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Medicinal Plants for Prevention and Treatment of Liver Cancer

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ABSTRACT

Hepato cellular carcinoma (HCC), in particular, persists as one of the most prevalent forms of cancer related fatalities internationally. The potential therapeutic value of medicinal plants and their compounds that are bioactive in the prevention and treatment of liver cancer has attracted an extensive amount of attention in recent years. Turmeric, or *Curcuma longa*, garlic, *Zanthoxylum schinifolium*, *Zingiber officinale*, *Prunus salicina*, *Ribes nigrum L* and Cruciferous Vegetables are well-documented for their ability to protect hepatocytes against toxin-induced damage and suppress tumorigenesis through regulation of detoxifying enzymes and suppression of angiogenesis. These plants are abundant in phytochemicals, such as glycosides, phenolics, alkaloids, terpenoids, flavonoids, and saponins. These chemical substances have a variety of biological purposes, including pro-apoptotic, anti-inflammatory, antioxidant, and anti-proliferative properties. Through various kinds of procedures, several types of therapeutic plants have shown significant hepatoprotective and anti-cancer properties. Combining herbal extracts alongside traditional chemotherapeutic pharmaceuticals might improve therapeutic efficacy and reduce toxicity, according to preclinical and clinical research, suggesting a synergistic approach to the management of liver cancer.

Keywords: Liver cancer; Medicinal plants; Active components; Anticancer, Cellular homeostasis

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Introduction

Cancer develops when cells escape normal growth controls, multiply uncontrollably, and invade distant tissues (Saini et al., 2020). Left untreated, the disease kills. Hepatocellular carcinoma rates are climbing fastest in poorer countries, where it has become a serious public health problem. Scientists have grown more interested in medicinal plants because their compounds can reduce inflammation, slow tumor growth, and fight viral infections activities that could help treat liver cancer.With the ongoing growth of science, many herbal remedies are significantly useful for treating liver cancer (Ghosh et al., 2011).

Traditional treatments, which include a liver transplant, radiation, chemotherapy, and resection by surgery, frequently suffer from limitations associated with recurrence, high toxicity, and drug resistance. Alternative or additional methods of therapy that are safe and effective are therefore desperately needed. Traditional healthcare systems have utilized medicinal herbs for millennia, and their hepatoprotective and anticancer properties are now being confirmed by science. Several compounds generated by plants, including andrographolide from Andrographis paniculata, curcumin from Curcuma longa, and silymarin from Silybum marianum, have demonstrated potential in preventing the advancement of cancer while minimizing liver damage. Many methods, such as antioxidant activity, apoptotic regulation, signaling pathway enhancement, and detoxification enzyme enhancement are carried out by these phytochemicals. The research and study of medicinal plants offers an achievable path toward accelerating the development of breakthrough liver cancer treatments that integrate conventional knowledge with innovative biomedical technology that can improve patient outcomes and minimize adverse reactions associated with therapy.

Curcumin

Turmeric, or *Curcuma longa*, is a root plant of natural habitat in regions such as Southeast Asia, the Indian subcontinent, and other regions with a tropical climate (Chanda et al., 2019).It belongs to the same family as ginger and is widely cultivated as a herb. Most of the turmeric available worldwide comes from India. Turmeric has been utilized in Ayurvedic medicine for quite some time due to its ability to inhibit swelling, fight harmful bacteria, ease joint pain, and facilitate wound healing. It is

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also believed to protect the liver, lower blood sugar, improve cardiovascular health, reduce toxic fats, and even inhibit cancer (Blotner et al., 1929).

Curcumin is the main curcuminoid found in turmeric. It is composed of different types of compounds known as phenolics, among which the curcuminoid is the most important. It is also known as diferuloyl methane. Curcumin has been extensively studied and used to treat various diseases such as diabetes, autoimmune disorders, liver disease, and cancer over the past 20 years, including tests on mice (Wang et al., 2017). Mice studies using carcinogen exposure showed that curcumin limited tumor development. When researchers gave mice this compound before exposing them to hepatotoxic chemicals, fewer liver tumours formed. Xeno graft experiments—where human cancer cells were transplanted into rodents—demonstrated slower tumor expansion in curcumin-treated animals compared with controls. Most studies have investigated curcumin's ability to prevent cancer in both mice and human cells. It was observed to suppress the migration and spread of liver cancer cells by reducing the level of matrix metalloproteinase-9 (MMP-9) protein. Curcumin and its analogues also blocked cancer cell formation and induced cell death (Abadi et al., 2022).

Garlic

Several studies show that garlic has various anticancer potential (Stępień, 2024; Mohapatra, P., & Chandrasekaran, N., 2025). Fleischauer et al. (2011) found that major compounds of garlic, including allicin, alliin, and diallyl sulfide, have anticancer properties. High-allicin garlic powder from high-allicin garlic reduced DNA damage in chemically injured rats with liver injury. Allyl mercaptan also reduced DNA damage caused by dimethyl nitro samine. Morris et al. (2004) found that garlic lowered the growth rate of liver cells and prevented pre-malignant liver changes. Some human trials showed that garlic extract can increase the activity of natural killer (NK) cells. Epidemiological studies have shown that consuming large amounts of garlic can lower the incidence of many types of cancer, as reported by Dorant et al. (1993).Some of garlic's unique bioactive chemicals, known as organosulphur compounds (OSC), such as alliin, allicin, diallyl disulfide, diallyl sulfide, allyl mercaptan, and S-allylcysteine, are believed to be responsible for its cancer-fighting potential. For example, when rats were treated with garlic powder,

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DNA damage to the liver was reduced by 35% to 60%, according to a comet assay. This effect was attributed to the concentrated levels of alliin in the garlic. Later, some of these OSC compounds were tested by scientists for their ability to reduce DNA damage in HepG2 cells. All the compounds, except allyl mercaptan, helped reduce the damage caused by aflatoxin B1, while allyl mercaptan was effective in reducing the damage caused by dimethylnitrosamine. Guyonnet et al. (2002) found that diallyl disulfide also acted effectively against the toxic effect of benzo (α) pyrene. All the OSC compounds tested were effective in inhibiting DNA damage from direct-acting chemicals such as hydrogen peroxide and methyl methane sulfonate. In a study on rat liver cancer cells, sodium 2-propenyl thiosulfate greatly enhanced the activity of an enzyme known as quinone reductase. In a liver cancer cell line called Hep3B, garlic extracts increased the production of reactive oxygen species (ROS), which disrupted the mitochondrial membrane potential and induced cell death. Allicin caused cell death by increasing ROS levels in the same cancer cells. Since liver cancer tends to Meta stasise and recur, S-allyl cysteine was shown to suppress the metastasis and growth of liver cancer in a metastatic cell line called MHCC97L and in a mouse model of liver cancer, as found by Xiao et al. (2018).

The possible mechanisms of S-allyl cysteine include: (1) inhibiting cancer cell migration and spread by down regulating VEGF and up regulating E-cadherin; (2) inducing cancer cell apoptosis by decreasing Bcl-2 and Bcl-xl and activating caspase-3 and caspase-9; and (3) inhibiting cell cycle progression. In another study, water-soluble garlic extracts were found to be superior to the oily compound diallyl disulfide in preventing the growth of HepG2 cells. Bensam et al. (2023) reported that water-soluble extracts caused the cells to arrest at the G2/M phase of the cell cycle and induced cell death through a mechanism involving p53 and p21.

Pepper

Laboratory studies have identified that pepper extracts can prevent liver cancer cells from surviving without harming healthy cells (Zhou et al., 2016). This effect is possible because pepper lowers the levels of toxic chemicals (ROS), and damages cancer cells. A protein present in one variety of pepper, *Zanthoxylum piperitum*, helped combat cancer by inducing the self-destruction of cancer cells and enhancing the immune system in rats. Oils extracted from *Zanthoxylum schinifolium* showed

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antitumor properties against hepatic malignancies, with geranyl acetate, citronellal, and sabinene as major constituents (Paik et al., 2005). Researchers isolated a 24 Kd a glycoprotein from *Zanthoxylum piperitum* that protected against carcinogen-induced hepatic tumours through immune modulation and programmed cell death activation; mice receiving diethyl nitrosamine followed by 20 mg/kg glycoprotein treatment showed increased perforin and granzyme B expression alongside elevated natural killer cell function, while the glycoprotein also reduced pro-apoptotic proteins—Bid, caspase-3, and cytochrome c—in hepatic tissue. Metastatic spread requires extracellular matrix breakdown through metalloproteinases MMP-2 and MMP-9, whose endogenous inhibitors TIMP-1 and TIMP-2 correlate with restricted metastasis (Bauvois et al., 2012), and *Zanthoxylum avicennae* extracts blocked HA22T hepatoma cell proliferation through cell cycle arrest and apoptosis induction while decreasing migration and invasion as MMP-2 and MMP-9 levels dropped and TIMP-1 and TIMP-2 rose, with subsequent work identifying phosphatase 2A as a key mediator. Pericarp oil from *Z. schinifolium*, containing predominantly geranyl acetate, citronellal, and sabinene, increased ROS generation in HepG2 cells, triggering cell death, and xenograft models using human hepatic cancer cells confirmed antitumor activity in vivo(Yang et al., 2019).

Ginger

Zingiber officinale extracts demonstrate anti proliferative effects in hepatic malignancy models, with daily administration of 50 mg/kg reducing hepatic tissue proliferative markers in rodent studies. The bioactive constituent's 6-shogaol and 6-gingerol block hepatoma cell expansion and trigger oxidative stress-mediated apoptosis (Annamalai et al., 2016). Rats given diethyl nitrosamine to induce hepato carcinogenesis showed decreased circulating tumour markers—specifically alpha-fetoprotein and carcino embryonic antigen—when treated with 50 mg/kg daily ginger extract, alongside reduced hepatic growth factor expression through anti-inflammatory pathways and apoptosis activation (Habib et al., 2018). Higher doses at 100 mg/kg suppressed inflammatory mediators, including nuclear factor kappa B and malignant necrosis factor alpha, in hepatocarcinoma models, while a concentration-dependent inhibition of HEp-2 cells was observed with an IC_{50} of

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900 µg/mL, driven by reactive oxygen species accumulation and subsequent cell death.

Gas chromatography-mass spectrometry analysis identified geraniol, pino strobin, and clavatol among the phytochemical constituents (Vernin et al., 2016), and both 6-shogaol and 6-gingerol specifically suppressed hepatoma metastasis. They achieved this by reducing MMP-9 and urokinase-type plasminogen (in the presence of 6-shogaol) and increasing TIMP-1 levels. In addition, 6-shogaol also induced cancer cell death by increasing ROS and activating caspase-dependent apoptosis in a resistant type of liver cancer cell (Pan et al., 2018).

Plum

Peeled plums from the *Prunus salicina* plant contain a variety of compounds that can inhibit and deactivate tumour cells and protect the body against damage (Bahrin et al., 2022). When tested on a liver cancer cell line known as HepG2, plum extracts prevented the activation of cancer-associated genes and hindered the entry of toxic proteins into the cell nucleus. These extracts also reduced the biological invasion of cancer cells by enhancing the body's ability to detoxify harmful substances and minimizing the toxic effects of chemicals that cause cancer in animal models.

Immature plums belong to *Prunus salicina* are rich in natural phenolics that act as antioxidants feasibility of inhibiting cancer (Stacewicz et al., 2013). Plum peel extracts containing predominantly (−)-epicatechin (34.7%) and (−)-gallocatechin gallate (28.6%) triggered death receptor-mediated apoptosis in HepG2 hepatoma cells through sequential activation of initiator caspases-8 and -10 followed by executioner caspase-3, culminating in chromosomal DNA fragmentation. These extracts also blocked HepG2 cell motility by down regulating matrix metalloproteinase-9 gene transcription (Bellosta et al., 2003), achieved through preventing nuclear translocation of transcription factors nuclear factor kappa-B and activator protein-1. Hepatic transformation occurs in two principal phases. Phase I oxidative metabolism often produces reactive intermediates from xenobiotics, while Phase II conjugation reactions promote their detoxification and excretion. In experimental models, pretreatment with immature plum extracts conferred protection against benzo (α) pyrene-induced hepatotoxicity, indicating that poly

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phenolic constituents modulate hepatic xenobiotic metabolism to mitigate chemical injury. This was because the plum extracts enhanced the synthesis of detoxifying enzymes in the body (Igwe et al., 2016).

Black Currant

Black currant, *Ribes nigrum L.* is a commonly consumed food well-known for having strong antioxidant and anti-inflammatory abilities. This is because it contains a large amount of anthocyanins, approximately 250 mg for every 100 grams of fresh fruit (Horbowicz et al., 2008). . In a laboratory test using HepG2 cells, the part of black currant with the most anthocyanins was found to slow down the growth of the cells. The skin of the black currant, known as BCSE, has more anthocyanins than other parts, and the main anthocyanin in it is called cyanidin-3-O-rutinoside.

In a study with rats that had liver cancer caused by a chemical called diethyl nitrosamine (DEN), giving BCSE at doses of 100 or 500 mg/kg for two weeks helped reduce liver tumors in a dose-dependent manner (Ghufran et al., 2021). BCSE also helped decrease lipid peroxidation and the activity of some proteins, such as cyclooxygenase-2, heat shock proteins (HSP70 and HSP90), inducible nitric oxide synthase, and 3-nitrotyrosine, while boosting the activity of several liver enzymes that assist with antioxidant and detoxification functions, such as glutathione S-transferase, quinone oxidoreductase, and uridine diphosphate glucurono syltrans ferase is enzymes (Chen et al., 2020).

Cruciferous Vegetables Members of the *Cruciferae* (*Brassicaceae*) family, widely cultivated and consumed as vegetables, have been associated with a reduced risk of several malignancies. Epidemiological and experimental studies suggest that regular consumption of cruciferous vegetables such as cauliflower, broccoli, watercress, and Brussels sprouts exerts chemo preventive effects primarily through their high content of glucosinolates and their bioactive derivatives, isothiocyanates. Radishes (*Raphanus sativus*), belonging to the same family as brussels, are rich in similar phytochemicals, including glucosinolates, isothiocyanates, and polyphenols. Among these, 4-methylsulfanyl-3-butenyl glucosinolate (glucoraphasatin) is particularly abundant and has been identified as a key bioactive compound. The anticancer potential of these metabolites is thought to involve the upregulation of endogenous detoxification and antioxidant systems, mediated through enzymes such

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as NAD (P) H: quinone oxidoreductase-1 (NQO1), glutathione-S-transferase, and phenol sulfotransferases, thereby enhancing cellular defense against carcinogenic effect. These enzymes help the body break down and eliminate harmful substances. Studies of Sharma et al., (2025) have found that glucosinolates can enhance the activity of these detoxification enzymes, thereby assisting the body in removing dangerous chemicals. However, some studies suggest that it is actually the isothiocyanates, rather than the glucosinolates themselves, that exert the real cancer-fighting effects in middle-aged patients (Narra et al., 2025).For instance, experiments using rat liver slice models demonstrated that low concentrations of gluco raphasatin and its corresponding is othiocyanate derived from radish sprouts significantly enhanced the activity of Phase II detoxification enzymes involved in the metabolism of toxic compounds, including mycotoxins, heterocyclic amines, and polycyclic aromatic hydrocarbons.(Stoian et al., 2025). Moreover, sulforaphane, an isothiocyanate found in high concentrations in broccoli, has been shown to increase the expression of CYP1A1 in specific liver cells in a time- and dose-dependent manner (Yamaguchi et al., 2024).However, in humans, sulforaphane is highly reactive and quickly converts into a compound called N-acetyl-L-cysteine (NAC). The NAC form of sulforaphane was found to be more effective at inhibiting the growth of mouse liver cancer cells and increasing the activity of quinone reductase, another enzyme involved in the body's detoxification process (Fahey et al., 1999).

Conclusion

Therefore, considering their natural origin, low toxicity, and multitargeted pharmacological properties, medicinal plants represent an attractive frontier in liver cancer prevention and therapy. The production of revolutionary plant-based hepatoprotective and anticancer drugs may be made achievable through the integration traditional herbal scientific knowledge with present molecular research. A complete understanding of the phytochemical pathways along with how they operate in combination with traditional medications can assist with develop safer, less expensive, and more effective liver cancer therapy plans that also enhance patient outcomes.

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