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Boerhavia diffusa as a multi-targeted anticancer agent: Insights from Siddha Medicine and molecular oncology

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Abstract
Cancer remains one of the leading causes of mortality worldwide despite major advances in chemotherapy, radiotherapy, and targeted therapies. Limitations associated with conventional treatments, including systemic toxicity, drug resistance, tumour recurrence, and high treatment costs, have stimulated interest in alternative and integrative therapeutic approaches. Traditional medicinal systems, particularly Siddha medicine, offer a holistic perspective in disease management through restoration of physiological balance, detoxification, and rejuvenation. In Siddha literature, cancer-like conditions (Putru Noi) are associated with disturbances in the three humours—Vatham, Pitham, and Kapham—along with impaired metabolic activity (Agni) and accumulation of toxins (Ama).

*Boerhavia diffusa (*Punarnava), an important medicinal herb used in Siddha medicine, has attracted considerable scientific attention because of its diverse pharmacological properties. The plant contains several bioactive phytoconstituents, including flavonoids, alkaloids, retinoid, phenolic compounds, lignin's, and phytosterols, which contribute to its antioxidant, anti-inflammatory, immunomodulatory, anti-proliferative, anti-metastatic, and apoptosis-inducing activities. Experimental studies have demonstrated that *Boerhavia diffusa* modulates multiple molecular pathways involved in carcinogenesis, including NF-κB, PI3K/Akt, VEGF, mitochondrial apoptotic pathways, and matrix metalloproteinases (MMPs). These mechanisms collectively contribute to inhibition of tumour growth, suppression of metastasis, induction of apoptosis, and reduction of oxidative stress and inflammation.

The present review critically examines the botanical, pharmacognostic, phytochemical, pharmacological, and therapeutic significance of *Boerhavia diffusa* in cancer management from both Siddha and modern biomedical perspectives. In addition, the review discusses its potential role in integrative oncology as a complementary therapeutic agent capable of enhancing immune response, reducing treatment-associated toxicity, and improving patient quality of life. Although preclinical findings strongly support its anticancer potential, further clinical studies, standardization of formulations, and safety evaluations are necessary before its widespread therapeutic application. Overall, *Boerhavia diffusa* represents a promising bridge between traditional Siddha knowledge and evidence-based modern oncology, offering potential for the development of safer and multi-targeted cancer therapies.

Keywords: *Boerhavia diffusa*, Punarnava, Siddha Medicine, integrative oncology, cancer therapy, phytochemicals, apoptosis, antioxidant activity, anti-inflammatory activity, metastasis inhibition, herbal medicine, complementary therapy, molecular pathways, traditional medicine, anticancer activity

Introduction

Cancer is a highly intricate and multifactorial disorder marked by abnormal and uncontrolled cell growth, resistance to apoptosis, continuous formation of new blood vessels, and the ability to spread to distant organs through metastasis (Aggarwal BB, *et al.*, 2021). Despite remarkable progress in modern cancer treatments, including chemotherapy, radiotherapy, and targeted therapeutic approaches, cancer continues to pose a significant global health challenge. Although these therapies have enhanced patient survival, their effectiveness is frequently constrained by adverse side effects, development of drug resistance, expensive treatment costs, and recurrence of tumours (Ahmad I, *et al.*, 2021) [1]. These shortcomings underscore the necessity for the development of safer, cost-effective, and multi-targeted therapeutic alternatives.

Recently, there has been growing scientific interest in herbal and plant-derived medicines rooted in traditional systems of healthcare (Sharma R, *et al.*, 2025) [31]. Among these, Siddha medicine, one of the most ancient indigenous medical traditions, adopts a holistic approach focused on preserving bodily equilibrium, detoxification, and rejuvenation. Siddha philosophy attributes disease development to disturbances in the balance of the three vital humours—Vatham, Pitham, and Kapham—along with the accumulation of toxins (Amar) and dye function of digestive and metabolic processes (Agni) (Ahmad I, *et al.*, 2021) [1]. Therefore, Siddha therapies are designed not only to alleviate disease symptoms but also to re-establish systemic balance and strengthen the body's natural healing mechanisms.

Medicinal plants constitute a fundamental component of Siddha medicine because of their ability to exert therapeutic effects through multiple bioactive compounds acting on various biological targets. Among these medicinal herbs, *Boerhavia diffusa*, popularly referred to as Punarnava, has long been utilized in traditional healthcare practices for treating inflammatory conditions, hepatic disorders, and several chronic ailments (Atanasov AG, *et al.*, 2021) [3]. The term "Punarnava," which translates to "restoration of the

body," signifies its recognized rejuvenating potential. In Siddha medicine, it is regarded as a Kayakalpa drug because of its reputed capacity to facilitate tissue regeneration, detoxify the body, and strengthen immune function.

From the perspective of contemporary biomedical science, *Boerhavia diffusa* has gained significant research interest owing to its broad spectrum of pharmacological properties, such as antioxidant, anti-inflammatory, immunoregulatory, anti-proliferative, and anti-metastatic activities (Bibi Y, *et al*., 2026) [6]. Recent studies indicate that the phytochemical constituents present in this plant may influence several molecular signalling pathways associated with cancer development and progression, highlighting its possible utility as a supportive agent in cancer management.

Consequently, combining the holistic concepts of Siddha medicine with advances in modern molecular research may provide an innovative and less toxic approach to cancer treatment (Sinan KI, *et al.,* 2003). In this context, *Boerhavia diffusa* emerges as a promising link between traditional medicinal knowledge and modern oncological research, emphasizing the need for further detailed scientific investigation (Das S, Dutta S, Paul S, *et al.,* 2023) [8].

Siddha Interpretation of Cancer (Putru Noi)

Tridosha Theory: Role of Vatham, Pitham, and Kapham

Siddha medicine is founded on the concept of the Tridosha system, which includes Vatham, Pitham, and Kapham, the three fundamental humours responsible for maintaining physiological harmony within the body. Vatham is primarily associated with movement, nervous regulation, and functional coordination, whereas Pitham regulates metabolic activities, digestion, and biochemical processes. Kapham contributes to structural integrity, lubrication, and immune protection (Das S, *et al*., 2023) [8]. The balanced interaction of these three humours is considered essential for sustaining health and normal bodily functions.

According to Siddha principles, disease develops when the equilibrium among the Tridoshas is disturbed. In relation to cancer, referred to as Putru Noi in Siddha literature, the condition is mainly linked to the aggravation of Pitham and Kapham. Such imbalance is believed to trigger abnormal cellular proliferation, chronic inflammation, and excessive tissue accumulation. Siddha texts also associate this pathological state with weakened digestive and metabolic activity (Agni) and the accumulation of toxic metabolic waste products known as Ama, which collectively facilitate disease initiation and progression (Das S, *et al.,* 2023) [8].

The therapeutic strategy in Siddha medicine therefore focuses on correcting Tridosha imbalance, detoxifying the body, enhancing metabolic function, and rejuvenating affected tissues. These principles support the use of medicinal herbs such as *Boerhavia diffusa* in the supportive management of cancer and related disorders (Dina J, *et al.,* 2024) [12].

Significance of Agni (Metabolic Function) and Amar (Toxic Accumulation) in Siddha Medicine

Within Siddha philosophy, Agni is regarded as the vital metabolic force responsible for digestion, biochemical transformation, nutrient assimilation, and maintenance of cellular energy homeostasis. Amar, on the other hand, refers to toxic metabolic residues formed as a result of incomplete digestion and impaired metabolic activity. When Agni becomes weakened or dysfunctional, these harmful substances accumulate within the body, interfere with normal physiological processes, and contribute to the onset of various diseases (Dina J, *et al*., 2024) [12].

From the Siddha perspective of cancer development, the disturbance of Agni and the excessive accumulation of Amar may be associated with altered cellular metabolism, oxidative damage, chronic inflammation, and the persistence of toxic intermediates that support uncontrolled cellular proliferation. Such pathological changes are believed to create a favourable environment for tumour initiation and progression. Consequently, Siddha treatment approaches focus on enhancing metabolic efficiency, restoring digestive balance, and removing accumulated toxins in order to re-establish overall physiological harmony (Fulda S, *et al.,* 2024).

Traditional medicinal herbs such as *Boerhavia diffusa* are widely employed in Siddha medicine because of their reputed detoxifying and metabolism-supporting properties. These therapeutic effects may aid in maintaining systemic balance and contribute to the prevention and management of chronic disorders, including cancer (Greenwell M, Rahman Greenwell M, Rahman, 2020) [15].

Therapeutic Importance of Punarnava in Siddha Medicine

In Siddha therapeutics, *Boerhavia diffusa* is recognized as an important Kayakalpa herb known for its rejuvenating and restorative properties. The herb has traditionally been employed to improve vitality, maintain physiological equilibrium, and manage ailments associated with chronic inflammation, oedema, and long-standing systemic disorders (Gunaseelan D, *et al.,* 2022) [16].According to Siddha principles, Punarnava plays a significant role in balancing the Tridoshas, especially by pacifying aggravated Pitham and Kapham. It is also believed to support healthy metabolic activity and facilitate the removal of accumulated toxins from the body. Traditional applications of the herb include enhancement of tissue regeneration, improvement of digestive efficiency, stimulation of detoxification pathways, and reinforcement of immune defence mechanisms.

Because of these diverse therapeutic properties, *Boerhavia diffusa* is considered beneficial in the management of chronic and degenerative diseases, including conditions comparable to abnormal or tumour-like growths described in Siddha medical literature (Gunaseelan D, *et al.,* 2022) [18].

Botanical and Pharmacognostic Characteristics of *Boerhavia diffusa*

Boerhavia diffusa, popularly referred to as Punarnava, is a perennial medicinal herb belonging to the family Nyctaginaceae. The plant is extensively found across tropical and subtropical regions, where it commonly grows as a creeping or trailing herb with widely spreading branches. It generally develops close to the soil surface and is frequently observed in open wastelands, roadside areas, agricultural lands, and other disturbed habitats (Hanahan D., 2022) [19].

Morphological Features of *Boerhavia diffusa*

- **Growth Habit:** A perennial herb that commonly grows in a prostrate manner, though it may also exhibit ascending growth under certain conditions.
- **Root System:** The roots are thick, fleshy, cylindrical, and spindle-shaped with a yellowish-brown appearance,

and they constitute the primary medicinally valuable part of the plant.

- **Stem:** The stem is delicate, highly branched, and often displays a purplish coloration with characteristic swollen nodes.
- **Leaves:** Leaves are arranged oppositely and are generally ovate to nearly circular in shape. Leaf pairs are usually unequal in size and may appear smooth or slightly pubescent.
- **Flowers:** The plant bears small flowers that range in colour from pink to reddish and are typically grouped in clusters.
- **Fruits:** Fruits are minute, glandular structures containing a single seed, commonly described as anthocarps.

Pharmacognostic Properties of *Boerhavia diffusa*

Macroscopic Characteristics

The roots are typically long, tapering, and cylindrical in appearance, possessing a distinct characteristic odour and a mildly bitter taste. Their external surface is rough in texture and exhibits a light brown coloration.

Microscopic Characteristics

Microscopic examination of the root transverse section demonstrates a prominently developed cork layer, secondary cortex, and well-organized vascular tissues composed of xylem vessels and phloem elements. Starch granules along with calcium oxalate crystals are also frequently identified within the tissues.

Powder Analysis

The powdered root material contains identifiable fragments of cork cells, lignified vascular elements, fibres, and abundant starch grains. These microscopic components are considered important diagnostic markers for the authentication of the plant drug.

Identification and Standardization Criteria of *Boerhavia diffusa*

Parameters Used for Identification

- **Organoleptic Evaluation**
  Assessment of sensory characteristics such as colour, odour, and taste is carried out to establish the authenticity and purity of the crude drug.

- **Microscopic Diagnostic Features**
  Identification of characteristic anatomical structures, including vascular tissues and crystalline deposits, serves as an important tool for confirming the plant material.

- **Physicochemical Analysis**
  Determination of physicochemical parameters such as ash values and extractive values is performed to evaluate the quality, purity, and consistency of the herbal drug.

The detailed botanical and pharmacognostic characterization of *Boerhavia diffusa* plays a crucial role in its accurate identification, quality assurance, and standardization. These evaluations are important to ensure the safety, efficacy, and reproducibility of the plant when utilized in traditional Siddha preparations as well as in contemporary phytopharmaceutical formulations.

Phytochemical Composition of *Boerhavia diffusa*

Principal Bioactive Constituents

Table 1: Major Bioactive Compounds Identified in *Boerhavia diffusa*

Compound / Class	Biological Activity	Mechanism of Action
Punarnavine (Alkaloid)	Immunomodulatory, anti-inflammatory	Enhances immune cell activity; suppresses inflammatory mediators
Boeravinones (Retinoid)	Cytotoxic, anti-proliferative	Inhibits cancer cell growth; interferes with cell cycle progression
Quercetin (Flavonoid)	Antioxidant, pro-apoptotic	Scavenges free radicals; activates apoptotic pathways (capsizes)
Kaempferol (Flavonoid)	Anti-inflammatory, anticancer	Modulates signalling pathways; inhibits proliferation and angiogenesis
Phenolic compounds	Antioxidant	Neutralizes reactive oxygen species; protects DNA from oxidative damage
Lignin's	Anti-inflammatory, anticancer	Regulates cell signalling and reduces inflammatory responses
β-sit sterol (Sterol)	Anti-inflammatory, anti-tumour	Stabilizes cell membranes; modulates immune and inflammatory pathways

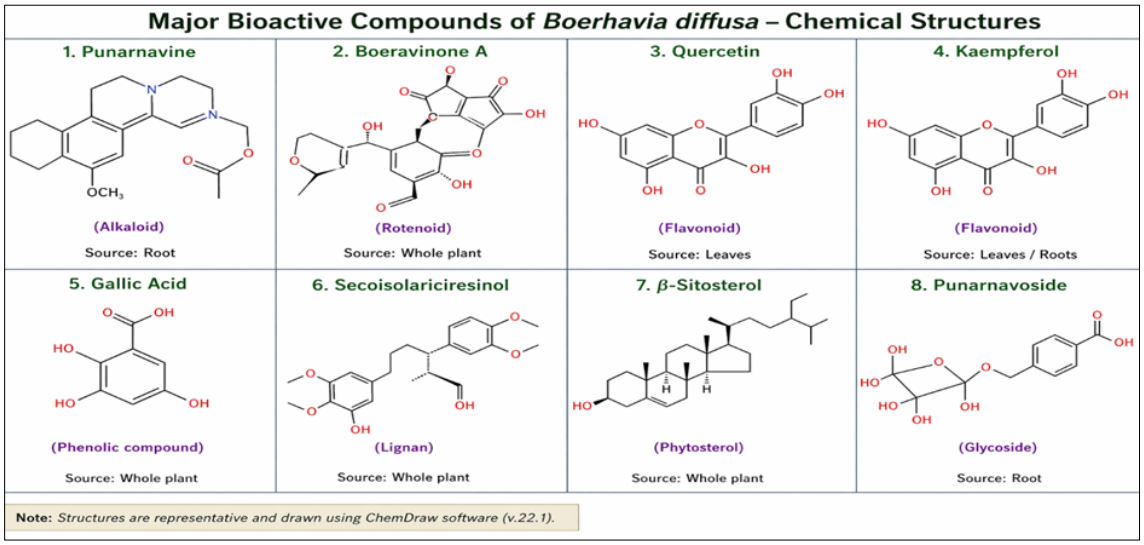

Fig 1: Chemical Structures of the Principal Phytoconstituents Present in *Boerhavia diffusa*

The therapeutic potential of *Boerhavia diffusa* is mainly attributed to the presence of diverse phytoconstituents possessing antioxidant, anti-inflammatory, immunomodulatory, and anticancer activities. These bioactive molecules are believed to contribute synergistically to the plant's pharmacological effects and support its application in traditional Siddha medicine as well as modern phytotherapeutic research.

Phytochemical Importance of *Boerhavia diffusa:* The medicinal value of *Boerhavia diffusa* is primarily associated with its abundant and chemically diverse phytoconstituents, including alkaloids, flavonoids, retinoid, phenolic compounds, lignins, and phytosterols (James JM, *et al*., 2025) [20]. The combined action of these bioactive molecules is believed to account for the plant's wide range of pharmacological properties, especially its potential role in cancer management.

Flavonoids and phenolic constituents present in the plant exhibit potent antioxidant activity by scavenging reactive oxygen species and reducing oxidative stress–induced DNA damage, which is closely linked to carcinogenesis (Krishnamoorthy S, *et al*., 2025) [24]. Alkaloidal compounds such as punarnavine are known for their immunomodulatory and anti-inflammatory actions, thereby helping to control inflammation associated with tumour progression. In addition, retinoid compounds, particularly boeravinones, have demonstrated cytotoxic and anti-proliferative effects that may suppress the growth and multiplication of cancer cells (Milosević N, *et al*., 2022) [16].

Multifaceted Phytochemical Actions of *Boerhavia diffusa* in Cancer Therapy

The phytoconstituents present in *Boerhavia diffusa* are known to modulate several cellular signalling pathways associated with cancer development and progression, including mechanisms involved in apoptosis, regulation of the cell cycle, and inflammatory responses. Through their combined biological activities, these compounds produce a multi-targeted therapeutic effect, offering a significant benefit when compared with conventional synthetic drugs that often act on a single molecular target (Newman DJ, Cragg GM., 2020) [28].

From the viewpoint of integrative medicine, the cooperative interaction among these bioactive constituents reflects the holistic philosophy of Siddha medicine, in which multiple therapeutic components function synergistically to restore physiological balance and strengthen the body's inherent defence systems (Patel N, *et al*., 2025) [29]. Consequently, the extensive phytochemical diversity of *Boerhavia diffusa* supports its promising role as a complementary therapeutic agent in cancer management.

Pharmacognostic Properties of *Boerhavia diffusa*

Table 2: Pharmacognostic Features of *Boerhavia diffusa*

Parameter	Macroscopic (Organoleptic Features)	Microscopic (Anatomical Features)	Powder Characteristics
Root	Cylindrical, tapering, yellowish-brown; rough surface; bitter taste	Cork layer present; secondary cortex well developed; vascular bundles with xylem and phloem	Fragments of cork cells, lignified vessels, fibres
Stem	Slender, branched, purplish; swollen nodes	Epidermis with cuticle; vascular bundles arranged in a ring	Epidermal fragments, vascular tissues
Leaves	Opposite, ovate, smooth or slightly hairy; green	Presence of stomata; mesophyll with chloroplasts; vascular strands	Leaf fragments, trachoma's, epidermal cells
Crystals	Not visible macroscopically	Calcium oxalate crystals present	Crystal fragments visible
Storage Materials	Not visible	Starch grains present in parenchyma cells	Starch granules observed
Diagnostic Features	Characteristic odour and bitter taste	Distinct cork cells and vascular tissues	Mixed fragments of fibres, vessels, and starch grains

Mechanistic Basis of Anticancer Activity

Antioxidant Potential

DPPH Free Radical Scavenging Method

A 0.1 mm solution of DPPH was freshly prepared using methanol as the solvent. Subsequently, 1.0 ml of the DPPH solution was mixed with 1.0 ml of the plant extract at different concentrations ranging from 50–300 µg/ml. The prepared mixtures were then kept under dark conditions at room temperature for approximately 30 minutes to allow the reaction to occur. After incubation, the absorbance values were recorded at 517 nm using methanol as the blank solution. Ascorbic acid served as the reference standard for comparison (Sahu SN, *et al*., 2025).

The radical scavenging activity was determined by calculating the percentage inhibition using the following equation:

$$\% \text{ Inhibition} = [Ac - As/Ac] \times 100$$

Where:

- Ac represents the absorbance of the control sample
- As represents the absorbance of the test sample

This assay is commonly employed to evaluate the antioxidant capacity of plant extracts based on their ability to neutralize free radicals.

ABTS Radical Cat ion Decolourization Assay

The ABTS radical cat ion was produced by combining a 7 mm ABTS solution with 2.45 mm potassium percolate, followed by incubation of the mixture in dark conditions at room temperature for approximately 12–16 hours. Prior to analysis, the resulting ABTS solution was diluted using ethanol until an absorbance value of 0.70 ± 0.02 was achieved at 734 nm.

For the assay procedure, 1.0 ml of the prepared ABTS reagent was mixed with 100 µl of the plant extract at varying concentrations. The reaction mixture was allowed to stand for 6 minutes, after which the absorbance was measured at 734 nm. Ascorbic acid was employed as the reference standard for antioxidant comparison (Sinan KI, *et al.,* 2003). This method is widely utilized to assess the free

radical scavenging potential of plant extracts based on their ability to reduce the ABTS radical cat ion and cause decolourization of the reaction mixture.

Hydrogen Peroxide (H_2O_2) Radical Scavenging Assay

The scavenging ability against hydrogen peroxide was evaluated using a 40 mm H_2O_2 solution prepared in phosphate buffer (50 mm, pH 7.4). For the assay, 1 ml of the plant extract at different concentrations was combined with 0.6 ml of the hydrogen peroxide solution. The reaction mixture was then incubated at room temperature for 10 minutes. Following incubation, the absorbance was measured at 230 nm using a blank solution consisting of phosphate buffer without hydrogen peroxide. Ascorbic acid was employed as the standard reference antioxidant compound (Sinan KI, Zengin G, 2021) [38]. This assay is commonly applied to determine the antioxidant potential of plant extracts based on their capacity to neutralize hydrogen peroxide and reduce oxidative stress.

Superoxide Anion Radical Scavenging Assay

The superoxide radical scavenging activity was assessed using a reaction system composed of 1 mL of nitro blue tetrazolium (NBT, 156 µm), 1 ml of NADH solution (468 µm), and 1 ml of the plant extract at various concentrations (Sushma B, *et al*., 2023). The reaction was started by the addition of 100 µl of phenazine methosulfate (PMS, 60 µm). The prepared mixture was incubated at 25°C for 5 minutes, after which the absorbance was recorded at 560 nm against an appropriate blank solution. A reduction in absorbance value was considered indicative of enhanced superoxide radical scavenging potential of the plant extract. This assay is widely used to evaluate the capacity of bioactive compounds to neutralize superoxide anions and thereby reduce oxidative stress–related cellular damage.

Hydroxyl Radical Scavenging Assay

The hydroxyl radical scavenging activity was evaluated using a reaction mixture consisting of 0.45 ml phosphate buffer (50 mm, pH 7.4), 0.15 ml $FeSO_4$–EDTA solution (10 mm), 0.15 ml deoxyribose (10 mm), 0.15 mL hydrogen peroxide (10 mm), and 0.525 ml distilled water. To this mixture, 0.15 ml of the plant extract at different concentrations was added. The reaction system was then incubated at 37°C for 1 hour.

Following incubation, 0.75 ml of 2.8% trichloroacetic acid and 0.75 ml of 1% thiobarbituric acid were introduced into the reaction mixture. The tubes were subsequently heated at 90°C for 15 minutes to allow colour development. After cooling, the absorbance was measured at 532 nm (Milosevic N, *et al*., 2022) [26].This method is commonly employed to determine the ability of plant extracts to scavenge hydroxyl radicals, thereby indicating their potential protective effect against oxidative damage.

Nitric Oxide (NO) Radical Scavenging Assay

The nitric oxide scavenging activity was determined using sodium nitroprusside as the nitric oxide donor. In this method, 0.5 ml of sodium nitroprusside solution (10 mm) prepared in phosphate buffer (pH 7.4) was combined with 0.5 ml of the plant extract at varying concentrations. The reaction mixture was then incubated at 25°C for 150 minutes.

Following incubation, 0.5 ml of the reaction solution was mixed with an equal volume of Gris's reagent containing 1% sulphanilamide, 0.1% naphthyl-ethylenediamine hydrochloride, and 2% phosphoric acid. The absorbance of the resulting chromosphere was measured at 540 nm (Vander Heiden MG, *et al*., 2021) [41]. Ascorbic acid was used as the reference antioxidant standard. This assay is commonly utilized to evaluate the capacity of plant extracts to inhibit nitric oxide radicals, thereby reflecting their potential anti-inflammatory and antioxidant properties.

Anti-inflammatory Activity Assay

The anti-inflammatory potential of the plant extract was evaluated using the bovine serum albumin (BSA) denaturation method. Initially, 200 µl of 1% BSA was mixed with 800 µl of chilled normal saline and allowed to dissolve completely with gentle agitation. Subsequently, 1.3 ml of phosphate-buffered saline (PBS) along with 0.2 ml of either the standard drug (diclofenac sodium) or the plant extract at different concentrations was added to the prepared BSA solution. For the control setup, distilled water was used to adjust the final volume to 5 ml.

The reaction mixtures were incubated at 37 ± 2°C for 30 minutes, followed by heating in a water bath maintained at 70 ± 5°C for 15 minutes. After cooling to room temperature, the absorbance was measured at 280 nm using a UV–Visible spectrophotometer, with PBS serving as the blank solution (Krishnamoorthy S, *et al*., 2025) [24].This method is widely employed to assess anti-inflammatory activity based on the ability of the test sample to inhibit protein denaturation.

% of inhibition = OD of Control- OD of Test/ OD of Control x 100

Cell Viability Evaluation by MTT Assay

The cytotoxic effect and cell viability were determined using the MTT assay method. Cells were initially cultured in 96-well micro plates and exposed to different concentrations of *Boerhavia diffusa* extract. Following an incubation period of 24–48 hours, MTT reagent was introduced into each well and allowed to react further under suitable incubation conditions (Zitvogel L, *et al*., 2021) [42]

During the assay, viable cells converted the MTT reagent into insoluble purple Formosan crystals. These crystals were subsequently dissolved using dimethyl sulfoxide (DMSO), and the absorbance was recorded at 570 nm with the help of a micro plate reader. The measured absorbance values were used to estimate cell viability and cytotoxic activity of the plant extract.

Apoptosis Analysis by Annex in V–FITC/PI Staining

The extent of apoptosis was evaluated using Annex in V–FITC and propidium iodide (PI) dual staining followed by flow cytometric analysis. Both treated and untreated control cells were harvested and washed thoroughly with phosphate-buffered saline (PBS). The cells were subsequently stained with Annex in V–FITC and propidium iodide to differentiate viable, early apoptotic, late apoptotic, and necrotic cell populations (Gunaseelan D, *et al.*, 2021).After staining, the samples were subjected to flow cytometer for quantitative analysis of apoptotic changes. This method enabled the identification and measurement of both early-stage and late-stage apoptotic cells induced by the treatment.

TUNEL Assay for Detection of DNA Fragmentation

DNA fragmentation associated with apoptosis was examined using the TUNEL assay technique. Cells were initially fixed and permeabilized to facilitate the entry of the reaction components. Subsequently, the samples were treated with the TUNEL reaction mixture, which labels fragmented DNA ends characteristic of apoptotic cells. The stained cells were then observed under a fluorescence microscope for the identification and visualization of apoptosis.

Capsize Activity Assay

The activities of caspase-3 and caspase-9, key enzymes involved in the apoptotic pathway, were determined using commercially available colorimetric or fluorometric assay kits following the manufacturer's recommended procedure. An elevation in capsize enzyme activity was considered indicative of apoptosis induction in the treated cells (James JM, *et al.*, 2025) [20].

Assessment of Mitochondrial Membrane Potential (ΔΨm)

Alterations in mitochondrial membrane potential were investigated using JC-1 fluorescent dye staining. After treatment, the cells were incubated with JC-1 dye and subsequently examined under a fluorescence microscope. The transition of fluorescence from red to green was interpreted as an indication of mitochondrial membrane depolarization, which is a characteristic event associated with apoptosis (Sahu SN, *et al.*, 2022) [33].

Cell Cycle Evaluation

For cell cycle analysis, cells were first fixed using ethanol and then stained with propidium iodide. The stained samples were analysed through flow cytometer to determine the distribution of cells across various phases of the cell cycle. The appearance of an increased sub-G1 population was considered indicative of apoptotic cell death.

Preclinical Investigations:

***In -Vitro* Antioxidant Activity of *Boerhavia diffusa*.**

The ethanol extracts obtained from the leaves and stems of *Boerhavia diffusa* demonstrated remarkable antioxidant activity in a concentration-dependent manner across several *in vitro* free radical scavenging models, including DPPH, ABTS, hydrogen peroxide, superoxide, hydroxyl radical, and nitric oxide assays. Among the tested samples, the leaf extract consistently exhibited lower IC_{50} values than the stem extract, indicating comparatively stronger antioxidant effectiveness, which may be attributed to its higher concentration of phenolic and flavonoid compounds. The observed activity was comparable to that of the standard antioxidant, ascorbic acid, emphasizing the potent natural antioxidant capacity of the plant.

A marked increase in antioxidant activity was observed at 300 µg/ml, where the leaf extract produced the highest inhibitory effects across nearly all assay systems. The recorded inhibition values for the leaf extract included 88.32 ± 1.66% in the DPPH assay, 91.29 ± 1.70% in the hydrogen peroxide scavenging assay, and 85.40 ± 1.53% in the nitric oxide assay, values that closely approached the activity of standard ascorbic acid, which demonstrated 96.09 ± 1.85% inhibition in nitric oxide scavenging at the same concentration.

The DPPH radical scavenging assay measures the ability of antioxidants to donate hydrogen atoms or electrons to stabilize free radicals. The strong activity exhibited by the leaf extract suggests the presence of potent antioxidant phytochemicals, particularly phenolic compounds and flavonoids, which are recognized for their free radical neutralizing properties. Similarly, significant activity in the ABTS assay (88.40 ± 1.88%) confirmed the broad-spectrum antioxidant potential of the extract against both hydrophilic and lipophilic radicals.

The hydrogen peroxide and superoxide radical scavenging assays further demonstrated concentration-dependent increases in antioxidant activity, indicating that the phytochemicals present in *Boerhavia diffusa* may function as reducing agents and metal-chelating compounds capable of preventing hydroxyl radical generation through Fenton-type reactions. The hydroxyl radical scavenging assay also revealed substantial activity, with the leaf extract showing 83.72 ± 1.55% inhibition, highlighting its potential to protect cellular biomolecules such as DNA, proteins, and lipids from oxidative damage caused by highly reactive oxygen species.

Table 3: Evaluation of Free Radical Scavenging Potential of *Boerhavia diffusa.*

Concentration µG	DPPH	ABTS	H2O2	Superoxide	OH	Nitric oxide
Stem extract (SE) 50 µg	12.31±0.38	12.51±0.50	14.51±0.55	16.62±0.51	13.24±0.41	17.60±0.44
SE 300 µg	72.37±1.40	80.11±1.52	80.72±1.52	82.73±1.57	78.40±1.37	85.40±1.53
Leaf extract (LE) 50 µg	24.39±0.51	18.62±0.81	24.65±0.60	18.52±0.67	16.52±0.55	17.60±0.44
LE 300 µg	88.32±1.66	88.40±1.88	91.29±1.70	87.50±1.69	83.72±1.55	85.40±1.53
Ascorbic acid 50 µg	30.68±0.89	25.13±0.83	36.52±0.89	28.62±0.80	25.33±0.60	34.41±0.70
Ascorbic acid 300 µg	95.47±1.85	92.70±1.82	96.40±1.75	93.45±1.78	90.19±1.70	96.09±1.85

Considerable nitric oxide scavenging activity was also observed, with both extracts displaying 85.40 ± 1.53% inhibition at 300 µg/ml. This finding suggests that the bioactive constituents of *Boerhavia diffusa* may help regulate nitric oxide-mediated oxidative stress, thereby reducing inflammation and tissue injury.

Overall, the leaf extract consistently demonstrated superior antioxidant performance compared to the stem extract in all evaluated assays. This enhanced activity may be related to the higher abundance of bioactive compounds such as flavonoids, tannins, alkaloids, and phenolic acids in the leaves. These findings are in agreement with previous reports indicating that different parts of *Boerhavia diffusa* possess significant antioxidant, anti-inflammatory, and antimicrobial activities due to their rich phytochemical composition.

Among the plant parts, the leaves appear to exhibit the greatest antioxidant and anti-inflammatory potential because of their elevated total phenolic and flavonoid content

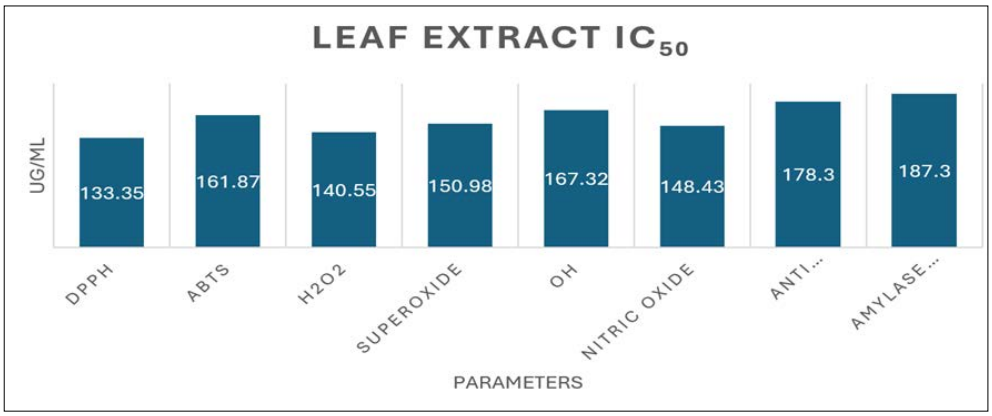

Fig 2: Bar diagram illustrating the IC_{50} values (µg/ml) obtained from different antioxidant and biological activity assays of the leaf extract of *Boerhavia diffusa.*

The updated and publication-ready IC_{50} chart has been prepared based on your provided values.

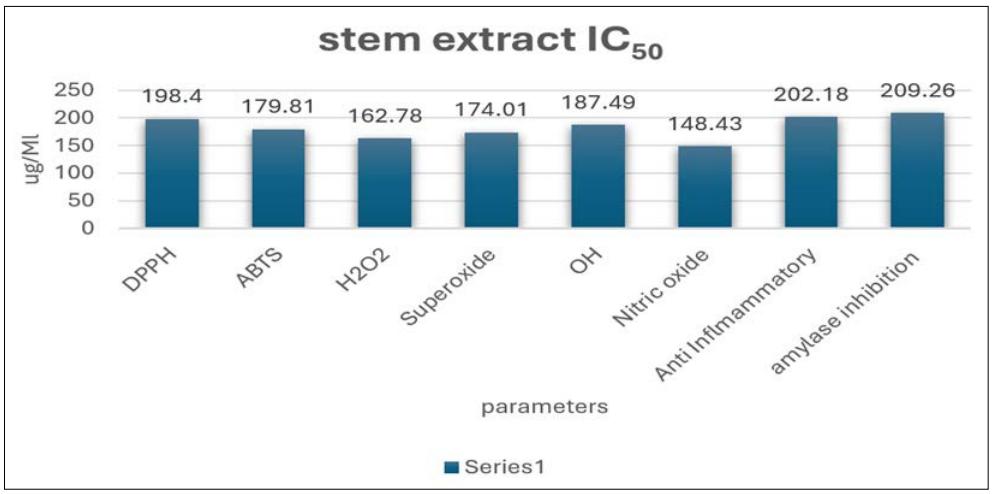

Fig 3: Bar chart depicting the IC_{50} values (µg/ml) recorded for different antioxidant and biological assays of the stem extract of *Boerhavia diffusa*.

Anti-inflammatory Activity of *Boerhavia diffusa* Extracts

The anti-inflammatory effects of leaf and stem extracts of *Boerhavia diffusa* were assessed by determining their percentage inhibition at different concentrations (50 and 300 µg/ml) and comparing the results with a standard anti-inflammatory agent such as ascorbic acid or diclofenac sodium. The findings presented in Table 2 revealed a concentration-dependent enhancement in anti-inflammatory activity for both extracts.

At the lower concentration of 50 µg/ml, the leaf extract produced an inhibition of 17.20 ± 0.45%, whereas the stem extract showed 13.52 ± 0.33% inhibition, both of which were considerably lower than the activity of the standard drug (34.12 ± 0.75%). A substantial increase in activity was observed at 300 µg/ml, where the leaf extract exhibited 79.90 ± 1.59% inhibition, demonstrating stronger activity than the stem extract, which showed 72.68 ± 1.33% inhibition. The activity of the leaf extract at this concentration approached that of the standard compound, which displayed 97.19 ± 1.77% inhibition.

The IC_{50} values further supported these observations. The leaf extract showed an IC_{50} value of 178.30 µg/ml, indicating greater anti-inflammatory potency compared to the stem extract, which exhibited an IC_{50} value of 202.18 µg/ml. In contrast, the standard drug demonstrated a lower IC_{50} value of 98.01 µg/ml, confirming its strong reference activity.

The comparatively superior anti-inflammatory effect observed in the leaf extract may be attributed to its higher concentration of bioactive phytochemicals. These findings are consistent with previous studies on *Boerhavia diffusa* that have reported notable *in vitro* and *in vivo* anti-inflammatory properties. Similarly, Ozay and Keleş (2024) demonstrated that extracts of the plant significantly inhibited nitric oxide generation and reactive oxygen species production in LPS-stimulated macrophages, thereby supporting the anti-inflammatory potential of the species.

Table 4: Inhibitory Percentage of Anti-inflammatory Activity Exhibited by *Boerhavia diffusa* Extracts.

Concentration µg	Leaf extract	Stem extract	Standard
50	17.20±0.45	13.52±0.33	34.12±0.75
300	79.90±1.59	72.68±1.33	97.19±1.77
IC_{50}Value µg/Ml	178.30	202.18	98.01

***In - Vivo* Studies**

Apoptosis-Inducing Potential of *Boerhavia diffusa*

Boerhavia diffusa (Punarnava) demonstrates notable anticancer properties through its ability to trigger apoptosis, a programmed and tightly regulated form of cell death essential for the removal of abnormal or malignant cells. In

contrast to necrosis, apoptosis occurs in an organized and energy-dependent manner, thereby minimizing inflammatory responses and restricting tumour progression

The apoptosis-inducing activity of the plant is mainly associated with the intrinsic mitochondrial pathway. Phytoconstituents such as flavonoids and retinoid are known to influence the expression of apoptotic regulatory proteins by increasing the ratio of pro-apoptotic Box to anti-apoptotic Bcl-2 proteins. This alteration promotes permeabilization of the mitochondrial membrane, resulting in the release of cytochrome *c* into the cytoplasm.

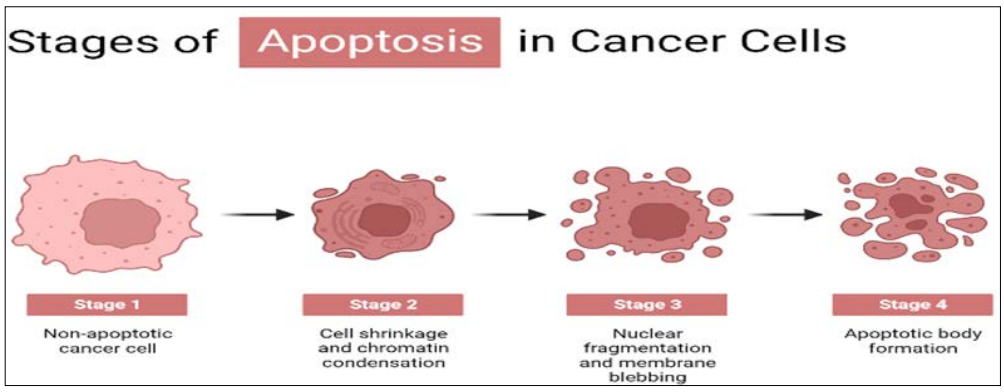

Fig 4: Apoptosis-inducing mechanism of *Boerhavia diffusa* in cancer cells

Released cytochrome *c* subsequently participates in the formation of the apoptosome complex, which activates caspase-9 and thereafter initiates caspase-3 activation, a major executioner enzyme involved in DNA fragmentation and apoptotic cell death. In addition, *Boerhavia diffusa* has been reported to modulate tumour suppressor proteins such as p53, there by further enhancing apoptotic responses in cancer cells.

The antioxidant properties of the plant also contribute significantly to apoptosis regulation by modulating intracellular oxidative stress. Through the regulation of reactive oxygen species (ROS), the plant may enhance apoptotic signalling pathways in malignant cells while simultaneously protecting normal cells from excessive oxidative injury.

Mechanistic Overview of Apoptosis Induction by *Boerhavia diffusa*

- Up regulation of pro-apoptotic Box expression accompanied by suppression of anti-apoptotic Bcl-2 levels
- Loss of mitochondrial membrane integrity and depolarization
- Release of cytochrome *c* from mitochondria into the cytoplasm
- Sequential activation of caspase-9 followed by caspase-3 signalling pathways
- Induction of DNA fragmentation leading to apoptotic death of cancer cells.

Therapeutic Relevance in Cancer Management

The apoptosis-promoting activity of *Boerhavia diffusa* emphasizes its promise as a potential anticancer therapeutic agent, particularly because many malignant cells develop resistance to apoptotic mechanisms. By reactivating programmed cell death pathways, Punarnava may contribute to:

- Targeted destruction of tumour cells with minimal effect on normal tissues
- Suppression of tumour progression and cellular proliferation
- Improvement of overall anticancer therapeutic outcomes.

Suppression of Tumour Progression and Metastatic Spread by *Boerhavia diffusa*

Boerhavia diffusa (Punarnava) has shown promising activity in inhibiting tumour development and reducing metastatic dissemination through a variety of molecular and cellular mechanisms. Cancer progression is characterized by abnormal and uncontrolled cellular proliferation, formation of new blood vessels (angiogenesis), and the capacity of malignant cells to invade adjacent tissues and migrate to distant organs.

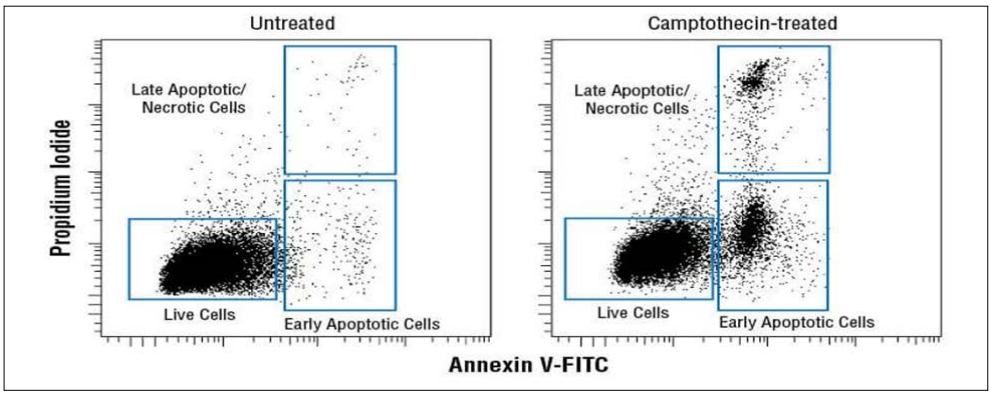

Fig 5: Apoptosis assay techniques employed for the evaluation of *Boerhavia diffusa.*

Anti-antigenic Effects of *Boerhavia diffusa* in Tumour Suppression

The pharmacologically active constituents present in *Boerhavia diffusa*, especially flavonoids and retinoid compounds, are known to interfere with multiple stages of tumour progression. A major anticancer mechanism of the plant involves suppression of angiogenesis, the process through which new blood vessels are formed to supply nutrients and oxygen to growing tumours. Studies have indicated that *Boerhavia diffusa* may inhibit the expression of vascular endothelial growth factor (VEGF) along with associated signalling pathways. By reducing antigenic activity, the plant restricts tumour vascularization, thereby limiting nutrient supply and ultimately suppressing tumour growth and expansion.

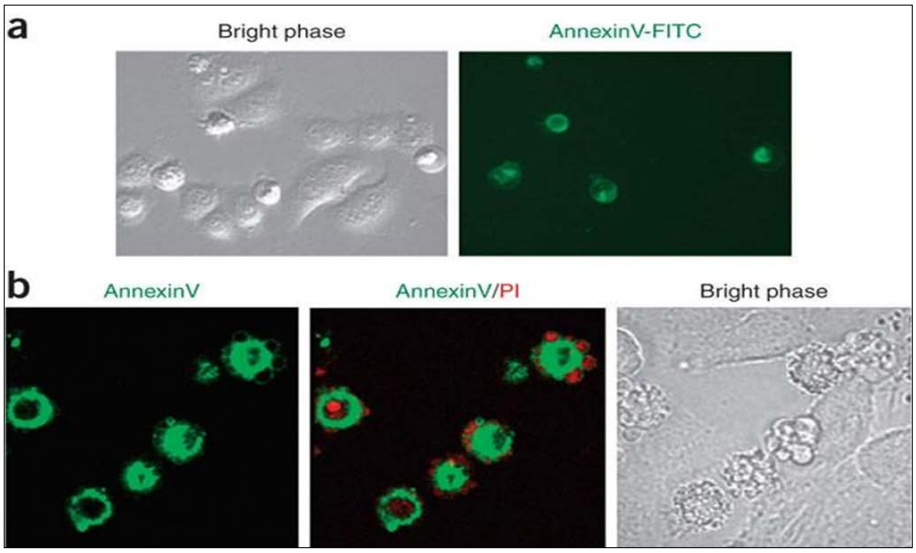

Fig 6: Detection of early apoptotic cells showing Annex in V positivity Inhibition of Tumour Invasion and Metastatic Signalling by *Boerhavia diffusa*

Boerhavia diffusa also exhibits anti-metastatic activity by inhibiting tumour invasion and the spread of cancer cells. One of the important mechanisms involves suppression of matrix metalloproteinases (MMPs), particularly MMP-2 and MMP-9, enzymes that facilitate degradation of the extracellular matrix during tumour invasion. By limiting extracellular matrix breakdown, the plant reduces the migratory and invasive capacity of malignant cells.

In addition, the plant extract has been reported to modulate critical intracellular signalling pathways such as PI3K/Akt and NF-κB, both of which play essential roles in cellular survival, proliferation, inflammation, and metastasis. Regulation of these pathways leads to decreased tumour cell growth and enhances the sensitivity of cancer cells to apoptotic mechanisms.

Moreover, the antioxidant and anti-inflammatory activities of *Boerhavia diffusa* may contribute to modification of the tumour microenvironment, thereby creating conditions that are less favourable for tumour development, progression, and metastatic dissemination.

Mechanistic Overview of Antitumor and Anti-metastatic Actions of *Boerhavia diffusa*

- Down regulation of VEGF signalling leading to suppression of angiogenesis
- Inhibition of MMP-2 and MMP-9 enzymes, thereby limiting tumour invasion and metastatic spread
- Regulation of PI3K/Akt and NF-κB signalling pathways associated with cancer progression
- Reduction in tumour cell growth and proliferative activity
- Modification of the tumour microenvironment to create conditions unfavourable for cancer development and dissemination

Therapeutic Importance in Cancer Management

The capacity of *Boerhavia diffusa* to suppress tumour progression as well as metastatic dissemination underscores its potential as a multi-targeted anticancer agent. Through modulation of several molecular pathways associated with cancer development, the plant may contribute to:

- Restriction of tumour growth and expansion
- Prevention of metastatic spread and secondary tumour development
- Improvement of the therapeutic efficacy of conventional anticancer treatments

Role of *Boerhavia diffusa* in Siddha Medicine

Siddha Perspective on Cancer and Neoplastic Disorders

In Siddha medicine, conditions comparable to cancer are described using terms such as “Putru,” “Kuttam,” and other forms of abnormal tissue growth. These disorders are considered manifestations of prolonged internal imbalance and pathological alterations within the body rather than a single isolated disease entity. Siddha philosophy attributes the development of such neoplastic conditions to disturbances in the three vital humours—Vali (Vatham), Azhal (Pitham), and Iyyam (Kapham).

According to Siddha concepts, severe derangement of these humours disrupts normal physiological and cellular activities, resulting in abnormal tissue proliferation, accumulation of toxic metabolic substances known as “Ama” or “Kazhichal,” and impairment of natural body functions. Factors such as unhealthy dietary habits, environmental influences, chronic inflammatory states, and weakened immune responses are considered important contributors to disease initiation and progression.

The Siddha approach to managing cancer-like disorders emphasizes restoration of humoural balance, detoxification

of accumulated toxins, rejuvenation of tissues, and enhancement of the body's defence mechanisms. Traditional herbal medicines, including Boerhavia diffusa, are extensively utilized for these purposes because of their reputed detoxifying, rejuvenating, and immune-supportive properties.

Therapeutic Uses of *Boerhavia diffusa* in Siddha Medicine

In Siddha therapeutics, *Boerhavia diffusa* is highly valued for its rejuvenative, detoxifying, and anti-inflammatory effects. The herb is traditionally employed to regulate abnormal tissue proliferation, support metabolic balance, and strengthen the body's immune defence system.

Additionally, the plant is widely used for maintaining healthy liver and kidney functions, thereby facilitating detoxification and promoting overall recovery and disease management. Its multifaceted therapeutic actions make it an important medicinal herb in Siddha formulations for chronic and degenerative disorders.

Integration with Modern Oncology: Complementary and Alternative Therapeutic Perspectives

The application of *Boerhavia diffusa* in contemporary oncology is increasingly being explored through an integrative medical approach, where traditional herbal therapies are combined with conventional cancer treatments to improve patient care and quality of life. Within traditional systems such as Siddha medicine, the plant has historically been regarded as a rejuvenating remedy capable of restoring physiological balance and supporting the body during chronic diseases.

As a complementary therapeutic agent, *Boerhavia diffusa* may assist in alleviating adverse effects associated with chemotherapy and radiotherapy, including oxidative stress, inflammation, fatigue, and immune suppression. The phytochemical constituents of the plant are believed to enhance immune responses and support overall systemic health, which may prove beneficial for individuals undergoing cancer treatment.

From an alternative medicine perspective, experimental and preclinical investigations have demonstrated that the plant possesses bioactive compounds capable of inhibiting tumour growth and reducing metastatic progression. Nevertheless, these observations are primarily derived from laboratory-based studies, and current clinical evidence remains insufficient to support the use of the plant as a substitute for established oncological therapies.

Therefore, incorporation of *Boerhavia diffusa* into cancer management should be undertaken carefully and only under appropriate medical guidance. At present, its most suitable role appears to be as a supportive adjunct within evidence-based oncology, where it may complement standard therapeutic strategies while additional clinical research continues to evaluate its safety, efficacy, and therapeutic potential in humans.

Synergistic Interaction with Conventional Cancer Therapies

The concurrent use of *Boerhavia diffusa* alongside standard oncological treatments is gaining attention because of its possible ability to enhance therapeutic efficacy. In integrative cancer care, synergism refers to the capacity of the plant's bioactive constituents to act in combination with therapies such as chemotherapy and radiotherapy, thereby improving treatment outcomes while minimizing adverse effects.

Experimental studies have suggested that phytochemicals present in *Boerhavia diffusa* may increase the sensitivity of cancer cells to anticancer drugs. Such interactions could contribute to improved suppression of tumour growth through enhanced induction of apoptosis and inhibition of malignant cell proliferation. Simultaneously, the antioxidant and anti-inflammatory properties of the plant may provide protective effects against damage to normal tissues caused by conventional cancer treatments.

Another promising aspect is its potential role in overcoming drug resistance, which remains a major obstacle in effective cancer therapy. Certain constituents of the plant are believed to modulate cellular signalling pathways associated with resistance mechanisms, thereby possibly improving the responsiveness of tumour cells to standard therapeutic agents. Furthermore, the immune modulatory activity of the plant may help strengthen host immune defence, supporting the overall anticancer response.

Despite these encouraging observations, most available evidence is currently limited to *in vitro* and preclinical investigations, while substantial clinical validation in humans remains insufficient. Therefore, *Boerhavia diffusa* should presently be regarded only as a supportive adjunct to conventional cancer therapy and used under professional medical supervision. Additional clinical studies are required to establish its synergistic efficacy, determine optimal dosage regimens, and confirm its long-term safety when combined with established oncological treatments.

Safety, Toxicological Profile, and Dosage Considerations of *Boerhavia diffusa*

Safety Profile

Boerhavia diffusa (Punarnava) is widely regarded as a relatively safe medicinal herb when administered within recommended therapeutic limits. The plant has been extensively utilized for centuries in traditional medical systems such as Siddha medicine for the management of various chronic ailments. Experimental investigations conducted so far have generally reported an absence of serious adverse effects at standard therapeutic doses.

Toxicity Considerations

Current scientific evidence suggests that the plant possesses a low toxicity profile. Experimental animal studies have demonstrated that administration of moderate to comparatively high doses does not produce significant toxic manifestations or severe harmful effects. Nevertheless, excessive consumption or prolonged unsupervised usage may occasionally result in mild adverse reactions, including gastrointestinal discomfort or disturbances in fluid and electrolyte balance. Since comprehensive human toxicity studies remain limited, cautious and medically supervised use is recommended.

Dosage Recommendations and Precautionary Measures for *Boerhavia diffusa*

Recommended Dosage Forms

The appropriate dosage of *Boerhavia diffusa* varies according to the type and concentration of the formulation being used:

- **Powder (Churna):** approximately 3–6 g daily
- **Decoction (Kashayam):** generally 20–50 mL per day
- **Standardized Extracts:** dosage depends on extract potency and formulation composition

For chronic illnesses and serious conditions such as cancer, the herb should preferably be administered under the guidance of a qualified healthcare practitioner or Siddha physician, particularly during prolonged treatment.

Precautions and Safety Measures

- Use during pregnancy and lactation should be avoided unless specifically recommended by a medical professional.
- Individuals with pre-existing kidney or liver disorders are advised to seek medical consultation before using the herb.
- The plant may interact with certain medications, especially diuretics and other long-term therapeutic drugs.
- Extended use should be periodically monitored to ensure safety and prevent possible adverse effects.

Overall, *Boerhavia diffusa* demonstrates a favourable safety profile and comparatively low toxicity when consumed appropriately. Nevertheless, accurate dosage regulation, professional supervision, and additional clinical investigations remain essential to ensure its safe and effective application in modern therapeutic practice.

Discussion and Critical Evaluation

The present review emphasizes the promising therapeutic role of *Boerhavia diffusa* (Punarnava) as an integrative approach in cancer therapy by combining the principles of Siddha medicine with contemporary biomedical research. The integration of traditional medicinal knowledge with modern molecular insights highlights the growing importance of multi-targeted phytotherapeutics in managing the complex biological nature of cancer.

From the Siddha viewpoint, cancer, referred to as Putru Noi, is regarded not simply as a localized abnormality but as a systemic disorder resulting from disturbances in the three humours—Vatham, Pitham, and Kapham—along with impaired metabolic activity (Agni) and the accumulation of toxic metabolic products (Ama). Interestingly, this traditional concept parallels current scientific understanding of cancer as a multifactorial condition associated with oxidative stress, chronic inflammation, metabolic imbalance, and immune dye regulation. The classification of Punarnava as a Kayakalpa or rejuvenate herb in Siddha medicine reflects its traditional role in restoring systemic harmony and strengthening bodily functions, concepts that correspond closely with supportive care and immune restoration strategies in modern oncology.

At the molecular level, *Boerhavia diffusa* has demonstrated significant anticancer potential through regulation of several critical signalling pathways, including NF-κB, PI3K/Akt, and mitochondrial-mediated apoptotic mechanisms. Such multi-target activity is particularly important because tumour development and progression involve interconnected and overlapping cellular pathways. Unlike conventional chemotherapeutic drugs that generally act on single molecular targets, the phytoconstituents present in the plant, including punarnavine, boeravinones, and flavonoids, exert diverse biological effects by simultaneously modulating inflammation, cellular proliferation, apoptosis, angiogenesis, and metastasis. These pleiotropic properties strengthen the scientific basis for considering herbal medicines as complementary agents in cancer management.

Despite the encouraging preclinical evidence, several important limitations remain. A major concern is that most studies demonstrating the anticancer properties of *Boerhavia diffusa* have been conducted using *in vitro* experimental models or animal systems, while clinical evidence in human subjects is still inadequate. Consequently, questions remain regarding the translation of these findings into clinical practice, particularly with respect to bioavailability, pharmacokinetic behaviour, therapeutic dosage, and long-term safety.

Another challenge involves variability in phytochemical composition, which may differ according to geographical origin, environmental conditions, harvesting period, and processing methods. Such variability complicates standardization and reproducibility of herbal formulations, making it difficult to achieve consistent therapeutic outcomes. The development of standardized extracts and validated quality-control parameters is therefore essential for future clinical application.

An additional issue is the limited availability of rigorous clinical trials investigating the use of *Boerhavia diffusa* as an adjunct to standard cancer therapies. Although preliminary findings indicate that the plant may help reduce chemotherapy-associated toxicity and support immune function, carefully designed randomized controlled studies are required to establish its efficacy, safety profile, and possible herb–drug interactions. Particular attention should be given to interactions with anticancer agents metabolized through hepatic pathways to avoid undesirable adverse effects.

From a pharmacological perspective, the synergistic interactions among multiple phytoconstituents represent both a therapeutic advantage and a scientific challenge. While synergism may enhance the overall anticancer effect, it also complicates the identification of individual active compounds and their precise molecular mechanisms. Advanced scientific approaches such as metabolomics, systems biology, and network pharmacology may therefore provide valuable insights into the complex interactions of these bioactive constituents and support the development of optimized therapeutic formulations.

Potential Role of *Boerhavia diffusa* in Integrative Oncology

Within the field of integrative oncology, *Boerhavia diffusa* appears to have considerable potential as a supportive therapeutic agent rather than an independent replacement for conventional cancer treatment. Its therapeutic value may be especially beneficial in:

- Strengthening and modulating immune function
- Lowering inflammation and minimizing oxidative stress
- Reducing adverse effects associated with chemotherapy and radiotherapy
- Enhancing overall well-being and quality of life in cancer patients

Furthermore, the incorporation of Siddha medicinal practices into contemporary healthcare systems should be

supported by rigorous scientific validation and evidence-based research. Establishing a connection between traditional medicinal knowledge and modern clinical investigation may contribute to the development of standardized, reliable, and safe herbal therapies with improved therapeutic effectiveness.

Concluding Remarks on the Discussion

In conclusion, *Boerhavia diffusa* serves as an important illustration of how traditional medicinal systems can contribute valuable insights to contemporary therapeutic development. Existing preclinical investigations strongly indicate its potential anticancer properties; however, successful application in clinical settings requires comprehensive scientific validation, proper standardization of herbal extracts, and carefully designed clinical studies.

Moreover, effective translation of its therapeutic potential into modern healthcare demands collaborative efforts among pharmacologists, oncologists, researchers, and experts in traditional medicine. Such interdisciplinary approaches are essential for accurately evaluating its efficacy, safety, and mechanisms of action. The future prospects of *Boerhavia diffusa* are closely linked to the advancement of evidence-based integrative oncology, where the integration of traditional knowledge with modern biomedical science may support the development of safer, more comprehensive, and patient-centred cancer treatment strategies.

Future Perspectives and Research Directions

- Performing comprehensive and well-structured clinical studies to confirm the therapeutic efficacy and safety profile of *Boerhavia diffusa* in human populations.
- Isolating and characterizing the specific phytochemical constituents responsible for the plant's pharmacological and anticancer activities through advanced analytical techniques.
- Establishing standardized, validated, and quality-assured herbal formulations to achieve consistent therapeutic performance and reproducible clinical outcomes.
- Exploring innovative drug delivery strategies, particularly nanotechnology-based delivery systems, to improve bioavailability, targeted delivery, and therapeutic efficiency of the bioactive compounds.
- Encouraging the integration of *Boerhavia diffusa* into evidence-based oncology by promoting multidisciplinary research that combines traditional Siddha knowledge with modern biomedical and clinical sciences.

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