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BHALLATAKA (*SEMECARPUS ANACARDIUM* L.F.): BRIDGING CLASSICAL AYURVEDIC KNOWLEDGE AND CONTEMPORARY EVIDENCE ON ANTICANCER ACTIVITY

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ABSTRACT

Bhallataka (*Semecarpus anacardium* L.f.), a medicinal plant widely described in Ayurveda, has long been recognized as a potent but potentially toxic drug requiring careful purification before therapeutic use. Classical texts including *Charaka Samhita*, *Sushruta Samhita*, *Ashtanga Hridaya*, and later nighantus document its use in disorders characterized by abnormal growth, chronic inflammation, metabolic derangement, and tissue morbidity—disease frameworks that partially overlap with present-day oncologic concepts. In modern pharmacological research, *S. anacardium* has attracted sustained attention for its cytotoxic, pro-apoptotic, antioxidant, anti-inflammatory, antimutagenic, and antimetastatic effects. Experimental studies demonstrate activity in hepatocellular carcinoma, breast cancer, leukemia, lymphoma, and lung cancer models. Mechanistic work suggests that Bhallataka-derived preparations and isolated compounds can induce apoptosis through mitochondrial depolarization, Bax/Bcl-2 modulation, cytochrome-c release, caspase activation, PARP cleavage, cell-cycle arrest, checkpoint kinase inhibition, suppression of migration, and modulation of oxidative stress and xenobiotic-metabolizing enzymes. Importantly, recent work indicates that traditional purification (*shodhana*) may not merely reduce toxicity but also improve pharmacological performance. Despite encouraging preclinical findings, the

current evidence remains predominantly experimental, with limited human data and insufficient standardization of extracts, dose, and formulations. This review integrates classical Ayurvedic descriptions with PubMed-indexed and Scopus-indexed modern literature to critically evaluate the anticancer promise of Bhallataka, its mechanistic basis, safety concerns, and translational challenges.[7,15-17]

KEYWORDS: Bhallataka; *Semecarpus anacardium*; Ayurveda; anticancer activity; apoptosis; shodhana; ethnopharmacology; phytochemicals.

INTRODUCTION

Cancer continues to demand safer, multi-targeted, and biologically intelligent therapeutics, especially for tumors resistant to conventional cytotoxic agents. In that context, medicinal plants with deep traditional use and emerging mechanistic validation remain highly relevant. Bhallataka, botanically identified as *Semecarpus anacardium* L.f. of the family Anacardiaceae, occupies a distinctive position because it is simultaneously described in Ayurveda as therapeutically powerful and intrinsically hazardous in its raw state. That duality is scientifically important: it invites a translational model in which traditional processing, formulation, and indication logic are examined alongside molecular oncology.[5-7,15] Modern reviews identify four major cancer domains repeatedly associated with *S. anacardium* research: hepatocellular carcinoma, breast cancer, blood malignancies, and lung cancer. Across these models, the plant has shown the ability to reduce proliferation, induce apoptosis, suppress invasion and migration, and modulate inflammatory and oxidative pathways. Such breadth suggests that Bhallataka may function less as a single-target botanical and more as a multi-component anticancer platform.[7,13,16,17]

MATERIALS AND METHODS

This review was carried out by collecting and analyzing information on *Bhallataka (Semecarpus anacardium L.f.)* from both classical Ayurvedic texts and modern scientific literature. Relevant articles were searched from databases such as PubMed, Scopus, Google Scholar, and ScienceDirect up to the year 2025 using keywords like “Bhallataka,” “Semecarpus anacardium,” “anticancer activity,” and “shodhana.” Only peer-reviewed and English-language studies related to anticancer activity, phytochemistry, and safety were included, while unrelated or non-scientific sources were excluded. Classical texts including Charaka Samhita, Sushruta Samhita, Ashtanga Hridaya, and Bhavaprakasha Nighantu were referred to for traditional knowledge and therapeutic use. The collected information was then

organized and reviewed under different headings such as phytochemical properties, mechanisms of action, and safety, and finally interpreted in a simple narrative manner to connect traditional Ayurvedic concepts with modern scientific findings.

Classical Ayurvedic understanding of Bhallataka

Classical Ayurvedic literature places Bhallataka among potent drugs requiring discernment, purification, and careful patient selection. Standard texts and lexicons describe it under multiple synonyms and emphasize properties broadly corresponding to *ushna* (hot), *tikshna* (penetrating), *deepana* (digestive/metabolic kindling), and *lekhana* (scraping or reducing pathological accumulations). It is repeatedly mentioned in formulations for *arsha*, *kushtha*, *gulma*, *grahani*, *prameha*, and *vata*-related disorders, while later compilations also preserve instructions on collection, storage, antidotes, dietary restrictions, and adverse-effect prevention. These details are striking because they portray Bhallataka not as a casual herb but as a drug whose efficacy is inseparable from pharmaceutical handling.[1,5] Although classical Ayurvedic texts do not speak in the language of "oncogenes," "metastasis," or "cell-cycle arrest," they do repeatedly associate Bhallataka with disease states involving abnormal masses, chronic inflammation, induration, metabolic dysfunction, and difficult-to-treat lesions. For a modern reader, that matters less as a forced one-to-one mapping to cancer and more as evidence that Bhallataka belonged to the traditional therapeutic repertoire for stubborn, proliferative, and tissue-destructive conditions. This historical continuity partly explains why modern anticancer research on *S. anacardium* did not emerge in a vacuum but from a long medicinal memory.[1,5]

Phytochemistry of *Semecarpus anacardium*

The anticancer interest in Bhallataka is supported by a chemically rich profile that includes catechol derivatives, anacardic acid-related constituents, bhilawanols, flavonoids, and phenolic lipids. One of the most important mechanistic advances was the isolation of the catechol compound **3-(8′Z,11′Z-pentadecadienyl) catechol (SA-3C)** from the kernel, which displayed cytotoxicity against tumor cell lines, including multidrug-resistant lines, and showed synergy with doxorubicin. Such findings move the evidence beyond crude ethnobotanical claims toward chemically attributable pharmacology.[7,13] What makes the phytochemistry especially compelling is that the same class of compounds likely underlies both efficacy and toxicity. Vesicant phenolics and related lipophilic compounds contribute to the plant's irritant potential, including blistering and contact dermatitis, yet these reactive

constituents may also influence membrane dynamics, redox biology, and tumor-cell vulnerability. This is precisely why Ayurvedic *shodhana* deserves serious scientific attention: it may reshape the chemical fingerprint rather than merely dilute a poison.[5,15]

Experimental anticancer evidence in hepatocellular carcinoma

The hepatocellular carcinoma evidence for *S. anacardium* is among the oldest and most coherent. In aflatoxin B1-induced hepatocellular carcinoma models, nut or milk extracts restored several tumor-associated biochemical abnormalities toward normal values. These included tumor marker enzymes such as lactate dehydrogenase, aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase, and gamma-glutamyl transpeptidase, supporting a genuine antitumor rather than merely symptomatic effect.[8] Subsequent mechanistic studies in the same broad experimental context showed that *S. anacardium* enhanced antioxidant defenses, increasing vitamin C, vitamin E, glutathione-related parameters, total thiols, and cytochrome P450 content in tissues compromised by carcinogenesis. Another study demonstrated normalization of both phase I and phase II biotransformation enzymes, suggesting that the plant may interfere with carcinogen activation, detoxification failure, and oxidative injury simultaneously. In other words, Bhallataka appears capable of acting not only against tumor burden but also against the biochemical environment that sustains carcinogenesis.[9,10] A further study on glucose-metabolizing enzymes reported that *S. anacardium* decreased glycolytic enzyme activity and increased gluconeogenic enzyme activity toward near-normal levels in aflatoxin B1-induced hepatocellular carcinoma. This is noteworthy because it anticipates, in a rudimentary experimental way, modern interest in targeting tumor metabolic reprogramming. More recent full-text synthesis has also suggested that Ayurvedic milk extract may show efficacy alone and in combination with chemotherapy in hepatocellular carcinoma models, although these findings still remain preclinical and require far stronger translational validation.[10,18]

Experimental anticancer evidence in breast cancer

Breast cancer models have provided some of the strongest apoptotic evidence for Bhallataka. In T47D cells, *S. anacardium* nut extract induced apoptosis through rapid intracellular calcium mobilization, altered mitochondrial transmembrane potential, decreased Bcl-2, increased Bax, cytochrome-c release, caspase activation, PARP cleavage, and internucleosomal DNA fragmentation. This is a mechanistically persuasive profile because it links phenotypic cytotoxicity to the intrinsic apoptotic pathway rather than to nonspecific cell

injury alone.[11] In a chemically induced mammary carcinoma model, nut extract treatment restored altered xenobiotic-metabolizing enzyme systems, including CYP1A1, CYP1A2, CYP1B1, and multiple phase II enzymes. This suggests that Bhallataka may exert part of its anticancer effect by modulating carcinogen metabolism and host detoxification, a mechanism particularly relevant in tumors driven or promoted by environmental toxicants.[12] More recently, attention has shifted from the nut alone to the leaf as a potentially safer anticancer source. An ethyl acetate leaf extract showed selective cytotoxicity toward cancer cells, with marked potency in MCF-7 breast cancer cells, induction of apoptosis, cell-cycle arrest, suppression of migration, and in vivo inhibition of tumor growth with prolonged survival in tumor-bearing mice. The relative insensitivity of non-malignant cells to the leaf extract is especially encouraging, because selectivity remains one of the biggest challenges in botanical anticancer development.[16]

Activity in hematologic malignancies and multidrug-resistant models

The isolation study of SA-3C is arguably the clearest evidence that *S. anacardium* contains constituents with drug-development potential. SA-3C was active against tumor cell lines with IC50 values reported to be lower than doxorubicin, retained activity against multidrug-resistant tumor lines, induced dose-dependent apoptosis in leukemia cells, and caused S- and G2/M-phase arrest associated with checkpoint kinase inhibition. Synergy with doxorubicin further raises the possibility that Bhallataka-derived molecules could serve as chemosensitizers rather than as stand-alone agents only.[13] Evidence in lymphoma models reinforces this multi-mechanistic pattern. In lymphoma-transplanted mice, aqueous nut extract increased the activity of antioxidant enzymes such as catalase, superoxide dismutase, and glutathione transferase while decreasing lactate dehydrogenase, a marker associated with anaerobic metabolism and tumor activity. Interestingly, the authors reported stronger effects than doxorubicin on some biochemical parameters, though that result should be interpreted cautiously because biochemical normalization is not equivalent to clinical superiority.[14]

Emerging evidence in lung cancer and metastasis

The newest mechanistic layer in Bhallataka research comes from proteomics. In lung adenocarcinoma models, Bhallataka taila reduced colony formation, proliferation, and migration while increasing apoptosis. Tandem mass tag-based proteomic analysis detected broad alterations in protein expression, with changes linked to progression, invasion, metastasis, and epithelial-mesenchymal transition. This is important because it shifts the

conversation from gross cytotoxicity toward network pharmacology and systems-level pathway regulation.[17] Source This lung cancer work also strengthens the idea that Bhallataka is best understood as a multi-target intervention. Instead of acting on a single receptor or pathway, it appears to influence an interconnected set of proteins governing cell survival, motility, and metastatic behavior. For natural-product oncology, this kind of systems evidence is valuable because it matches the biological complexity of both botanical extracts and cancer itself.[17]

Shodhana, toxicity, and formulation relevance

Any serious discussion of Bhallataka must confront toxicity. Raw *S. anacardium* is well known to cause irritation, blistering, and contact dermatitis, and this vesicant potential has historically limited careless use. Rather than treating this as a reason to dismiss the drug, the Ayurvedic pharmaceutic tradition treats it as a reason for disciplined processing. Classical sources repeatedly emphasize purification, appropriate adjuvants, and dietary restrictions during administration.[1,5] Source Modern evidence now supports that classical intuition. In an Ehrlich Ascites Carcinoma model, purified Bhallataka showed chemical profile changes on LC-MS and better anticancer activity than the raw sample. This finding is unusually important in integrative pharmacology because it suggests that *shodhana* may be a bioactive pharmaceutical transformation step—one that alters efficacy and safety together. That insight should influence future standardization strategies, regulatory frameworks, and formulation science.[15]

DISCUSSION

Taken together, the literature suggests that Bhallataka's anticancer promise lies in five converging domains: apoptosis induction, cell-cycle arrest, redox modulation, carcinogen detoxification, and suppression of migration/metastatic behavior. Few medicinal plants show this degree of mechanistic breadth across multiple tumor models. Just as importantly, several studies connect traditional processing and formulation logic with measurable biochemical or pharmacological consequences, offering a rare bridge between classical Ayurveda and modern translational oncology.[7,17] At the same time, the evidence base remains overwhelmingly preclinical. Most studies use different plant parts, extraction methods, solvents, dosing schedules, and model systems, which makes direct comparison difficult. Human evidence is sparse, robust randomized cancer trials are lacking in the accessible literature reviewed, and standardized phytochemical markers are still not uniformly adopted.

These limitations do not negate Bhallataka's potential, but they do mean that current evidence supports it as a **promising investigational anticancer botanical**, not yet as a validated clinical anticancer drug.[7,15,16,18] The most sensible path forward is not indiscriminate clinical use, but disciplined translational research: authenticated raw material, standardized purified formulations, defined marker compounds, comparative pharmaceutics of raw versus purified drug, organ-specific toxicity profiling, pharmacokinetics, interaction studies with chemotherapy, and phase-wise clinical trials in carefully selected indications such as hepatocellular carcinoma, breast cancer adjunctive care, or drug-resistant hematologic malignancies. In that sense, Bhallataka deserves neither romantic overstatement nor skeptical dismissal; it deserves rigorous development.[7,13,15,17,18]

CONCLUSION

Bhallataka stands out as one of the most conceptually rich examples of an Ayurvedic drug whose classical identity aligns meaningfully with modern experimental oncology. The plant's traditional reputation as a powerful, penetrating, and carefully processed medicine is echoed in contemporary findings showing apoptosis induction, modulation of detoxification enzymes, correction of oxidative imbalance, cell-cycle blockade, and inhibition of migration and metastasis. Among the strongest modern signals are the hepatocellular carcinoma studies, the breast cancer apoptosis data, the isolation of SA-3C with activity against multidrug-resistant cells, the improved performance of purified Bhallataka, and recent proteomic evidence in lung cancer. Yet the bridge from laboratory promise to bedside relevance remains incomplete. The future of Bhallataka in oncology will depend on whether traditional pharmaceutics and modern biomedical methods can be integrated with sufficient rigor to convert a historically revered medicine into a reproducible, safe, and clinically meaningful anticancer intervention.[5,7,13,15-18]

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