

Biotechnological insights into medicinal plants for hepatocellular carcinoma therapy: an overview

S M Yahaya^{1*} and M A Yakasai¹

¹ Assistant Professor, Department of Biology, Sri Krishnadevaraya University, Anantapur, Andhra Pradesh, India

Correspondence Author: S M Yahaya

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Abstract

Hepatocellular carcinoma (HCC) is one of the most prevalent liver cancers and ranks among the leading causes of cancer-related mortality worldwide. The liver's critical role in metabolism and detoxification makes it particularly vulnerable to carcinogenic insults. Herbal medicine has long been explored for liver protection and cancer management, offering potential therapeutic benefits with reduced toxic side effects compared to conventional chemotherapy. Numerous medicinal plants have demonstrated promising *in vitro* and *in vivo* anticancer activities, yet their clinical efficacy and underlying mechanisms remain under-investigated. Bioactive compounds derived from these plants are gaining attention as potential hepatoprotective and anticancer agents. Experimental studies over the past century have revealed that several plant species exhibit cytotoxic, antioxidant, and apoptosis-inducing effects against liver cancer cells. This review highlights key medicinal plants evaluated for HCC, focusing on their bioactive constituents, mechanisms of action, and therapeutic potential. By consolidating current findings, the study aims to guide future research toward the discovery and development of novel plant-derived molecules for sustainable and effective management of hepatocellular carcinoma.

Keywords: Medicinal plants, Liver cancer, HepG2 cell line, Phytochemicals

Introduction

Cancer is a common term encompassing a wide range of malignant diseases that can affect various organs of the body. These diseases are characterized by the uncontrolled proliferation of abnormal cells, which can accumulate and spread, causing damage to tissues and organs. This process continues unchecked unless therapeutically controlled [1].

The liver, the largest glandular organ in the human body, plays a critical role in metabolism. It produces essential blood coagulation factors such as prothrombin and fibrinogen, as well as heparin, a sulfated mucopolysaccharide that prevents clot formation. Additionally, the liver synthesizes bile, regulates glucose metabolism, and performs numerous detoxification processes [2].

Liver diseases are a major cause of morbidity and mortality worldwide, with hepatotoxicity being one of the most common underlying factors. Hepatocellular carcinoma (HCC) is among the deadliest forms of cancer, causing approximately 745,000 deaths annually and ranking as the second leading cause of cancer-related mortality globally [3]. Over the past decades, the prevalence of liver cancer has doubled, with the majority of cases occurring in developed countries. Treatment of HCC is complex and depends on tumor characteristics, liver function, vascular invasion, and patient surgical eligibility [4].

Therapeutic options for HCC range from locoregional interventions such as intratumoral ethanol injection, microwave coagulation, and Yttrium-90 microarterial therapy to surgical resection, liver transplantation, and

chemotherapeutic agents like sorafenib [5]. Despite these approaches, conventional chemotherapy often exhibits limited efficacy, prompting increased interest in alternative and complementary therapies, particularly herbal medicines. Herbal remedies are widely believed to offer natural, targeted treatment options, reinforcing their integration into supportive cancer care [6, 7].

Natural treatments for liver cancer

Medicinal plants contain a variety of phytochemicals with potent antioxidant properties, including flavonoids (e.g., isoflavones, flavonones, anthocyanins, catechins, quercetin), terpenoids, polyphenols (e.g., ellagic acid, gallic acid, tannins), alkaloids, saponins, minerals (selenium, zinc, manganese, chromium, iodine), enzymes (superoxide dismutase, catalase, glutathione peroxidase), and polysaccharides [8, 9]. These compounds protect cells from oxidative damage by scavenging free radicals and can contribute to disease prevention and therapy.

Curcumin

Curcumin (diferuloylmethane), extracted from turmeric, exhibits strong antioxidant, anti-inflammatory, and anticancer properties. Studies have demonstrated its inhibitory effects on angiogenesis in HCC models, suggesting a key mechanism in its anticancer activity [10, 11].

Allium sativum (Garlic)

Garlic is one of the oldest cultivated medicinal plants, rich in organosulfur compounds such as S-allylcysteine and S-allylmercaptocysteine, which exhibit chemopreventive properties. Experimental studies have shown that garlic extracts reduce tumor growth and progression in animal models [12, 13].

Camptotheca acuminata

Camptothecin, an alkaloid derived from the Chinese tree *C. acuminata*, exhibits anticancer and antiviral activities. Root cultures of this plant produce camptothecin and its derivative 10-hydroxycamptothecin, which are effective and relatively low in toxicity [14].

Azadirachta indica (Neem)

Neem extracts promote caspase-mediated apoptosis, induce reactive oxygen species (ROS) generation, modulate macrophage polarization, inhibit tumor angiogenesis, and restore redox balance in cancer cells [15, 16].

Phyllanthus amarus

Phyllanthus amarus exerts anticancer effects by arresting the cell cycle, promoting DNA repair, and modulating carcinogen metabolism, contributing to tumor suppression [17].

Withania somnifera

Withanolides, particularly Withanolide A, are bioactive compounds in *W. somnifera* leaves that induce apoptosis in cancer cells. This plant modulates immune responses, enhances cytotoxicity in tumor-bearing models, and increases expression of cytokines such as IL-2 and IFN- γ [19, 20].

Conclusion

Cancer remains a significant global health challenge, with conventional therapies often limited by toxicity and low selectivity toward cancer cells. Medicinal plants offer a rich source of bioactive compounds with potential anticancer properties. Phytochemicals from these plants provide a promising avenue for liver cancer treatment, although further research is required to validate their efficacy, elucidate mechanisms of action, and ensure pharmacological standardization. Despite advances in modern medicine, plant-derived therapeutics continue to play a critical role in liver disease management and hold potential for integration into sustainable and effective cancer care strategies.

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