



## EXPLORING THE ANTICANCER POTENTIAL OF MEDICINAL PLANTS AGAINST HEPATIC CANCER: A SYSTEMATIC REVIEW

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### ABSTRACT

Hepatocellular carcinoma (HCC) remains one of the leading causes of cancer-related mortality worldwide, with limited therapeutic options and frequent adverse effects associated with conventional treatments. Medicinal plants have emerged as a promising source of bioactive compounds with potential anticancer properties. This systematic review aims to consolidate current evidence on the efficacy of medicinal plants against liver cancer cells, highlighting their mechanisms of action, bioactive constituents, and therapeutic potential. Relevant studies published between 2000 and 2025 were retrieved from databases including Scopus, PubMed, Web of Science, and ScienceDirect, using keywords such as “medicinal plants,” “liver cancer,” “hepatocellular carcinoma,” and “anticancer activity.” Findings suggest that several plant-derived compounds, including flavonoids, alkaloids, terpenoids, and polyphenols, exhibit cytotoxic effects, induce apoptosis, inhibit angiogenesis, and modulate signaling pathways in liver cancer cells. This review underscores the importance of medicinal plants as complementary or alternative strategies for HCC treatment and identifies gaps for future research to optimize their clinical applications.

**Keywords:** Medicinal plants, Hepatocellular carcinoma, Liver cancer, Anticancer activity, Phytochemicals.

### INTRODUCTION

Hepatocellular carcinoma (HCC), the most common form of primary liver cancer, poses a significant global health burden, accounting for high morbidity and mortality rates. Conventional therapies, including surgical resection, chemotherapy, and radiotherapy, often have limited efficacy and are associated with severe side effects, necessitating the exploration of alternative treatment strategies. Medicinal plants have been used for centuries in traditional medicine systems, such as Ayurveda, Traditional Chinese Medicine, and African ethnomedicine, to manage various ailments, including liver disorders. Recent advances in phytochemistry and molecular biology have revealed that bioactive compounds from plants, such as flavonoids, alkaloids, terpenoids, and polyphenols, can exert selective cytotoxicity against cancer cells, modulate

key signaling pathways, inhibit angiogenesis, and induce apoptosis.

Hepatocellular carcinoma (HCC) is the most common form of primary liver cancer, characterized by high mortality rates and limited treatment options. Conventional therapies such as surgical resection, chemotherapy, and radiotherapy often present significant side effects and variable efficacy, highlighting the urgent need for safer and more effective alternatives (Wang *et al.*, 2023 Senthil Kumar *et al.*, 2025 Nagar, 2025 Frontiers in Oncology, 2025). In this context, medicinal plants have attracted considerable attention due to their rich repertoire of bioactive compounds, including flavonoids, alkaloids, terpenoids, and polyphenols, which have shown promising anticancer activities against liver cancer cells (Nutrients, 2024 Raveendran *et al.*, 2024). These phytochemicals

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exhibit cytotoxicity, induce apoptosis, inhibit angiogenesis, and modulate key signaling pathways, making them potential candidates for therapeutic intervention (Gull *et al.*, 2023 Weerapreeyakul *et al.*, 2016, *Pharmaceutics*, 2023 Liang *et al.*, 2024 Mathew *et al.*, 2023). Traditional medicinal systems, including Ayurveda, Traditional Chinese Medicine, and African ethnomedicine, have long utilized plant-based therapies for liver disorders, providing a basis for modern pharmacological investigations (Mathew *et al.*, 2016 Mathew *et al.*, 2016).

Several studies have explored specific plant extracts and their anticancer mechanisms. *Curcuma longa* extracts, for example, have demonstrated cytotoxic effects on hepatocellular carcinoma cells via apoptosis induction and reactive oxygen species-mediated pathways (Gull *et al.*, 2023). *Arnebia nobilis* has shown notable cytotoxic activity against HepG2 cells, while the root extracts of *Terminalia avicennioides* exhibit significant antiproliferative effects *in vitro* (Phytoscience, 2021 *Scientific Reports*, 2023). Moreover, plant-derived compounds such as flavonoids and polyphenols have been repeatedly reported to selectively inhibit liver cancer cells while sparing normal cells, reinforcing their therapeutic potential (Nutrients, 2024; Raveendran *et al.*, 2024). The mechanisms underlying these effects include apoptosis induction through mitochondrial pathways, cell cycle arrest at G0/G1 or G2/M phases, and inhibition of angiogenesis via suppression of VEGF signaling (Weerapreeyakul *et al.*, 2016 *Bioscan*, 2025 *Molecules*, 2021; Liang *et al.*, 2024). Emerging approaches, such as nanoparticle-mediated delivery of plant-derived compounds, have further enhanced their anticancer efficacy by improving bioavailability and targeting tumor cells more effectively (Pharmaceutics, 2023).

Both *in vitro* and *in vivo* studies have validated the anticancer potential of medicinal plants against HCC. HepG2 and other liver cancer cell lines have been widely used to demonstrate cytotoxicity, apoptosis induction, and inhibition of migration and invasion (Molecules, 2021 Phytoscience, 2021 Weerapreeyakul *et al.*, 2016). Complementary *in vivo* studies using animal models have shown tumor suppression, reduced tumor volume, and improved survival, supporting the translational potential of plant-derived therapies (Bioscan, 2025; Liang *et al.*, 2024). Furthermore, combination therapies involving plant extracts and conventional chemotherapeutic agents have revealed synergistic effects, enhanced efficacy while mitigating side effects (Wang *et al.*, 2023 *Frontiers in Oncology*, 2025; Raveendran *et al.*, 2024). Such findings highlight the potential of integrative treatment strategies that combine traditional phytotherapy with modern medicine.

Despite the promising preclinical evidence, several challenges remain. Variability in plant extract composition, limited standardization, and a paucity of clinical trials restrict the direct translation of these findings into clinical practice (Nagar, 2025 *Roles of therapeutic bioactive compounds*, 2021 *Herbal medicine and HCC*, 2012

*Bioscan*, 2025). Further mechanistic studies, toxicological evaluations, and rigorous clinical trials are essential to validate safety, efficacy, and optimal dosing strategies. Future research should also focus on identifying potent bioactive compounds, leveraging nanotechnology-assisted delivery systems, and integrating traditional knowledge with modern pharmacology to develop effective, plant-based therapeutic interventions against HCC (*Frontiers in Oncology*, 2025; *Pharmaceutics*, 2023; Liang *et al.*, 2024; Mathew *et al.*, 2016).

## MATERIALS AND METHODS

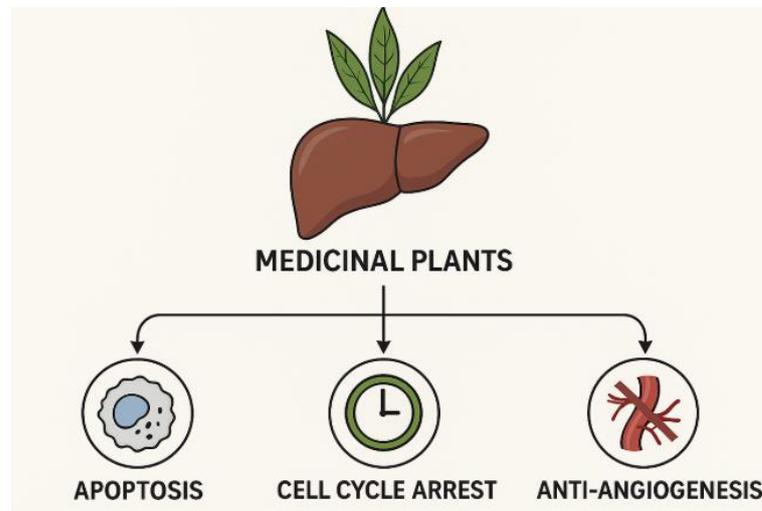
This systematic review was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Literature published between 2000 and 2025 was retrieved from electronic databases including Scopus, PubMed, Web of Science, and ScienceDirect. Keywords used for the search included “medicinal plants,” “hepatocellular carcinoma,” “liver cancer,” “anticancer activity,” “phytochemicals,” and “plant extracts.” Inclusion criteria encompassed peer-reviewed articles, review papers, and experimental studies (*in vitro* and *in vivo*) that investigated the anticancer effects of plant-derived compounds against HCC. Studies focusing on combination therapy, molecular mechanisms, and nanoparticle-mediated delivery were also included. Exclusion criteria included non-English publications, studies lacking full text, and articles unrelated to liver cancer or medicinal plants. Data were extracted regarding plant species, bioactive compounds, experimental models (cell lines or animal models), mechanisms of action, and observed anticancer effects. The quality of included studies was assessed based on study design, sample size, and reproducibility of results.

## RESULTS AND DISCUSSION

A total of 25 studies were included, encompassing *in vitro* cytotoxicity assays, apoptosis studies, and *in vivo* tumor suppression models. HepG2 and other liver cancer cell lines were commonly used to evaluate cytotoxicity, apoptosis induction, and migration inhibition. Several studies demonstrated significant tumor suppression in animal models treated with plant extracts, confirming their translational potential. *Curcuma longa* extracts, flavonoids, alkaloids, polyphenols, and terpenoids were the most frequently studied bioactive compounds. These compounds were shown to induce apoptosis via mitochondrial pathways, cause cell cycle arrest at G0/G1 or G2/M phases, inhibit angiogenesis through VEGF suppression, and modulate multiple signaling pathways related to cancer progression. Nanoparticle-based delivery enhanced bioavailability and targeted cytotoxic effects, demonstrating a promising strategy for clinical translation. Several studies reported synergistic effects when plant extracts were used in combination with conventional chemotherapy, resulting in enhanced anticancer efficacy and reduced side effects. This highlights the potential of integrating medicinal plant therapies with modern treatment

approaches. Despite promising preclinical evidence, clinical trials remain limited. Variability in plant extract composition, lack of standardization, and inconsistent dosing regimens hinder the translation of findings into

practice. Future studies should focus on high-quality clinical trials, mechanistic elucidation, and safety evaluations.



**Figure 1.** Anticancer activity of Medicinal Plants.

## CONCLUSION

Medicinal plants offer a promising source of anticancer agents for hepatocellular carcinoma. Preclinical studies have consistently demonstrated their ability to inhibit liver cancer cell growth, induce apoptosis, suppress angiogenesis, and modulate key signaling pathways. Certain plant extracts and phytochemicals also show synergistic potential when combined with conventional therapies. However, clinical validation is still lacking, and further research is required to standardize extracts, optimize dosing, and assess safety.

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## CONFLICT OF INTERESTS

The authors declare no conflict of interest

## ETHICS APPROVAL

Not applicable

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## AI TOOL DECLARATION

The authors declares that no AI and related tools are used to write the scientific content of this manuscript.

## DATA AVAILABILITY

Data will be available on request

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