Review Article

# ANTIOXIDANT AND ANTICANCER POTENTIAL OF CALOTROPIS GIGANTEA AND BAUHINIA VARIEGATA: A COMPREHENSIVE REVIEW



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#### Abstract

Background: Calotropis gigantea and Bauhinia variegata are medicinal plants reported to possess antioxidant and anticancer activities, but evidence has not been critically synthesized. **Objectives**: To systematically review and critically evaluate preclinical evidence on the phytochemistry, antioxidant potency, and anticancer mechanisms of C. gigantea and B. variegata, and to identify translational gaps and priorities. Methods: A narrative literature search (PubMed, Scopus, Google Scholar) was performed for articles published between 2000–2025 using the keywords "Calotropis gigantea", "Bauhinia variegata", "antioxidant", "anticancer", "phytochemical", and related terms. Inclusion criteria: original in vitro, in vivo, or clinical studies reporting antioxidant assays or anticancer outcomes for either species; English-language articles. Data extracted included phytochemical classes, assay types, reported IC<sub>50</sub> values, molecular pathways, and model systems. **Results**: C. gigantea methanolic extracts show consistently potent antioxidant activity (DPPH/ABTS IC<sub>50</sub> range ~6.7–21.4 μg/mL across leaves/flowers/latex) and induce apoptosis, caspase activation, mitochondrial dysfunction and cell-cycle arrest in multiple cancer cell lines. B. variegata demonstrates significant antioxidant and cytotoxic activity but quantitative potency is less consistently reported. Reported mechanisms for both species include ROS modulation, Bcl-2/Bax regulation, and inhibition of migration/invasion (MMP suppression). Major limitations include heterogeneous extraction methods, inconsistent quantitative reporting, toxicity concerns (cardenolides), and absence of clinical data. **Conclusions**: Preclinical data support the antioxidant and anticancer potential of both plants, particularly C. gigantea, but standardized phytochemical profiling, dose–response in vivo studies, toxicity assessment, and translational research are urgently needed.

**Keywords:** Calotropis Gigantea, Bauhinia Variegata, Antioxidant, Anticancer, Phytochemicals, Cardiac Glycosides, Flavonoids, ROS, Apoptosis.

# 1. Introduction

Cancer remains one of the leading causes of death globally, accounting for nearly 10 million deaths in

2020 alone, with projections indicating a continual rise in incidence[1]. Although conventional therapeutic approaches such as chemotherapy, radiotherapy, and immunotherapy have improved cancer survival rates, their limitations—including drug resistance, adverse effects, and limited target specificity—have prompted researchers to explore alternative strategies[2,3]. Natural products derived from medicinal plants have long been recognized as a rich source of bioactive compounds with chemo preventive and therapeutic potential, particularly due to their antioxidant and cytotoxic properties[4-6].

Oxidative stress, characterized by an imbalance between reactive oxygen species (ROS) and endogenous antioxidant systems, plays a central role in the pathogenesis of cancer by inducing DNA damage, lipid peroxidation, and protein oxidation[7,8]. Antioxidants from plant sources are known to scavenge ROS, enhance antioxidant defence mechanisms, and interfere with carcinogenic processes at multiple levels[9,10]. In this context, *Calotropis gigantea* and *Bauhinia variegata* have attracted growing interest due to their traditional usage in folk medicine and reported pharmacological activities, including antioxidant and anticancer properties[11].

# 1.1 Botanical Overview of *Calotropis gigantea* and *Bauhinia variegata*

Calotropis gigantea (L.) R. Br., belonging to the family Apocynaceae, is a perennial shrub widely distributed in tropical Asia and Africa. Traditionally, it has been used to treat inflammation, skin ailments, respiratory conditions, and gastrointestinal disorders. Phytochemical studies have shown the presence of cardenolides, flavonoids, terpenoids, and alkaloids, many of which exhibit free radical scavenging and cytotoxic effects[12].

Bauhinia variegata L., a deciduous tree from the Fabaceae family, is widely used in Ayurveda and Unani medicine for the treatment of tumours, ulcers, and microbial infections[13]. Its bark, flowers, and leaves are rich in flavonoids, glycosides, saponins, and phenolic acids—compounds known for their antioxidant and anticancer potential[14,15] an anti-

inflammatory agent used in traditional medicine, has been shown to suppress cellular transformation, proliferation, invasion, angiogenesis, and metastasis through a mechanism not fully understood. Because several genes that mediate these processes are regulated by nuclear factor-κB (NF-κB.

This review aims to compile and critically evaluate the available scientific literature on the antioxidant and anticancer activities of *Calotropis gigantea* and *Bauhinia variegata*, highlighting their bioactive constituents, proposed mechanisms of action, and therapeutic potential in cancer prevention and treatment.

# 2. Phytochemical Constituents

Phytochemicals are bioactive secondary metabolites that largely determine the therapeutic potential of medicinal plants. Both *Calotropis gigantea* (CG) and *Bauhinia variegata* (BV) contain diverse classes of compounds—including flavonoids, alkaloids, terpenoids, cardiac glycosides, phenolics, and saponins—that contribute to their reported antioxidant and anticancer activities.

In *C. gigantea*, cardenolides such as calotropin and uscharin, together with triterpenoids (lupeol,  $\beta$ -amyrin), have been frequently implicated in cytotoxicity and apoptosis induction. By contrast, *B. variegata* is particularly rich in flavonoids such as kaempferol, quercetin, and myricetin, which are strongly associated with free radical scavenging and modulation of cancer-related signaling pathways.

A comparative overview of the major phytochemical classes identified in both species, along with their reported plant parts and references, is presented in Table 1. This tabular summary highlights the overlap in common classes (flavonoids, phenolics, steroids) while also underscoring species-specific features—namely, the abundance of potent cardiac glycosides in *C. gigantea* and the dominance of flavonoids in *B. variegata*. These distinctions provide a biochemical basis for the differential antioxidant and anticancer activities discussed in subsequent sections.

Phytochemical Calotropis gigantea (CG)		Bauhinia variegata (BV)	Key References
Flavonoids	Isorhamnetin derivatives; rutin, quercetin	Kaempferol, quercetin, myricetin	Ahmad 2020; Alafnan 2021; K. Sharma 2024
Alkaloids	Present in leaves, latex, roots (mudarine, others)	Present in leaves, bark, flowers (minor alkaloids reported)	Ahmad 2020; Bhargav 2019
Triterpenoids / Terpenoids	Lupeol, β-amyrin, taraxasterol (aerial parts, root bark)	Lupeol, β-sitosterol, phytosterols (bark, leaves)	Ghorpade 2025; Bhargav 2019
Cardiac Glycosides	Calotropin, calotoxin, uscharin (latex, roots, leaves)	Cardiac glycosides (less defined, bark extracts)	Saha 2022; Nair 2022
Phenolic Compounds	Gallic acid, tannins, catechols (leaves, bark)	Protocatechuic acid, gallic acid, polyphenols (bark, leaves)	Ahmad 2020; Nair 2022
Saponins	Latex and leaf extracts (antimicrobial, cytotoxic activity)	Bark and leaves; moderate levels	Ahmad 2020; K. Sharma 2024
Steroids	Stigmasterol, β-sitosterol (root bark, aerial parts)	Stigmasterol, β-sitosterol (bark, leaves)	Saha 2022; Bhargav 2019

(leaves)

Table 1: Comparative overview of the major phytochemical classes identified in CG, BV

## 3. Antioxidant Activities

Fatty acids /

**Coumarins** 

**Esters** 

#### 3.1 Phytochemical Basis and Mechanisms

latex)

Both Calotropis gigantea (CG) and Bauhinia variegata (BV) contain abundant flavonoids, phenolics, terpenoids, and alkaloids that underpin their antioxidant activity. These compounds act via free radical scavenging, metal ion chelation, and inhibition of lipid peroxidation, thereby protecting cellular macromolecules from oxidative stress. Importantly, oxidative stress is closely linked to carcinogenesis, positioning antioxidant activity as a mechanistic bridge to anticancer potential.

Palmitic, oleic acids (seeds,

Not well reported

# 3.2 Comparative Assay Results

Evidence indicates that CG generally demonstrates stronger and more consistently quantified antioxidant activity than BV across standard assays.

A. DPPH radical scavenging: CG methanolic extracts show IC<sub>50</sub> values of 6.74 μg/mL (leaves), 14.44 μg/mL (latex), and 21.35 μg/mL (flowers), while another study reported a higher IC<sub>50</sub> of 268.8 μg/mL (methanolic leaves), underscoring variability based on extraction methods[16,17]. For BV, ethanolic

and aqueous leaf extracts exhibit significant DPPH scavenging, but no IC<sub>50</sub> values have been reported to date[18,19].

Saha 2022; Nair 2022

Nair 2022

Stearic acid, hexadecenoic acid

Moderate amounts in leaves

B. FRAP assay: CG methanolic leaf extracts outperform aqueous and petroleum ether extracts, showing high ferric reducing capacity[20,21]. BV extracts demonstrate dose-dependent reducing power and metal ion chelation at 10–40 μg/mL, but again, quantitative IC<sub>50</sub> values are missing[18].

C. ABTS assay: CG leaf extracts display potent ABTS scavenging (IC<sub>50</sub> 6.74–21.25 μg/mL), while silver nanoparticles synthesized from CG show an IC<sub>50</sub> of 137 μg/mL[22]. For BV, ABTS activity has been reported qualitatively as "significant," but no IC<sub>50</sub> values are available[18].

D. Hydroxyl radical scavenging: CG-derived AgNPs achieved an IC<sub>50</sub> of 52.12 µg/mL, comparable to quercetin[22]. No hydroxyl radical scavenging data have been published for BV.

E. Lipid peroxidation inhibition: CG methanolic flower extract inhibited lipid peroxidation in vitro[23]. BV extracts demonstrated antioxidant activity in the

β-carotene bleaching assay, but no TBARS-specific IC<sub>50</sub> values were reported[18].

F. In vivo evidence: BV leaf extracts reduced lipid peroxidation (MDA levels) and enhanced glutathione (GSH) in mice, demonstrating systemic antioxidant effects[24] Passive evasion Paradigm, Morris water maze and Actophotometer; thus biochemical parameters of brain homogenate such as acetyl cholinesterase (AChE. Comparable in vivo antioxidant data for CG remain scarce.

#### 3.3 Critical Evaluation

Overall, CG extracts consistently yield low IC<sub>50</sub> values across DPPH and ABTS assays, confirming strong radical scavenging activity. BV shows reproducible antioxidant activity, but the lack of quantitative IC<sub>50</sub> data limits direct comparison. The wide variability in CG IC<sub>50</sub> values (6.7 vs. 268 μg/ mL) highlights the urgent need for standardized extraction and assay protocols. Notably, BV provides

stronger in vivo antioxidant evidence, whereas CG data are largely confined to in vitro assays.

A comparative summary of antioxidant activities of *C. gigantea* and *B. variegata* across standard assays is presented in Table 2. These findings highlight the consistently strong activity of *C. gigantea* in in vitro assays, contrasted with the less quantified but biologically significant activity of *B. variegata*, particularly in vivo.

#### 3.4 Implications

Given the role of oxidative stress in carcinogenesis, the antioxidant properties of CG and BV likely contribute to their reported anticancer effects. Future work should emphasize direct correlation of antioxidant potency with cellular outcomes (e.g., ROS modulation, DNA damage prevention), employ standardized reporting of IC<sub>50</sub> values, and extend in vivo validation.

Table 2: Comparative summary of antioxidant activities of C. gigantea and B. variegata.

Assay	C. gigantea (IC50 / activity)	B. variegata (IC <sub>50</sub> / activity)	Model	Reference(s)
DPPH	6.74 μg/mL (leaves, methanol); 14.44 μg/mL (latex)	Data not available (reported as significant)	In vitro (extract assays)	Prabhu 2020; Mishra 2013
FRAP	Methanolic leaf extract > Dose-dependent increase (no IC50)		In vitro	Venkatesan 2022; Mishra 2013
Hydroxyl radical	AgNPs: 52.12 μg/mL	Data not available	In vitro (nanoparticle assays)	Rengarajan 2024
Lipid peroxidation	Inhibition in methanolic flowers	β-carotene bleaching assay positive	In vitro	Kumar 2015; Mishra 2013
Antioxidant enzyme modulation	↑ GSH, ↓ MDA (murine brain tissue)	↑ GSH, ↓ MDA	In vivo (mice)	Khare 2021

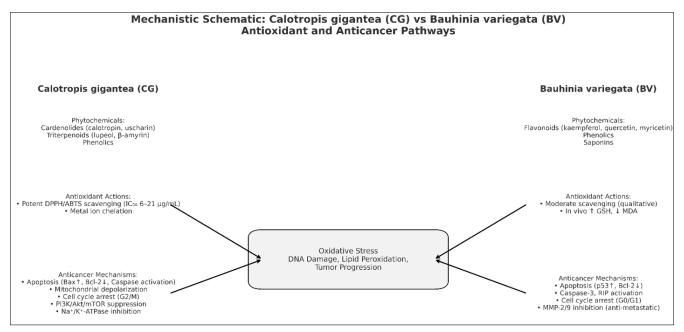


Figure 1: Map showing the State of Uttar Pradesh [Source: (1)]

# 4. Anticancer Activities

Evidence indicates that both *C. gigantea* and *B. variegata* exert anticancer effects through multiple, partially overlapping pathways. These include induction of apoptosis, activation of caspase cascades, cell cycle arrest, modulation of ROS and mitochondrial function, and inhibition of metastatic processes. Grouping the data by mechanistic pathway highlights where the two species share common targets (e.g., caspase activation) and where they diverge (e.g., CG's Na<sup>+</sup>/K<sup>+</sup>-ATPase inhibition vs. BV's MMP suppression).

#### **4.1 Apoptosis Induction**

A. C. gigantea: Methanolic extracts induce apoptosis in MCF-7 and HepG2 cells (TUNEL assay, phosphatidylserine externalization), accompanied by Bax/Bak upregulation and Bcl-2 downregulation[25,26].

B. B. variegata: Ethanolic bark extract induces apoptosis in HeLa cells with G0/G1 arrest; volatile oils from flowers trigger p53 upregulation and mitochondrial dysfunction in A549 cells[27,28].

# **4.2 Caspase Cascade Activation**

A. C. gigantea: Poly-caspase activation (caspase-3, -8, Apaf-1) in a dose-dependent manner confirms engagement of both intrinsic and extrinsic

A. B. variegata: Stem fractions trigger caspase-3 and RIP activation, suggesting both apoptotic and

# 4.3 Cell Cycle Arrest

necroptotic pathways[29].

pathways[25,26].

A. C. gigantea: G2/M arrest in MCF-7 cells, resembling paclitaxel, with additional effects on glycolytic metabolism[30].

B. B. variegata: Bark extract produces G0/G1 arrest in HeLa cells, consistent with p53 upregulation[28].

### 4.4 ROS Modulation and Mitochondrial Dysfunction

A. C. gigantea: Cardenolides elevate ROS levels, disrupt mitochondrial membrane potential, and inhibit Na<sup>+</sup>/K<sup>+</sup>-ATPase, promoting selective cancer cell death[31,32].

B. B. variegata: Flavonoids (e.g., baicalin) induce mitochondrial depolarization, increase ROS, and downregulate Bcl-2 while upregulating p53[33].

#### 4.5 Metastasis Inhibition

A. C. gigantea: Calotropin reduces migration and invasion by suppressing PI3K/Akt/mTOR and TGF-β/ERK signaling pathways[26,30].

B. B. variegata: Stem fractions inhibit MMP-2 and MMP-9 activity, reducing HeLa cell migration and invasion[29].

,	Table 3: Summa	ry of principa	l pathways mo	odulated by CG, I	3V

Pathway	C. gigantea	B. variegata	Model	Reference(s)
Apoptosis induction	TUNEL assay, Bax↑, Bcl-2↓	p53↑, mitochondrial depolarization	In vitro (MCF-7, HepG2, HeLa, A549 cells)	Kharat 2019; Awaed 2025
Caspase activation	Caspase-3, -8, Apaf-1 activation	Caspase-3, RIP activation	In vitro	Tian 2018; Santos 2018
Cell cycle arrest	G2/M arrest (MCF-7)	G0/G1 arrest (HeLa)	In vitro	Kharat 2019; Kumar 2014
ROS modulation	ROS↑, mitochondrial permeability changes	ROS↑, p53 upregulation	In vitro	Khosravi 2021; Sharma 2025
Antimetastatic effects	PI3K/Akt/mTOR and TGF-β/ERK suppression	MMP-2/9 inhibition	In vitro	Jayaraman 2023; Santos 2018

The anticancer activities of Calotropis gigantea and Bauhinia variegata have been reported across diverse models, targeting multiple pathways including apoptosis induction, caspase activation, cell cycle arrest, ROS modulation, and inhibition of metastatic processes. However, these findings are fragmented across studies and vary in methodological quality. To provide a clearer comparison, Table 3 summarizes the principal pathways modulated by both species, the experimental models used (in vitro or in vivo), and the associated phytoconstituents. This organization highlights overlapping mechanisms, such as caspase activation and ROS involvement, while also underscoring species-specific differences—for example, C. gigantea's inhibition of Na+/K+-ATPase versus B. variegata's suppression of MMP-2/9 activity.

# 5. Challenges and Research Gaps

# 5.1 Standardization of Phytochemical Profiles

One of the major challenges in advancing *Calotropis* gigantea and Bauhinia variegata into therapeutic use is the lack of phytochemical standardization. Both species exhibit wide variability in secondary metabolite content depending on geographic origin, seasonal factors, soil type, and extraction method. For example, cardenolide concentrations in *C. gigantea* and flavonoid levels in *B. variegata* differ significantly across reported studies, making reproducibility and comparative analysis difficult.

Without universally accepted quality-control markers, standardization of extracts remains elusive.

#### 5.2 Lack of Clinical Evidence

Although a substantial number of in vitro and a few in vivo studies have demonstrated antioxidant and anticancer potential, there are no clinical trials validating safety or efficacy in humans. The current evidence base remains entirely preclinical, limiting translational application. This gap highlights the urgent need for carefully designed pharmacokinetic and pharmacodynamic studies in humans.

#### **5.3 Toxicity and Safety Concerns**

The therapeutic use of *C. gigantea* is complicated by the presence of potent cardiac glycosides, including calotropin and uscharin, which can be cardiotoxic if not carefully dosed. Toxicity studies are sparse, with little information available on long-term safety, dose—response thresholds, or herb—drug interactions. Until systematic toxicological evaluations are performed, clinical adoption will remain risky.

# 5.4 Sustainability and Conservation Issues

Overharvesting, especially of roots and bark, poses a conservation threat to wild populations of both plants. At present, there are no large-scale cultivation protocols or conservation strategies to ensure sustainable use. Developing controlled cultivation practices and propagation methods is essential to prevent depletion of natural resources.

#### 5.5 Unexplored Synergistic and Formulation Potentials

Most pharmacological investigations have focused on crude extracts or isolated compounds, while synergistic effects between phytoconstituents remain largely untested. Similarly, advanced formulation approaches such as nanoparticles, liposomes, or polyherbal combinations have received little attention. Exploring these strategies could enhance bioavailability and therapeutic efficacy.

# 5.6 Incomplete Mechanistic Understanding

Although antioxidant and apoptotic effects are frequently reported, detailed molecular targets and pathway interactions remain poorly defined. Few studies employ omics-based tools such as transcriptomics, proteomics, or metabolomics to comprehensively map mechanisms of action. Without such integrative approaches, it will be difficult to establish a robust mechanistic foundation for clinical translation.

# 6. Conclusion

This review highlights the complementary antioxidant and anticancer properties of *Calotropis gigantea* and *Bauhinia variegata*, supported by diverse preclinical studies. *C. gigantea*, rich in cardenolides and triterpenoids, consistently demonstrates strong in vitro antioxidant activity and potent pro-apoptotic and cell-cycle—modulating effects across cancer cell lines. *B. variegata*, characterized by high flavonoid and phenolic content, exhibits reproducible in vivo antioxidant activity and anti-metastatic mechanisms, including inhibition of MMP-2/9 and modulation of p53. Together, these findings suggest that both plants may contribute valuable leads for the development of natural product—based oncotherapeutics.

Despite encouraging evidence, translation remains limited by variability in extract preparation, lack of standardized phytochemical markers, incomplete mechanistic data, and the absence of clinical validation. Future research should prioritize standardized extract profiling, omics-based mechanistic investigations, advanced formulations such as nanoparticles, and rigorous in vivo efficacy—

toxicity studies. Addressing these gaps will be critical to establish safety and therapeutic relevance.

In conclusion, *C. gigantea* and *B. variegata* represent promising but underexplored candidates for integrative oncology, warranting carefully designed translational studies to realize their clinical potential.

# 7. Funding Declaration: None

# 8. Conflict of Interest: None

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