
# Plant-Based Therapies for Viral Infections

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**Abstract**
Viral infections constitute one of the foremost challenges to global public health, imposing substantial morbidity, mortality, and socioeconomic burden across diverse geographic settings. Despite considerable progress in antiviral pharmacotherapy, current conventional strategies—including nucleoside analogues, protease inhibitors, and neuraminidase inhibitors—are undermined by rapidly emerging drug resistance, restricted therapeutic spectra, and adverse side-effect profiles that limit long-term applicability. Against this backdrop, plant-based therapies have attracted intensified scientific scrutiny as potential sources of novel antiviral agents endowed with multi-target pharmacological capabilities. This review critically examines the antiviral properties of phytochemicals, with particular focus on the major bioactive classes encompassing flavonoids, alkaloids, terpenoids, and polyphenols. The mechanisms by which these compounds exert antiviral activity are evaluated in depth, encompassing inhibition of viral attachment and cellular entry, suppression of replication machinery, interference with protein synthesis and viral assembly, and immunomodulatory modulation of host defence responses. Evidence derived from in vitro experimental systems, animal models, and early-phase clinical investigations is synthesised and critically appraised. Special attention is directed to translational challenges including pharmacokinetic limitations, bioavailability constraints, variability in phytochemical composition, and regulatory hurdles that impede clinical advancement. Contemporary formulation strategies, including nanoparticulate delivery platforms and standardised extract technologies, are discussed in the context of improving therapeutic efficacy. This review concludes by identifying priority areas for future investigation and underscoring the considerable translational promise of plant-derived antiviral compounds.

**Keywords:** Plant-based therapies, Viral infections, Antiviral agents, Phytochemicals, Immunomodulation, Translational research

## 1. Introduction

Viral infections collectively represent a leading cause of human morbidity and mortality worldwide, with their impact spanning acute epidemic events, endemic disease cycles, and the emergence of pandemic pathogens capable of rapid global dissemination [1]. The burden imposed by viruses such as influenza, human immunodeficiency virus (HIV), severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), hepatitis B and C viruses (HBV, HCV), herpes simplex virus (HSV), and dengue virus encompasses not only immediate clinical consequences but also long-term sequelae that challenge health systems globally [2]. Despite decades of sustained pharmaceutical investment, the antiviral armamentarium remains constrained by a narrow range of approved agents, most of which target specific viral enzymes or structural proteins and are therefore effective against only a limited spectrum of pathogens [3].

The emergence of antiviral drug resistance constitutes a critical limitation of current therapeutic paradigms. The high mutation rates inherent to RNA viruses, combined with selective pharmacological pressure, facilitate the rapid selection of resistant viral variants capable of evading established treatment regimens [4]. Furthermore, many licensed antiviral agents are associated with significant adverse effects, including nephrotoxicity, hepatotoxicity, haematological disturbances, and teratogenicity, which reduce patient tolerability and restrict clinical applicability [5]. These combined limitations have created an urgent imperative to identify and develop novel antiviral agents capable of acting through diverse mechanistic pathways and demonstrating improved safety profiles.

Medicinal plants have served as a foundational resource for therapeutic discovery throughout human history, and contemporary pharmacological investigation has confirmed that plant-derived secondary metabolites possess potent and multifaceted biological activities [6]. The chemical diversity represented within the plant kingdom provides an unparalleled reservoir of structurally varied bioactive compounds, many of which have demonstrable effects on viral replication cycles, host immune responses, and cellular signalling pathways relevant to infection [7]. Notably, several clinically deployed antiviral agents—including oseltamivir, derived from shikimic acid obtained from star anise, and compounds derived from artemisinin chemistry—trace their origins to botanical sources [8]. This pharmacognostic precedent reinforces the rational basis for investigating plant-derived compounds as sources of novel antiviral therapeutics.

This review aims to provide a comprehensive and critically evaluated synthesis of current knowledge pertaining to plant-based antiviral therapies, encompassing the biological basis of plant compound activity, the virological mechanisms underlying their antiviral effects, translational research findings, and the challenges and opportunities associated with their development into clinical applications [9].

## 2. Biology of Viruses: Structure, Replication, and Host–Virus Interactions

A thorough understanding of viral biology is essential for the rational evaluation of plant-based antiviral strategies. Viruses are obligate intracellular parasites characterised by their structural simplicity and absolute dependence upon host cellular machinery for replication. The fundamental structural components of a virus particle—termed the virion—comprise a nucleic acid genome encapsidated within a proteinaceous capsid, which in enveloped viruses is further surrounded by a lipid bilayer membrane derived from the host cell and embedded with viral glycoproteins [10]. These surface glycoproteins mediate recognition of host cell receptors and initiation of the infection cycle, and represent primary targets for both immune recognition and antiviral intervention.

The viral replication cycle proceeds through a series of sequential and interconnected stages. Initial attachment occurs through specific interaction between viral surface proteins and cognate cellular receptors, a process governed by high-affinity molecular recognition [11]. Following attachment, viral entry is accomplished by membrane fusion, endocytosis, or direct injection of genetic material, depending on the viral family. Intracellular uncoating liberates the viral genome, which subsequently directs the synthesis of viral proteins using host ribosomes and enzymatic machinery. DNA viruses typically replicate within the nucleus, whereas RNA viruses, which constitute the majority of clinically significant pathogens, replicate predominantly within the cytoplasm using virus-encoded RNA-dependent RNA polymerases (RdRp) [12]. Viral assembly involves the coordinated packaging of newly synthesised genomes within nascent capsid structures, followed by maturation and release of progeny virions via budding or cell lysis.

Host-virus interactions extend beyond the direct mechanics of replication to encompass complex immunological dynamics. Infected cells mount innate immune responses mediated by pattern recognition receptors (PRRs) such as toll-like receptors (TLRs) and retinoic acid-inducible gene I (RIG-I), culminating in the production of type I interferons (IFNs) and pro-inflammatory cytokines [13]. Many viruses have evolved sophisticated mechanisms to evade or suppress these innate defences, including degradation of interferon signalling components, inhibition of antigen presentation, and exploitation of host immune regulatory pathways. Plant-derived compounds that interfere with these viral evasion mechanisms or augment host immune responses therefore represent a particularly valuable class of potential antiviral agents [14].

## 3. Plant-Based Bioactive Constituents and Pharmacological Relevance

The pharmacological activity of medicinal plants derives from their secondary metabolites, which are biosynthesised as ecological adaptations to environmental stressors including microbial pathogens, herbivores, and abiotic challenges [15]. These compounds are classifiable into several major chemical categories, each encompassing a diverse array of structurally distinct molecules with established or emerging antiviral properties.

### 3.1. Flavonoids

Flavonoids constitute one of the most extensively studied classes of plant-derived antiviral compounds. This polyphenolic family encompasses flavones, flavonols, flavanones, catechins, and isoflavones, characterised by a common C6-C3-C6 carbon skeleton with variable hydroxylation and glycosylation patterns [16]. Quercetin, kaempferol, luteolin, epigallocatechin gallate (EGCG), and apigenin have demonstrated antiviral activity against a broad spectrum of clinically relevant pathogens in experimental systems. The antiviral mechanisms of flavonoids are multifaceted and include direct virucidal activity through disruption of viral envelope integrity, inhibition of viral attachment to host cell receptors, suppression of viral polymerase activity, and interference with post-translational processing of viral proteins [17].

### 3.2. Alkaloids

Alkaloids are nitrogen-containing heterocyclic compounds biosynthesised primarily from amino acid precursors, and are represented by diverse structural families including indole, isoquinoline, purine, and quinoline alkaloids [18]. Several alkaloids have demonstrated significant antiviral activity; berberine, an isoquinoline alkaloid abundant in Berberis and Coptis species, has been shown to inhibit replication of influenza virus, HSV, and HCV through interference with viral entry, RNA synthesis, and protein expression. Lycorine, derived from Amaryllidaceae species, displays broad-spectrum antiviral activity including activity against

coronaviruses and flaviviruses, partly through inhibition of viral protein synthesis at the translational level [19].

### 3.3. Terpenoids

Terpenoids, biosynthesised via the mevalonate and non-mevalonate pathways, represent the largest class of plant secondary metabolites and include monoterpenes, sesquiterpenes, diterpenes, and triterpenes [20]. Betulinic acid and ursolic acid, pentacyclic triterpenes with widespread distribution in plant species, have demonstrated inhibitory activity against HIV, HCV, and herpes viruses through mechanisms including interference with viral protein-protein interactions and suppression of viral protease function. Artemisinin and its derivatives, sesquiterpene lactones originally characterised as antimalarials, have been shown to possess antiviral activity against several RNA viruses including SARS-CoV-2, mediated in part by reactive oxygen species generation and disruption of viral replication complexes [21].

### 3.4. Polyphenols and Other Bioactive Classes

Beyond the flavonoid subclass, polyphenols include hydroxycinnamic acids, stilbenes, lignans, and tannins, many of which demonstrate antiviral properties [22]. Resveratrol, a stilbene found in grape skin and various berries, inhibits replication of influenza virus, HIV, and herpes viruses through modulation of cellular signalling pathways including activation of sirtuin deacetylases and inhibition of NF-kB signalling. Ellagic acid and tannic acid, representative tannins, demonstrate potent virucidal activity and inhibition of viral attachment. Additional noteworthy antiviral phytochemicals include saponins, which disrupt viral envelopes through membrane-active properties, lectins with hemagglutinin-inhibitory activity, and sulphur-containing compounds such as allicin from Allium sativum with broad-spectrum antiviral effects [23].

## 4. Mechanisms of Antiviral Action

### 4.1. Inhibition of Viral Entry and Attachment

Interference with the initial stages of viral infection—attachment and entry—represents one of the most extensively characterised antiviral mechanisms of phytochemicals. Viral glycoprotein-receptor interactions, which are obligatory for cellular tropism and infection initiation, offer multiple pharmacological targets [24]. Flavonoids including quercetin and EGCG have been shown to bind directly to viral surface proteins, including influenza hemagglutinin and SARS-CoV-2 spike protein, thereby sterically blocking receptor engagement. Polyphenolic compounds further disrupt viral attachment through electrostatic interactions with heparan sulphate proteoglycans on host cell surfaces, which serve as initial low-affinity attachment factors for numerous viruses including HSV, HIV, and cytomegalovirus [25].

### 4.2. Suppression of Viral Replication

Viral replication enzymes, particularly RNA-dependent RNA polymerases and DNA polymerases, represent high-priority antiviral targets owing to their essential roles in genome amplification and their structural distinctions from host polymerases [26]. Several phytochemicals demonstrate competitive or non-competitive inhibition of viral polymerases; EGCG has been reported to inhibit the RdRp of poliovirus and other enteroviruses, while baicalein and luteolin suppress HCV NS5B polymerase activity. Terpenoids and alkaloids additionally interfere with reverse transcriptase activity in retroviruses, constituting a mechanistic basis for their anti-HIV activity. Beyond direct enzyme inhibition, phytochemicals may disrupt the assembly of viral replication complexes or interfere with genome circularisation events required for efficient RNA synthesis [27].

### 4.3. Interference with Viral Assembly and Release

Following genome replication, the assembly of progeny virions and their subsequent release from infected cells represent additional vulnerable stages of the viral lifecycle. Betulinic acid has been shown to inhibit HIV-1 maturation by targeting the viral protease, preventing correct processing of the Gag-Pol polyprotein precursor and generating non-infectious immature particles [28]. Quercetin and other flavonoids disrupt the function of neuraminidase in influenza virions, impeding the release of progeny particles from the surface of infected cells and thereby limiting intercellular viral spread. Additionally, plant-derived compounds that stabilise host cell membranes or interfere with the budding machinery may reduce the efficiency of enveloped virus release.

### 4.4. Immunomodulatory Effects

A distinct and therapeutically significant dimension of plant-based antiviral activity involves modulation of host immune responses. Many phytochemicals enhance innate antiviral defences by stimulating interferon production, activating natural killer cells, and augmenting macrophage-mediated antiviral functions [29]. Andrographolide, a diterpene lactone from Andrographis paniculata, activates NF-kB signalling and augments type I IFN responses while simultaneously suppressing excessive pro-inflammatory cytokine production, thereby potentially ameliorating virus-associated pathological inflammation. Echinacea-derived alkylamides and polysaccharides stimulate innate immune pathways and have been associated with reduced severity and duration of upper respiratory viral infections in clinical studies [30].

## 5. Preclinical and Translational Research

### 5.1. In Vitro Evidence

The foundation of antiviral evidence for the majority of plant-derived compounds rests upon in vitro experimental systems utilising cell culture models of viral infection. Such studies enable controlled mechanistic investigation of antiviral activity, selectivity index determination, and structure-activity relationship analyses [31]. Cell-based assays employing virus-infected Vero, HEK293, or primary human cell lines have been utilised to demonstrate antiviral activity of flavonoids against dengue virus, Zika virus, and coronaviruses, among others. While in vitro data provide mechanistic insights of considerable value, they are subject to well-recognised limitations including the absence of pharmacokinetic processes, simplified immunological milieux, and potential artefacts associated with high compound concentrations unachievable *in vivo*.

### 5.2. Animal Models

Animal model studies provide the critical bridge between in vitro findings and clinical development by enabling evaluation of antiviral efficacy in the context of physiological pharmacokinetics, immune competence, and tissue distribution [32]. Murine models of influenza, herpes, HIV,

and flavivirus infection have been employed to assess the *in vivo* antiviral activity of numerous phytochemicals. Quercetin has demonstrated significant reduction in influenza viral titres and mortality rates in mouse models, while glycyrrhizin from Glycyrrhiza glabra has shown efficacy in reducing SARS-associated lethality in animal studies. Critically, concordance between in vitro and *in vivo* outcomes is frequently imperfect, underscoring the importance of animal model validation prior to clinical investigation.

### 5.3. Pharmacokinetics and Bioavailability Challenges

The translation of preclinical antiviral activity to clinical efficacy is substantially complicated by pharmacokinetic limitations inherent to many phytochemicals. Oral bioavailability is often poor owing to limited aqueous solubility, extensive first-pass hepatic metabolism, rapid intestinal degradation, and inefficient gastrointestinal absorption [33]. Quercetin, for instance, undergoes extensive Phase II conjugation in the intestinal epithelium and liver, reducing its systemic bioavailability and potentially altering its pharmacological profile. Curcumin, which has demonstrated antiviral activity in vitro, is characterised by extremely low oral bioavailability attributable to its rapid metabolic transformation and poor aqueous solubility. These pharmacokinetic constraints necessitate the development of formulation strategies capable of enhancing systemic exposure to bioactive phytochemicals at therapeutically relevant concentrations.

## 6. Current Clinical Applications and Evidence

The clinical evidence base for plant-based antiviral therapies, while expanding, remains less robust than that supporting conventional antiviral agents. A limited number of standardised botanical preparations have been subjected to rigorous randomised controlled trials, and the methodological quality of available clinical studies is variable [34]. Preparations standardised for andrographolide content have demonstrated statistically significant reductions in duration and severity of symptoms associated with upper respiratory viral infections in several randomised controlled trials, with a favourable safety profile and no significant adverse events reported. Echinacea preparations have similarly been evaluated in multiple clinical trials for prevention and treatment of viral rhinitis, with meta-analyses suggesting modest but statistically significant benefits for symptom reduction and prevention of recurrent infections, although effect sizes and statistical significance vary by preparation type and clinical endpoint [35].

Green tea catechins, particularly EGCG, have been assessed in clinical contexts for prevention of influenza infection in healthcare workers, with a double-blind placebo-controlled trial demonstrating a significant reduction in influenza incidence in the catechin-supplemented group. Glycyrrhizin-containing preparations have been applied clinically in Japan for management of chronic HCV and HBV infection, with evidence of transaminase normalisation and histological improvement, although antiviral activity as reflected by suppression of viral load has been less consistently demonstrated [36]. The clinical applicability of plant-based antiviral agents is further complicated by batch-to-batch variability in phytochemical composition, particularly for whole plant extracts and complex botanical formulations, which undermines dosing consistency and complicates the interpretation of clinical trial outcomes.

## 7. Formulation Strategies and Advanced Delivery Systems

Recognition of the pharmacokinetic limitations of plant-derived antiviral compounds has driven substantial innovation in drug delivery technology aimed at enhancing their therapeutic performance. Nanoparticulate delivery systems have emerged as the most extensively investigated approach, encompassing polymeric nanoparticles, lipid-based nanocarriers including liposomes and solid lipid nanoparticles, and inorganic nanostructures such as gold and silica nanoparticles [37]. Encapsulation of curcumin within liposomal formulations has been demonstrated to increase oral bioavailability by orders of magnitude relative to unformulated curcumin, with concomitant improvements in antiviral efficacy observed in animal models. Quercetin-loaded PLGA nanoparticles similarly demonstrate enhanced cellular uptake and sustained intracellular drug retention compared to free quercetin.

Self-emulsifying drug delivery systems (SEDDS), cyclodextrin inclusion complexes, and solid dispersion technologies have been applied to improve the aqueous solubility and dissolution rate of poorly soluble phytochemicals. Phospholipid complexation, as exemplified by the phytosome technology, has been employed to improve absorption of polyphenolic compounds by enhancing their membrane permeability [38]. Beyond oral delivery, inhalation formulations represent a promising route for plant-based antiviral agents targeting respiratory viral infections, enabling direct delivery to the site of viral replication and potentially reducing the systemic exposure required for therapeutic effect. Each of these strategies requires careful optimisation to ensure physicochemical stability, preservation of biological activity, and biocompatibility of excipients.

## 8. Regulatory, Safety, and Commercialisation Challenges

The regulatory framework governing plant-based antiviral agents presents distinctive and often formidable challenges that differ fundamentally from those applicable to synthetic small-molecule drugs. In many jurisdictions, botanical preparations are classified as dietary supplements, herbal medicines, or traditional medicines rather than pharmaceutical drugs, subjecting them to less stringent evidentiary requirements for market authorisation but also limiting the health claims that may be made regarding their therapeutic application [39]. The regulatory pathway for development of a standardised plant-derived compound as a registered antiviral drug—requiring demonstration of quality, safety, and efficacy through formal clinical trials—entails substantial financial investment and technical complexity that may exceed the resources of many developers, particularly in low- and middle-income countries where medicinal plant research is most actively pursued.

Safety considerations for plant-based antiviral agents encompass potential herb-drug interactions mediated through modulation of cytochrome P450 enzymes and drug transporter proteins, variable toxicity profiles dependent upon preparation method and dosage, and theoretical risks of adulteration or contamination of plant-sourced materials with heavy metals, pesticides, or microbial pathogens [40]. Standardisation of botanical raw materials and finished products through validated analytical methods including high-performance liquid chromatography and mass

spectrometry-based metabolomic profiling is essential to address quality control challenges. Commercialisation of plant-based antivirals additionally requires resolution of intellectual property considerations related to traditional knowledge, equitable benefit-sharing arrangements with source communities, and development of sustainable and traceable supply chains for botanical raw materials.

## 9. Conclusion and Future Directions

The body of evidence reviewed herein substantiates the considerable antiviral potential of plant-derived compounds and underscores the pharmacological richness of the plant kingdom as a source of novel antiviral therapeutics. Flavonoids, alkaloids, terpenoids, and polyphenols collectively engage viral targets at multiple points in the replication cycle, and their immunomodulatory properties confer additional therapeutic value that distinguishes them from single-target conventional antiviral agents. The multimodal mechanisms of action characteristic of many phytochemicals may confer inherent resistance-suppressing properties that are particularly advantageous for management of rapidly mutating RNA viruses.

Future research priorities should encompass rigorous mechanistic characterisation of antiviral action at the molecular level, expanded and methodologically robust clinical trials employing standardised preparations, and systematic pharmacokinetic investigations in human subjects. Development of validated analytical standards and internationally harmonised quality benchmarks for botanical antiviral preparations is urgently required to enable cross-study comparison and regulatory advancement. The integration of computational approaches including molecular docking, virtual screening of natural product libraries, and systems pharmacology modelling offers transformative potential for accelerating the identification of plant-derived leads with optimised antiviral activity and selectivity.

Ultimately, the realisation of the therapeutic promise of plant-based antiviral agents will require sustained interdisciplinary collaboration encompassing ethnobotany, phytochemistry, virology, pharmacology, clinical medicine, regulatory science, and drug delivery engineering. Investment in this research agenda, supported by equitable international partnerships and appropriate regulatory frameworks, holds the prospect of delivering novel, accessible, and effective antiviral therapies capable of addressing the global burden of viral infectious disease.

## Figures

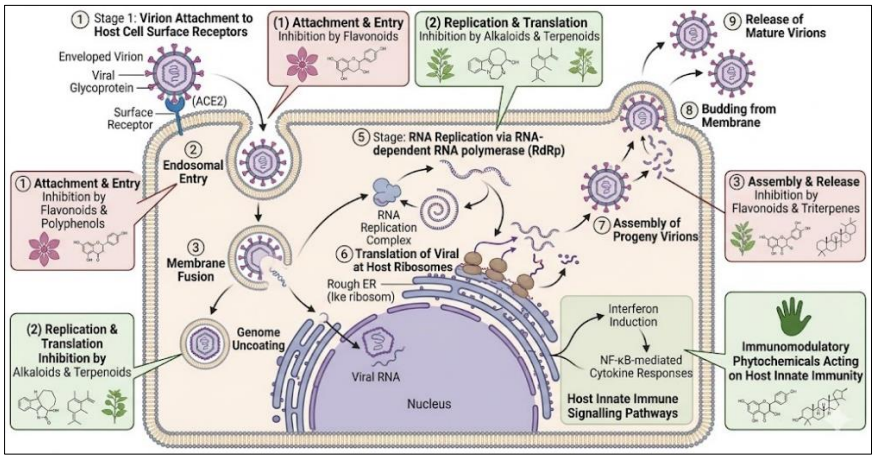


**Fig 1:** Schematic representation of the viral life cycle and sites of action of plant-derived antiviral compounds.

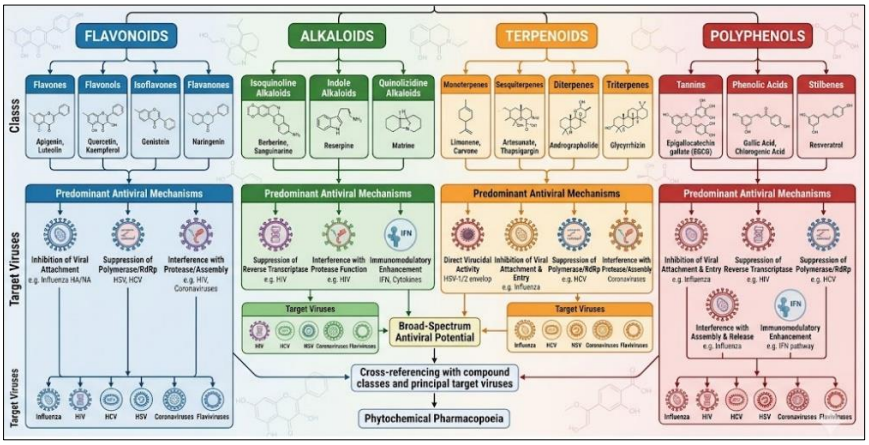


**Fig 2:** Classification of plant-derived antiviral compounds and their principal mechanisms of antiviral action.

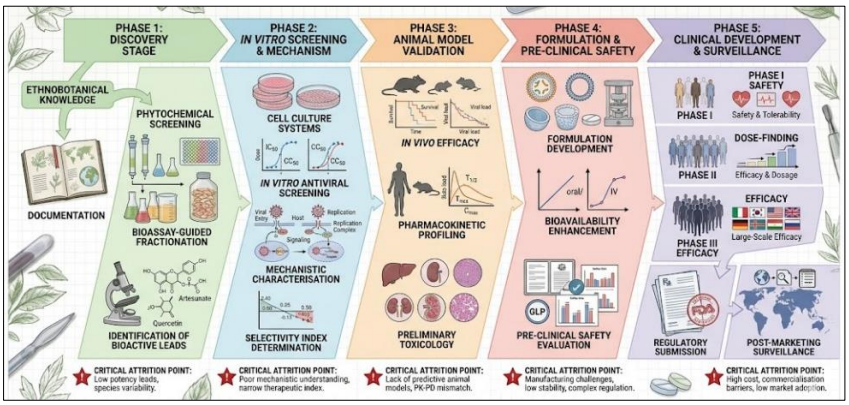


**Fig 3:** Translational pathway from plant compound discovery to antiviral drug development and clinical application.

## Tables

**Table 1:** Comparison of Plant-Based Antiviral Compounds, Their Sources, and Mechanisms of Action

| Compound | Plant Source | Chemical Class | Primary Mechanism | Target Virus Examples |
|---|---|---|---|---|
| Quercetin | Allium cepa, Camellia sinensis | Flavonol | Inhibition of viral entry; RdRp suppression | Influenza, SARS-CoV-2, Zika |
| EGCG | Camellia sinensis | Catechin/Flavonoid | Virucidal; envelope disruption; polymerase inhibition | Influenza, HCV, HIV |
| Berberine | Berberis vulgaris, Coptis chinensis | Isoquinoline Alkaloid | RNA synthesis inhibition; viral entry blockade | Influenza, HSV, HCV |
| Lycorine | Narcissus spp., Lycoris radiata | Amaryllidaceae Alkaloid | Protein synthesis inhibition; antiviral cytokine induction | SARS-CoV-2, Dengue, Zika |
| Betulinic Acid | Betula spp., Platanus spp. | Pentacyclic Triterpene | Viral protease inhibition; maturation arrest | HIV-1, HSV, HCV |
| Artemisinin | Artemisia annua | Sesquiterpene Lactone | ROS generation; replication complex disruption | SARS-CoV-2, Dengue, Influenza |
| Resveratrol | Vitis vinifera, Polygonum cuspidatum | Stilbene Polyphenol | NF-κB inhibition; sirtuin activation; virucidal | Influenza, HIV, HSV |
| Glycyrrhizin | Glycyrrhiza glabra | Triterpenoid Saponin | Inhibition of viral entry; antiviral cytokine induction | SARS, HBV, HCV |
| Andrographolide | Andrographis paniculata | Diterpene Lactone | IFN induction; NF-κB modulation | Influenza, HIV, HCV |
| Allicin | Allium sativum | Organosulphur Compound | Virucidal; inhibition of viral enzyme activity | Influenza, HSV, CMV |

**Table 2:** Summary of Antiviral Activity Against Different Viruses and Therapeutic Spectrum

| Phytochemical | Virus Family/Type | Model System | Key Finding | Reference Compounds |
|---|---|---|---|---|
| Quercetin | Orthomyxoviridae (Influenza A/B) | In vitro / Murine | Reduced viral titre; enhanced survival | Oseltamivir |
| EGCG | Flaviviridae (HCV, Dengue) | Huh7 cells / Mice | Inhibited viral RNA replication by >80% | Ribavirin |
| Berberine | Herpesviridae (HSV-1, HSV-2) | Vero cells / Mice | Reduced plaque formation; decreased viral load | Acyclovir |
| Lycorine | Coronaviridae (SARS-CoV-2) | Calu-3 / Hamster | EC50 < 1 µM; inhibited spike-mediated entry | Remdesivir |
| Betulinic Acid | Retroviridae (HIV-1) | MT-2 cells / SCID mice | Suppressed p24 antigen production; IC50 ~1 µM | Lopinavir |
| Artemisinin | Coronaviridae, Flaviviridae | Vero E6 / Murine | Reduced SARS-CoV-2 replication; antiviral cytokines | Chloroquine |
| Resveratrol | Orthomyxoviridae (Influenza) | MDCK / Mice | Reduced viral shedding; attenuated lung pathology | Zanamivir |
| Glycyrrhizin | Hepadnaviridae (HBV) | HepG2.2.15 / Clinical | Reduced HBsAg; transaminase normalisation | Entecavir |
| Andrographolide | Paramyxoviridae | A549 / Mice | Antiviral cytokine induction; viral load reduction | Ribavirin |

**Table 3:** Advantages, Limitations, and Pharmacokinetic Considerations of Plant-Based Antiviral Agents

| Parameter | Advantages | Limitations | Mitigation Strategies |
|---|---|---|---|
| Mechanism of Action | Multi-target activity reduces resistance potential; immunomodulatory synergy | Off-target effects; lack of mechanistic selectivity for some classes | Structure-activity optimisation; analogue synthesis |
| Bioavailability | Some compounds orally bioavailable; tissue-selective distribution | Extensive first-pass metabolism; low aqueous solubility; rapid clearance | Nanoformulation; prodrug strategies; phospholipid complexation |
| Toxicity Profile | Generally favourable tolerability; historical ethnopharmacological safety data | Herb-drug interactions via CYP enzyme modulation; dose-dependent hepatotoxicity possible | Therapeutic drug monitoring; clinical pharmacokinetic studies |
| Spectrum of Activity | Broad-spectrum activity across virus families; relevant for novel pathogens | Potency often lower than licensed antivirals; in vitro to *in vivo* correlation poor | Combination therapy; pharmacokinetic enhancement; *in vivo* model validation |
| Standardisation | Established HPLC/MS analytical methods available | Batch-to-batch compositional variability; seasonal and geographic phytochemical variation | Standardised extraction protocols; chemical marker quantification |
| Cost and Accessibility | Natural abundance; potential low-cost manufacturing in endemic regions | Sustainable sourcing; supply chain integrity; intellectual property complexity | Fair benefit-sharing frameworks; certified sustainable supply chains |

**Table 4:** Current Research Status and Development Stages of Plant-Based Antiviral Therapies

| Compound/Preparation | Target Infection | Development Stage | Regulatory Status | Key Research Gap |
|---|---|---|---|---|
| Quercetin (nanoformulated) | COVID-19 / Influenza | Phase I/II Clinical Trials | IND filed (select jurisdictions) | Optimal dosing regimen; PK/PD modelling in humans |
| EGCG / Green tea extract | Influenza / HCV | Phase II Clinical Trials | Dietary supplement (US); Traditional medicine (Asia) | Standardised preparation; efficacy confirmation in RCT |
| Andrographolide preparation | Respiratory viruses | Phase III Clinical Trials (Asia) | Licensed herbal medicine (Thailand, India) | Long-term safety data; antiviral vs. immunomodulatory mechanism |
| Glycyrrhizin (i.v.) | HBV / SARS | Clinical use (Japan) | Licensed pharmaceutical (Japan) | Controlled RCT for viral load endpoints; Western regulatory approval |
| Betulinic acid analogues | HIV-1 | Preclinical / Early Phase I | Investigational | Selectivity index improvement; CNS penetration data |
| Artemisinin derivatives | COVID-19 / Dengue | Phase II Clinical Trials | Licensed antimalarial; IND for antiviral indications | Antiviral-specific clinical efficacy; resistance profiling |
| Curcumin nanoformulations | HCV / Influenza | Preclinical / Phase I | Dietary supplement; Investigational antiviral | Antiviral-specific clinical trial design; bioavailability benchmarking |
| Resveratrol preparations | Influenza / HSV | Preclinical / Phase I | Dietary supplement | Clinical antiviral efficacy data; optimal delivery route |

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