats by intraperitoneal injection with 140 mg/kg body wt. with alloxan monohydrate dissolved in sterile, normal saline. Administration of *B. diffusa* leaf extract to the alloxan-induced diabetic rats decreased measured-plasma levels of TBARS, lipid peroxide, ceruloplasmin, and tocopherol, demonstrating an anti-peroxidative effect of *B. Diffusa leaf extract*.[45]

TOXICITY

On B. diffusa, several toxicological investigations were carried out.[46] investigated the acute oral toxicity of a crude extract made from the juice (JE) and decoction (DE) of fresh leaves that had been lyophilized. Up to a level of 5000 mg/kg of body weight, mice showed no signs of toxicity, and no weight gain in the body or organs was noticed either. The maximum tolerable dose of root extract administered to mice, according to Dhar et al., is roughly 1g/kg of body weight.[47] Pregnant albino female rats were given a daily dose of 250 mg/kg of B. diffusa ethanolic extract, and this dose demonstrated no teratogenic activity. Chandan et al. noted a potent choleretic activity that increased bile flow without manifesting any harmful effects up to a 2g/kg body weight oral dosage in mice.[48]

CONCLUSION

Ayurveda and Unani are two traditional medical systems that commonly recommend the well-known medicinal herb B. diffusa. Numerous pharmacological and clinical investigations describing the distinct bioactivity of plant extracts have confirmed the plant's numerous traditional benefits for treating a variety of Diseases.Plant extracts shown anti-diabetic, anti-fibrinolytic, analgesic, antioxidant, and adoptogenic properties in additional animal investigations. However, only in vitro testing employing lab animals have been used to evaluate the varied pharmacological effects of plant extract and extracted phytochemicals. It is still abundantly obvious that B. diffusa is a plant with huge broad use right now and also with amazing potential for the future, even though there are gaps in the studies done so far that need to be filled in order to realize the full therapeutic potential of this plant. To provide essential information for future study scope and for conservation of this priceless species, this review compiles anti diabetic studies completed on many aspects of B. diffusa by numerous authors and traditional healers.

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