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Phytotherapeutic Potential of Medicinal Plants Against Hepatitis C: A Review

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A B S T R A C T

Objective: Hepatitis C virus (HCV) infection remains a major global health challenge, contributing to chronic liver disease, cirrhosis, and hepatocellular carcinoma. Although direct-acting antivirals (DAAs) have markedly improved treatment outcomes, their high cost and potential adverse effects limit accessibility, particularly in low-resource settings. Consequently, there is increasing interest in exploring medicinal plants as alternative or complementary therapies for HCV management.

Methods: This systematic review analyzed 12 peer-reviewed studies investigating the therapeutic potential of medicinal plants with anti-HCV activity. Extracted data included plant species, bioactive compounds, mechanisms of action, and hepatoprotective properties.

Results: Several plants demonstrated notable antiviral and hepatoprotective effects, including *Citrus aurantium L., Cynara cardunculus L., Acacia nilotica, Marrubium peregrinum L., Camellia sinensis L., Olea europaea, Glycyrrhiza uralensis, Maytenus ilicifolia, Lamium album L., Artemisia annua L., and Silybum marianum* L. These botanicals exert therapeutic effects through diverse mechanisms, including inhibition of viral entry, suppression of viral replication, modulation of immune responses, antioxidant activity, and hepatocyte protection.

Conclusion: Medicinal plants exhibit promising anti-HCV and hepatoprotective activities, indicating their potential as affordable and well-tolerated therapeutic options. Nevertheless, further in vitro, in vivo, and clinical studies are required to validate efficacy, establish standardized dosages, and assess long-term safety. Integration of phytotherapy with conventional antiviral regimens may enhance treatment outcomes and reduce the global healthcare burden associated with hepatitis C.

Keywords: Hepatitis C, Medicinal plants, Antiviral, Hepatoprotection, Phytotherapy

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Introduction

Hepatitis C is a viral disease primarily affecting the liver and caused by the Hepatitis C virus (HCV) [1]. HCV is a small, positive-strand, enveloped RNA virus capable of evading the host immune system, allowing persistent replication over prolonged periods [1]. Infection may be acute or chronic, with a small proportion of patients spontaneously clearing the virus during the acute phase, while the majority progress to chronic liver disease [2]. Chronic infection can lead to liver tissue damage, hepatitis, and an increased risk of transmission to close contacts, which can be mitigated through adherence to health guidelines [2]. Major routes of HCV transmission include exposure to infected blood, sharing contaminated needles among drug users, tattooing with unsterile equipment, blood transfusions or organ transplants from infected donors, mother-to-fetus transmission, and sexual contact [3].

Early-stage hepatitis C is often asymptomatic or presents with nonspecific symptoms; however, as the disease progresses, patients may experience fatigue, fever, weight loss, anorexia, myalgia and arthralgia, abdominal discomfort, dark urine, pruritus, peripheral and abdominal edema, jaundice, and pale-colored stools [4]. Diagnosis relies on a thorough medical history and clinical evaluation, supported by laboratory tests detecting HCV antibodies and viral RNA, and in some cases, liver biopsy [5]. Currently, no vaccine exists for HCV, and treatment primarily involves antiviral medications such as interferon and ribavirin, which achieve sustained virologic responses in approximately 50–80% of patients. Contemporary regimens recommended by the American Association for the Study of Liver Diseases include glecaprevir (300 mg)/pibrentasvir (120 mg) for 8 weeks and sofosbuvir (400 mg)/velpatasvir (100 mg) for 12 weeks. According to the Centers for Disease Control and Prevention (CDC), modern antiviral therapies achieve cure rates exceeding 90% with minimal adverse effects [6].

Despite their high efficacy, chemical antivirals can cause significant side effects [6], prompting growing interest in alternative strategies to prevent HCV infection and inhibit viral entry into host cells. Medicinal plants and herbal remedies have attracted attention due to their cost-effectiveness and favorable safety profiles [7–12]. Plant-derived bioactive compounds have demonstrated therapeutic potential in HCV management, and when combined with antiviral therapy, herbal medicines and dietary supplements may help alleviate symptoms and protect hepatic function [13]. This review aims to provide a comprehensive overview of medicinal plants with demonstrated efficacy in the prevention and management of hepatitis C, based on evidence from previous studies.

Materials and Methods

This systematic review was conducted to evaluate the potential effects of medicinal plants on Hepatitis C virus (HCV) infection. Relevant studies published between 2008 and 2020 were identified through comprehensive searches of the PubMed, Google Scholar, and ScienceDirect databases. The search strategy employed a combination of keywords and Boolean operators, including ("Hepatitis C" OR "HCV") AND ("medicinal plants" OR "herbal medicine" OR "phytotherapy"), as well as ("Hepatitis C" AND "herbal treatment" OR "plant extract").

Inclusion criteria were as follows:

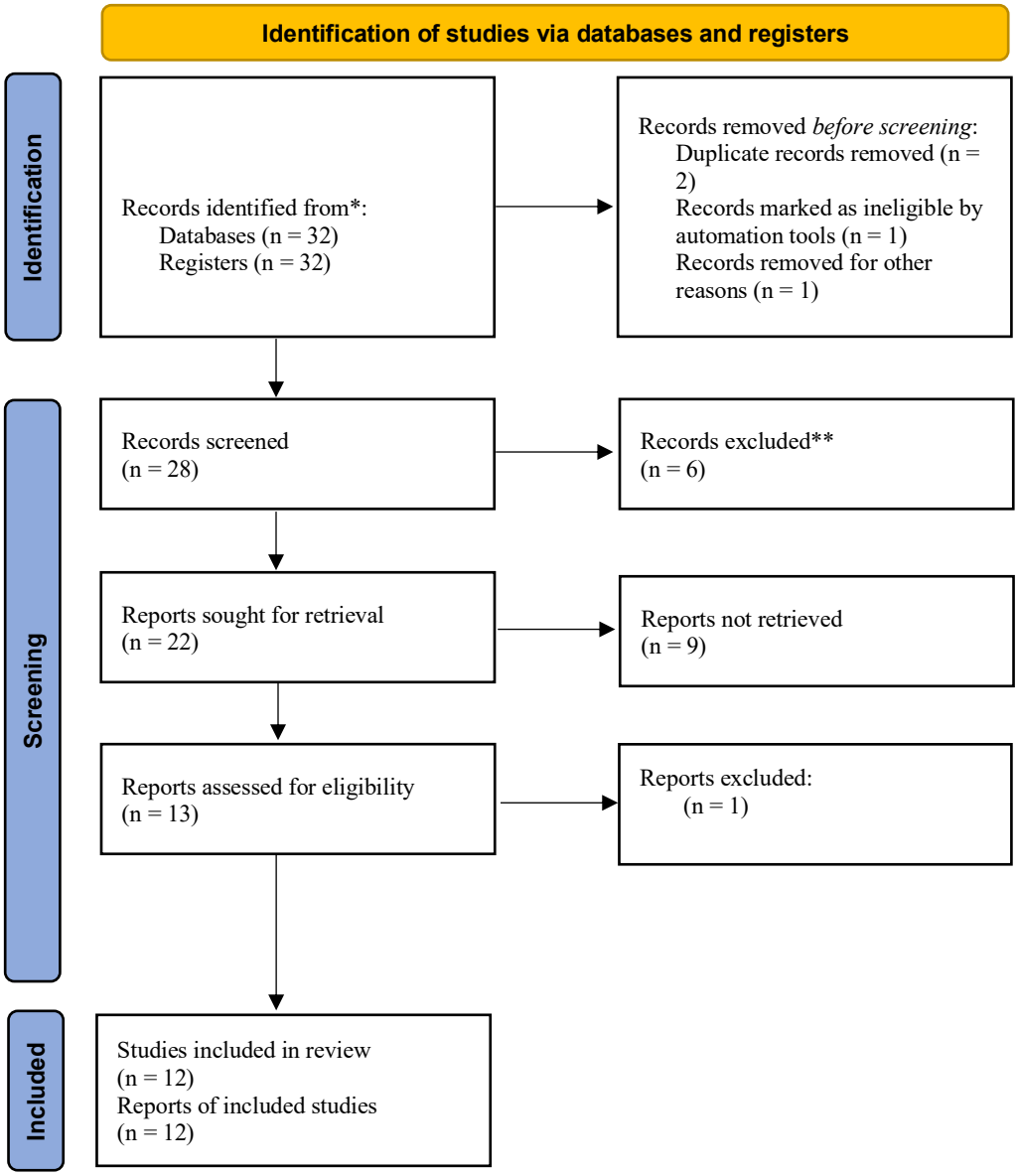
Original research articles published in peer-reviewed journals between 2008 and 2020. Studies investigating the antiviral or hepatoprotective effects of medicinal plants against HCV. Articles published in English or Persian.

Exclusion criteria included:

Reviews, abstracts, conference proceedings, or non-scientific publications. Duplicate or highly similar studies.

A total of 32 articles were initially identified. After screening titles, abstracts, and full texts, 12 studies were selected for detailed analysis. The study selection process is summarized in Figure 1 (Flowchart of Literature Screening and Selection).

Figure 1: Flowchart of Search Strategy



Results

The results of the literature review indicate that several medicinal plants have been utilized for the management and treatment of Hepatitis C. The medicinal plants identified as effective against HCV are summarized in Table 1. These include *Citrus*

aurantium L., *Cynara cardunculus* L., *Acacia nilotica* L., *Marrubium peregrinum* L., *Camellia sinensis* L., *Olea europaea* L., *Glycyrrhiza uralensis* Fisch., *Maytenus ilicifolia* Mart., *Artemisia annua* L., *Lamium album* L., and *Silybum marianum* L.

Table 1: List of herbal plants used for hepatitis C prevention or treatment

Scientific Name	Family	English Name	Active Compounds / Ingredients	Mechanism of Action
Citrus aurantium L.	Rutaceae	Grapefruit	Naringenin	Inhibits viral entry and replication [14]
Cynara cardunculus L.	Asteraceae	Artichoke	Oxalic, quinic, malic, citric, fumaric acids; palmitic, oleic, linoleic acids	Inhibits viral replication, modulates immune response, reduces oxidative stress, and improves liver function [15]
Acacia nilotica	Fabaceae	Gum Arabic Tree	Volatile oils, saponins, hydrolyzable tannins, flavonoids, triterpenoids, phenols	Modulates immune response and exhibits antiviral activity [16]
Marrubium peregrinum L.	Lamiaceae	White Horehound	Apigenin, cyclosporine, luteolin, ladenin	Inhibits viral replication [17]
Camellia sinensis L.	Theaceae	Green Tea	Epigallocatechin-3-gallate	Inhibits HCV entry and reduces viral replication [18]
Olea europaea	Oleaceae	Olive	Oleanolic acid, ursolic acid	Modulates immune response and inhibits viral replication [19]
Glycyrrhiza uralensis	Fabaceae	Liquorice	Glycyrrhizin	Inhibits HCV entry and replication [20]
Maytrenus ilicifolia	Celastraceae	Maytenus	Glycycoumarin, alkaloids, glycerol	Inhibits viral replication [21]
Lamium album L.	Lamiaceae	White Dead Nettle	Lamiridosin, iridoid aglycone epimer	Modulates immune response [22]
Artemisia annua L.	Asteraceae	Sweet Wormwood	Quercetin, polyphenols, triterpenes, sterols, d-caffeoylquinic acid	Inhibits viral replication and reduces inflammation [23]
Silybum marianum L.	Asteraceae	Milk Thistle	Silymarin, silibinin	Protects liver cells and promotes regeneration [24]

Table 2 presents a summary of medicinal plants with therapeutic potential against hepatitis C virus (HCV). It highlights their key active compounds and main biological properties related to antiviral and hepatoprotective effects.

Table 2: Therapeutic Medicinal Plants and Their Key Active Compounds

Scientific Name	Plant Part Used	Main Traditional Antimicrobial Uses [14-24]	Main Active Compound	Growth and Vegetative Pattern	Ecology / Habitat
Citrus aurantium L.	Fruit peel, flower, leaves	Antibacterial, antiviral	Synephrine	Small tree, perennial	Cultivated and wild in subtropical regions; well-drained soils
Cynara cardunculus L.	Leaves, flower, stem	Antibacterial, antioxidant	Cynarin	Perennial herb	Mediterranean climates; rocky and dry soils
Acacia nilotica	Bark, leaves, fruit, flower, root	Antibacterial, antiviral	Gallic acid	Tree, perennial	Tropical and subtropical regions; riverbanks, savannas
Marrubium peregrinum L.	Leaves, stem, flower	Antibacterial, anti-inflammatory	Marrubiin	Perennial herb	Dry meadows and rocky slopes
Camellia sinensis L.	Leaves	Antibacterial, antiviral	Epigallocatechin gallate (EGCG)	Evergreen shrub/tree, perennial	Subtropical/tropical highlands; well-drained acidic soils
Olea europaea	Leaves, fruit	Antibacterial, antiviral	Oleuropein	Evergreen tree, perennial	Mediterranean regions; well-drained, calcareous soils
Glycyrrhiza uralensis	Root	Antiviral, antibacterial	Glycyrrhizin	Perennial herb	Arid to semi-arid regions; sandy and loamy soils
Maytenus ilicifolia	Leaves, stem	Antibacterial, antioxidant	Maytenin	Evergreen shrub, perennial	Subtropical forests; well-drained soils

Lamium album L.	Leaves, flower	Antimicrobial, anti-inflammatory	Luteolin	Perennial herb	Meadows, roadsides, temperate climates
Artemisia annua L.	Leaves, flower	Antiviral, antibacterial	Artemisinin	Annual herb	Temperate to subtropical regions; sunny, well-drained soils
Silybum marianum L.	Seeds	Antioxidant, antibacterial	Silymarin	Biennial herb	Mediterranean regions; disturbed soils, fields, roadsides

Analysis of the results presented in Table 2 indicates that the majority of the studied species are perennial herbaceous plants. Their extended lifespan and ecological stability enable the accumulation of potent secondary metabolites, including flavonoids and terpenoids. These species are primarily distributed in Mediterranean and semi-tropical regions, which are recognized as rich habitats for medicinal plants and are characterized by high diversity in phenolic and flavonoid compounds associated with antibacterial and antiviral activities.

Among the chemical constituents, flavonoids and phenolic acids play key roles in inhibiting bacterial and viral pathogens, as well as in preventing cellular oxidative damage. All examined species demonstrated antibacterial activity, while more than half exhibited antiviral effects. These findings suggest that perennial herbaceous plants may be particularly effective in managing viral diseases, such as hepatitis C, due to their enhanced production of secondary metabolites and high metabolic diversity. Consequently, these plants represent promising natural sources for the treatment or prevention of viral infections in future pharmacological research.

Flavonoids and terpenoids emerged as the two dominant groups of bioactive compounds, playing critical roles in both antibacterial and antiviral activities. Table 2 highlights various bioactive constituents, including flavonoids, organic acids, tannins, saponins, and other phytochemicals, which have been extensively investigated for their antiviral potential, particularly against HCV. Many of these compounds exert their effects by inhibiting viral entry into host cells or suppressing viral replication.

Examining the plant families provides insight into biochemical similarities and differences among species, as closely related plants often contain comparable active compounds. For example, members of the Asteraceae family, such as artichoke and milk thistle, may share hepatoprotective mechanisms due to similar bioactive constituents. Notably, the Asteraceae, Fabaceae, and Lamiaceae families are frequently represented, underscoring their significance in medicinal, nutritional, and ornamental contexts. The pronounced antiviral activity of compounds from these families highlights their potential as sources for novel and effective HCV therapies, warranting further research and exploration.

Discussion

The present review highlights the antiviral and hepatoprotective potential of several medicinal plants against Hepatitis C virus (HCV) [25]. For instance, cynaropicrin from *Cynara cardunculus* exhibits antiviral activity by inhibiting the NF-κB-mediated inflammatory pathway, which is essential for viral replication and liver inflammation [26]. Extracts of *Acacia nilotica* demonstrated over 50% inhibition of HCV at non-toxic concentrations, underscoring their potential as safe antiviral agents [27]. *Marrubium peregrinum* L. interferes with RNA-dependent RNA polymerase NS5, thereby reducing viral replication [28]. Catechins from *Camellia sinensis* (EGCG, EGC, ECG, EC) have shown both antiviral and anti-oncogenic effects, suggesting a dual role in preventing HCV-induced liver damage and hepatocellular carcinoma [29].

Hepatoprotective activity has also been reported for *Olea europaea*, which protects liver cells against oxidative stress and inflammation [30]. Active compounds isolated from *Glycyrrhiza uralensis*, including glycycoumarin and licoiritigenin, inhibited HCV replication with IC_{50} values of 8–20 μg/mL, highlighting the importance of identifying and isolating bioactive phytochemicals for therapeutic use [31]. Iridoid analogs from *Lamium album* demonstrated significant anti-HCV activity, confirming the role of secondary metabolites in viral inhibition [32]. Additionally, diosgenin, a plant-derived sapogenin, effectively suppressed HCV subgenomic replication at micromolar concentrations without cytotoxicity [33].

Collectively, these findings indicate that plant-derived compounds can target multiple stages of the HCV life cycle, including viral entry, replication, and assembly. Compared to conventional antiviral

drugs, herbal treatments offer advantages such as lower toxicity, reduced side effects, and cost-effectiveness. However, challenges remain, including variability in bioactive compound concentrations, lack of standardized dosages, and limited clinical trials validating efficacy in humans [34–40].

Future research should focus on the isolation and characterization of active phytochemicals, elucidation of their precise molecular mechanisms, and well-designed clinical studies to assess safety and therapeutic effectiveness. Integrating medicinal plants with conventional antiviral therapies may provide synergistic effects, enhance patient outcomes, and reduce the overall burden of HCV treatment.

Conclusion

The antiviral activity of medicinal plants against Hepatitis C virus (HCV) is largely attributed to their hepatoprotective properties, which are mediated by bioactive compounds such as flavonoids, terpenoids, and polyphenols with potent antioxidant activity. These compounds can inhibit viral entry, suppress replication, modulate immune responses, and reduce oxidative stress, collectively contributing to liver protection. In clinical practice, incorporating herbal agents as adjuncts to conventional antiviral therapies may enhance treatment efficacy, mitigate drug-related side effects, and reduce overall healthcare costs. However, standardized dosing, stringent quality control, and rigorous clinical trials are essential to establish both safety and therapeutic effectiveness. Future research should focus on the isolation and characterization of active phytochemicals, elucidation of their molecular mechanisms, and evaluation of their clinical potential in well-designed human studies. Such investigations could facilitate the development of novel, cost-effective, and safe phytotherapeutic interventions for HCV, ultimately improving patient outcomes and quality of life.

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