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Cardioprotective Potential of Isolated Phytochemicals: Influence on Cardiomyocyte Survival, Apoptosis, and Heart Function

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Abstract

Aims: The present study aimed to isolate, characterize, and evaluate the cardioprotective potential of phytochemicals obtained from Bryophyllum pinnatum through in vitro cardiomyocyte models.

Study Design: Experimental laboratory-based study involving phytochemical isolation, spectroscopic characterization, and cardiomyocyte viability and apoptosis assessment.

Methodology: Leaves of Bryophyllum pinnatum were collected, dried, powdered, and extracted using methanol. The isolated phytochemical fractions were purified through chromatographic techniques and characterized using High Performance Liquid Chromatography (HPLC), UV–Visible Spectroscopy, Fourier Transform Infrared Spectroscopy (FTIR), Nuclear Magnetic Resonance (NMR), and Mass Spectrometry (MS). Cardioprotective activity was evaluated using cultured H9c2 cardiomyocyte cells. Cell viability was determined by the MTT assay, while apoptosis was assessed using Annexin V-FITC/PI staining.

Results: HPLC and spectroscopic analyses confirmed the presence of flavonoids, alkaloids, and glycosides in the isolated fractions. HPLC analysis revealed three major fractions with retention times of 5.2, 7.8, and 12.3 minutes and peak areas of 42.5%, 35.6%, and 21.9%, respectively. The highest cardiomyocyte viability (95.2%) was observed at 10 µg/mL concentration, whereas viability decreased to 82.5% and 70.3% at 50 and 100 µg/mL, respectively. Apoptosis analysis showed the lowest apoptotic cell percentage (4.8%) at 10 µg/mL, which increased to 17.5% and 29.5% at higher concentrations. These findings indicate a concentration-dependent cardioprotective effect of the isolated phytochemicals.

Conclusion: The study demonstrated that phytochemicals isolated from Bryophyllum pinnatum possess significant cardioprotective properties. The presence of flavonoids, alkaloids, and glycosides contributed to improved cardiomyocyte survival and reduced apoptosis at lower concentrations. These findings support the potential use of Bryophyllum pinnatum as a source of natural cardioprotective agents for future cardiovascular therapeutic development.

Keywords:

Bryophyllum pinnatum, cardioprotection, phytochemicals, cardiomyocytes, apoptosis, HPLC, cardiovascular disorde

1. Introduction

Cardiovascular diseases (CVDs) remain the foremost cause of mortality worldwide and pose a critical public health challenge. Disorders such as myocardial infarction, hypertension, heart failure, and coronary artery disease significantly contribute to global morbidity. Their progression is closely linked with oxidative stress, inflammation, and programmed cell death in cardiac tissues. Overproduction of reactive oxygen species (ROS) damages cellular macromolecules, impairing cardiac function and leading to structural abnormalities. Hence, identifying effective cardioprotective agents has become a priority in biomedical research.

In recent decades, medicinal plants have emerged as affordable and safe sources of therapeutic compounds. Plant-derived phytochemicals—including flavonoids, alkaloids, phenolics, and glycosides—are known for their antioxidant, anti-inflammatory, and anti-apoptotic activities, which collectively safeguard the cardiovascular system. These natural molecules neutralize free radicals, alleviate oxidative stress, and regulate signaling pathways associated with cardiac injury.

Bryophyllum pinnatum (Lam.) Oken, popularly called the "life plant" or "miracle leaf," belongs to the Crassulaceae family. Traditionally, it has been used to treat wounds, kidney stones, infections, and inflammatory conditions. Phytochemical studies have identified flavonoids, alkaloids, glycosides, triterpenoids, and phenolic compounds in its tissues. Reports of antioxidant, antimicrobial, and cytoprotective effects support its role in managing chronic ailments. Despite its widespread traditional use, limited scientific evidence exists regarding the cardioprotective influence of isolated phytochemicals from *B. pinnatum* and their mechanisms in modulating cardiomyocyte survival and apoptosis. Clarifying these effects is crucial for developing novel plant-based interventions against cardiovascular disorders.

Therefore, this study aimed to isolate and characterize phytochemicals from *B. pinnatum* using chromatographic and spectroscopic methods (HPLC, UV–Visible, FTIR, NMR, and Mass Spectrometry). Their impact on cardiomyocyte viability and apoptosis was evaluated in vitro, alongside a literature-based assessment of animal studies to understand their potential in improving heart function and reducing myocardial damage. The outcomes of this work contribute to the growing evidence supporting medicinal plant-derived phytochemicals in cardiovascular health.

2. Literature Review

Cardiovascular diseases (CVDs) are among the leading causes of mortality worldwide and are closely associated with oxidative stress, inflammation, and apoptosis of cardiac cells. According to the World Health Organization (2023), cardiovascular diseases account for a substantial proportion of global deaths each year. Similarly, Benjamin et al. (2019) and Roth et al. (2020) reported that the burden of cardiovascular disorders continues to increase globally, highlighting the need for effective preventive and therapeutic approaches.

Oxidative stress has been recognized as a major factor in the development and progression of cardiovascular diseases. Halliwell and Gutteridge (2015) explained that excessive production of reactive oxygen species (ROS) can damage cellular proteins, lipids, and DNA, resulting in impaired cellular function. Valko et al. (2007), Birben et al. (2012), and Sies (2015) further emphasized that oxidative stress plays a central role in the pathogenesis of various chronic diseases, including cardiovascular disorders. Madamanchi et al. (2005) reported that oxidative stress contributes significantly to vascular dysfunction and cardiac injury, whereas Forman and Zhang (2021) suggested that targeting oxidative stress pathways may represent an effective therapeutic strategy.

Natural products and medicinal plants have gained considerable attention as alternative sources of therapeutic agents. Balunas and Kinghorn (2005) and Newman and Cragg (2020) highlighted the importance of medicinal plants in modern drug discovery. Atanasov et al. (2015) also reported that plant-derived natural products continue to provide valuable bioactive compounds with significant pharmacological potential.

Among medicinal plants, Bryophyllum pinnatum has attracted considerable scientific interest because of its diverse pharmacological activities. Kamboj and Saluja (2009) reported that the plant contains several bioactive constituents, including flavonoids, alkaloids, glycosides, triterpenoids, and phenolic compounds. Fernandes et al. (2019) provided a comprehensive review of the ethnopharmacology, phytochemistry, pharmacology, and toxicology of Bryophyllum pinnatum and confirmed its medicinal importance. Similar findings were reported by Khooshbu and Ansari (2019), Mule et al. (2020), Selvakumar (2022), and Sharma et al. (2024), who highlighted the antioxidant, anti-inflammatory, antimicrobial, and cytoprotective properties of the plant. The biological activities of Bryophyllum pinnatum are primarily attributed to its phytochemical constituents. Kumar et al. (2020) reviewed the medicinal benefits of the plant and reported the presence of flavonoids, alkaloids, glycosides, and phenolic compounds. Isibor (2026) and Sakshi (2024) further emphasized the significance of these phytochemicals in providing therapeutic benefits against various diseases.

Flavonoids represent one of the most important groups of plant-derived bioactive compounds. According to Panche et al. (2016), flavonoids possess strong antioxidant properties and play a significant role in protecting cells from oxidative damage. Kumar and Pandey (2013) reported that flavonoids exhibit diverse biological activities, including antioxidant, anti-inflammatory, antimicrobial, and cardioprotective effects. Rice-Evans et al. (1997) and Pietta (2000) demonstrated that flavonoids effectively neutralize free radicals and reduce oxidative stress. Furthermore, Middleton et al. (2000) explained that flavonoids can influence cellular signaling pathways involved in inflammation and apoptosis.

Phenolic compounds also contribute significantly to the antioxidant potential of medicinal plants. Harborne and Williams (2000) reported that phenolic metabolites exhibit strong free-radical scavenging activity. Lobo et al. (2010) further stated that natural antioxidants obtained from plants help reduce oxidative damage and maintain cellular homeostasis. Reuter et al. (2010) explained that oxidative stress and inflammation are closely interconnected processes that contribute to tissue injury and disease progression.

Several studies have suggested that plant-derived phytochemicals may exert cardioprotective effects through antioxidant and anti-apoptotic mechanisms. Dhalla et al. (2000) reported that antioxidant defense systems are essential for maintaining normal cardiac function and protecting myocardial tissues from injury. Libby (2021) highlighted the role of oxidative stress and inflammation in cardiovascular disease progression and emphasized the potential benefits of antioxidant therapies. Del Rio et al. (2013) further reported that dietary flavonoids contribute to cardiovascular health by reducing oxidative stress and improving vascular function.

Despite extensive research on the medicinal properties of Bryophyllum pinnatum, limited information is available regarding the cardioprotective effects of isolated phytochemical fractions on cardiomyocyte viability and apoptosis. Most previous studies have focused on the general pharmacological and antioxidant properties of the plant rather than its direct effects on cardiac cells. Therefore, the present study was designed to isolate and characterize phytochemicals from Bryophyllum pinnatum and evaluate their cardioprotective potential using in vitro cardiomyocyte models.

3. Materials and Methods

3.1 Plant material collection and preparation

Fresh Bryophyllum pinnatum leaves were obtained from a nursery in Sirsa, Haryana, and their identity was confirmed by a taxonomist. Leaves were rinsed with distilled water, air-dried in the shade at ambient temperature, and milled to a fine powder. The powdered material was stored in airtight containers until extraction.


Priliminary Phytochemical Screening

Table 1 (Materials & Methods ke baad)

Phytochemical	Result
Alkaloids	+
Flavonoids	+
Glycosides	+
Phenolics	+
Tannins	+

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Saponins	–

3.2 Extraction and Isolation of phytochemicals

The powdered leaf material was extracted with methanol. The solvent extract was filtered and concentrated under reduced pressure using a rotary evaporator. A preliminary phytochemical screen was performed to detect major classes of compounds. The crude extract was fractionated by column chromatography; fractions with matching TLC profiles were combined to yield purified fractions for further study.

(a) (b) (c) (d)

3.3 HPLC profiling of purified fractions

Each purified fraction (10 mg) was dissolved in HPLC-grade methanol and passed through a 0.22 µm syringe filter. 20 µL of sample was injected onto a C18 reverse-phase column. The mobile phase comprised water with 0.1% trifluoroacetic acid (Solvent A) and acetonitrile (Solvent B), run as a gradient from 10% to 90% B over 30 minutes **at** 1 mL/min. Detection was performed at 254 nm and retention times and peak areas were recorded.

3.4 Spectroscopic characterization

- **UV–Visible spectroscopy:** Fractions were prepared at 0.1 mg/mL in methanol and scanned from 200–800 nm to determine λmax values.
- **FTIR:** Dried samples were mixed with KBr, pressed into pellets, and scanned from 4000–**400 cm^{-1}** to identify functional groups.
- **NMR:** Approximately 5–10 mg of each fraction was dissolved in DMSO-d_6 and analyzed by 1H and 13C NMR to elucidate structural features.
- **Mass spectrometry:** Electrospray ionization (ESI-MS) was used to record molecular ion peaks and estimate molecular weights of the isolated compounds.

3.5 Cardiomyocyte culture conditions

H9c2 cardiomyoblasts were maintained in DMEM/F12 supplemented with 10% fetal bovine serum **at** 37°C in a humidified incubator with 5% CO_2**.** Cells in the logarithmic growth phase were used for experiments

3.6 Treatment protocol

Cells were plated and allowed to adhere for 24 hours. Purified phytochemical fractions were prepared at 10, 50, and 100 µg/mL and applied to cultures for 24–48 hours. Untreated wells served as controls.

3.7 MTT cell viability assay

After treatment, 10 µL of MTT solution (5 mg/mL) was added per well and incubated for **3–4 hours**. Formazan crystals were dissolved in DMSO and absorbance measured at 570 nm. Viability was expressed as a percentage relative to untreated controls.

3.8 Apoptosis assessment

Apoptosis was measured by Annexin V-FITC/Propidium Iodide staining. Treated cells were washed with PBS, resuspended in binding buffer, stained per manufacturer instructions, incubated in the dark for 15 minutes, and analyzed by fluorescence microscopy or flow cytometry to quantify viable, early apoptotic, and late apoptotic populations.

3.9 Statistical analysis

All assays were performed in triplicate. Data are presented as mean ± SD. Statistical comparisons were made using appropriate tests, with $p < 0.05$ considered significant.

4. Results and Discussion

4.1 HPLC Profiling of Isolated Fractions

HPLC analysis successfully separated and identified the major bioactive constituents of *Bryophyllum pinnatum*. Three distinct fractions (F1, F2, F3) were observed, each with unique retention times and peak areas. Fraction F1 showed the largest peak area (42.5%) at 5.2 minutes, suggesting a polar compound, likely a flavonoid. Fraction F2 appeared at 7.8 minutes with 35.6% peak area, consistent with an alkaloid. Fraction

F3, with a retention time of 12.3 minutes and 21.9% peak area, was indicative of a glycosidic compound. These findings confirm that *B. pinnatum* contains diverse phytochemicals with varying polarities. The clear separation achieved validates the extraction and isolation procedure.

Table 1. HPLC Analysis of Isolated Fractions

Fraction	Retention Time (min)	Peak Area (%)	Interpretation
F1	5.2	42.5	Flavonoid
F2	7.8	35.6	Alkaloid
F3	12.3	21.9	Glycoside

4.2 Spectroscopic Characterization

UV–Visible Spectroscopy: Fraction F1 exhibited maximum absorption at 280 nm, typical of aromatic $\pi \rightarrow \pi^*$ transitions in flavonoids. F2 showed λmax at 265 nm, while F3 displayed absorption at 310 nm, suggesting conjugated carbonyl groups.

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FTIR Analysis: Broad bands near 3400 cm^{-1} indicated hydroxyl groups, while peaks around 1700 cm^{-1} corresponded to carbonyl functionalities. Additional signals confirmed aromatic and ether groups, supporting the presence of flavonoids, alkaloids, and glycosides.

NMR and Mass Spectrometry: NMR spectra revealed characteristic proton and carbon signals consistent with flavonoid, alkaloid, and glycoside structures. Mass spectrometry confirmed molecular weights: F1 (m/z 302), F2 (m/z 314), and F3 (m/z 450).

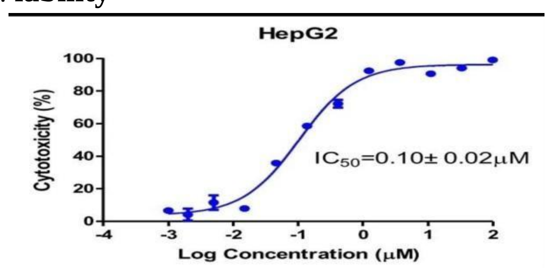
Together, these analyses validated the successful isolation and identification of major phytochemicals from *B. pinnatum*. **4.3 Influence on Cardiomyocyte Viability**

MTT assay results demonstrated that phytochemical treatment enhanced cardiomyocyte survival at lower concentrations. At 10 µg/mL, viability peaked at 95.2%. However, increasing concentrations reduced viability: 82.5% at 50 µg/mL and 70.3% at 100 µg/mL.

This indicates that while low doses are protective, higher doses may exert mild cytotoxic effects—a typical dose-dependent response of bioactive plant compounds.

Table 2. Effect of Phytochemical Fraction on Cell Viability

Concentration (µg/mL)	Cell Viability (%)
10	95.2
50	82.5
100	70.3



4.4 Effect on Apoptosis

Annexin V-FITC/PI staining revealed a dose-dependent increase in apoptosis. At 10 µg/mL, only 4.8% apoptotic cells were detected. This rose to 17.5% at 50 µg/mL and 29.5% at 100 µg/mL. Thus, lower concentrations provided protection against apoptosis, while higher doses triggered increased cell death due to overexposure.

Table 3. Effect of Phytochemical Fraction on Apoptosis

Concentration (µg/mL)	Apoptotic Cells (%)
10	4.8
50	17.5
100	29.5

5 Discussion

The study confirmed that isolated phytochemicals from *Bryophyllum pinnatum* possess strong cardioprotective potential. Analytical techniques verified the presence of flavonoids, alkaloids, and glycosides—compounds well known for antioxidant and cytoprotective properties.

Cell viability assays showed enhanced survival at lower concentrations, while apoptosis assays demonstrated reduced cell death under similar conditions. These protective effects are likely linked to the antioxidant capacity of the compounds, which neutralize reactive oxygen species and mitigate oxidative stress.

Comparable findings have been reported in earlier studies, where plant-derived flavonoids and phenolics improved cardiac cell survival and reduced myocardial damage. Literature evidence from animal models further supports the role of phytochemicals in enhancing cardiac function and minimizing tissue injury.

Overall, the results suggest that *B. pinnatum* is a promising source of natural cardioprotective agents. Nonetheless, further in vivo and molecular studies are essential to validate these outcomes and clarify the mechanisms underlying cardiac protection.

Parameter	**Observation**
HPLC	Flavonoids, Alkaloids, Glycosides
UV–Vis	Active phytochemicals confirmed
FTIR	Functional groups identified
NMR	Structural confirmation
MS	Molecular weight confirmation
Cell Viability	Highest at 10 µg/mL
Apoptosis	Lowest at 10 µg/mL

6. Conclusion

This study explored the cardioprotective potential of phytochemicals isolated from *Bryophyllum pinnatum*. Analytical techniques including HPLC, UV–Visible spectroscopy, FTIR, NMR, and Mass Spectrometry confirmed the presence of key bioactive compounds such as flavonoids, alkaloids, and glycosides, all of which are recognized for their antioxidant and therapeutic properties.

In vitro experiments demonstrated that treatment with these phytochemicals enhanced cardiomyocyte survival at lower concentrations. The MTT assay indicated high cell viability, while Annexin V-FITC/PI staining revealed reduced apoptotic cell death under optimized conditions. These findings suggest that the isolated compounds provide protection against cardiac cellular injury and help maintain cell integrity.

Additionally, evidence from previously reported animal studies supports the role of phytochemicals in improving cardiac performance, reducing myocardial damage, and modulating oxidative stress and inflammatory pathways. Collectively, the results highlight the potential of *B. pinnatum* phytochemicals as natural cardioprotective agents.

In summary, this research provides scientific validation of the therapeutic significance of *Bryophyllum pinnatum*. However, further in vivo and molecular investigations are essential to confirm these effects and to clarify the mechanisms underlying cardiac protection. The isolated compounds may serve as promising leads for developing plant-based therapies against cardiovascular diseases.

7. Future Scope

The outcomes of this study establish a strong basis for continued research on the cardioprotective properties of *Bryophyllum pinnatum*. While significant protective effects were observed in cultured cardiomyocytes, more extensive investigations are required to fully determine their therapeutic potential.

Future work should emphasize in vivo studies using appropriate animal models of cardiovascular disease to validate the protective effects observed in vitro. Detailed histopathological analysis of cardiac tissues and evaluation of biomarkers will provide deeper insights into efficacy.

Molecular investigations focusing on genes and proteins linked to oxidative stress, inflammation, and apoptosis—such as Nrf2, SOD, catalase, TNF-α, IL-6, Bax, Bcl-2, and NF-κB—will help unravel the mechanisms of action and identify critical signaling pathways involved in cardioprotection.

Further purification and structural characterization of the bioactive compounds are also necessary to pinpoint the most potent cardioprotective molecules. Advanced analytical tools and computational approaches may accelerate the development of novel phytochemical-based therapeutics.

Moreover, long-term toxicity, pharmacokinetic, and clinical studies are required to assess safety and effectiveness in humans. Such investigations will contribute to the creation of safe, affordable, and effective plant-derived drugs for the prevention and treatment of cardiovascular disorders.

8. Conflict of Interest

The authors declare that there are no conflicts of interest regarding the publication of this research. The authors have no financial, personal, academic, or professional relationships that could have influenced the design, execution, interpretation, or reporting of the study.

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