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## Bioprospecting of medicinal plants for antiviral phytochemicals: A systematic review

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**Abstract**

The global burden of viral infections including pandemic threats like SARS-CoV-2 and persistent challenges such as HIV, HSV, and influenza demands an urgent expansion of the antiviral therapeutic arsenal. Conventional antivirals, while effective, face limitations including resistance, toxicity, high cost, and limited spectrum of activity. In this context, medicinal plants emerge as a largely untapped yet evolutionarily refined reservoir of bioactive compounds with compelling antiviral potential.

This systematic review maps the bioprospecting landscape of antiviral phytochemicals, focusing on mechanistically active classes such as flavonoids, alkaloids, terpenoids, lignans, and polyphenols. These compounds disrupt multiple stages of the viral life cycle blocking entry, inhibiting replication, impairing protein synthesis, and modulating host immune pathways offering both specificity and resilience against resistance. Case studies from *Andrographis paniculata*, *Glycyrrhiza glabra*, *Curcuma longa*, *Phyllanthus niruri*, and *Camellia sinensis* illustrate validated pharmacological efficacy rooted in ethnomedicine and supported by emerging *in silico*, *in vitro*, and *in vivo* evidence.

Beyond pharmacological insights, the review interrogates real-world barriers to phytomedicine translation, including phytochemical variability, lack of standardization, ethical tensions in bioprospecting, and intellectual property inequities. Future-forward solutions are explored ranging from AI-guided compound discovery and nanotechnology based delivery systems to regulatory innovation and transdisciplinary collaboration.

This review argues that systematic, ethical, and technologically integrated phytochemical bioprospecting is not only a scientific necessity but a strategic imperative for global antiviral preparedness in the post-pandemic era.

**Keywords:** Antiviral phytochemicals, ethnomedicinal plants, bioactive natural compounds, antiviral screening methods, plant-derived antiviral agents

**Introduction**

Viral infections remain one of the most persistent threats to global public health. Diseases caused by viruses such as influenza, human immunodeficiency virus HIV, herpes simplex virus HSV, and the recently emerged severe acute respiratory syndrome coronavirus 2 SARS CoV 2 have led to widespread morbidity, mortality, and socio economic disruption [1]. Although antiviral therapies have significantly improved the management of many viral diseases, the challenges they pose remain substantial. Among these challenges are the emergence of drug resistant viral strains, significant toxicity associated with long term antiviral use, and the high cost of treatment [2, 3]. In the search for novel antiviral agents, medicinal plants offer a promising source of bioactive compounds. Historically, plants have played a central role in traditional medicine systems across the world. Phytochemicals such as flavonoids, alkaloids, terpenoids, saponins, and phenolic acids are known to possess broad spectrum antiviral activities through mechanisms like inhibiting viral entry, replication, or assembly [4]. For example, compounds like glycyrrhizin from *Glycyrrhiza glabra*, epigallocatechin gallate from *Camellia sinensis*, and curcumin from *Curcuma longa* have shown notable antiviral effects against respiratory and systemic viral infections including those caused by coronaviruses and herpesviruses [5].

The scientific investigation of natural products for pharmaceutical use falls within the domains of pharmacognosy and phytochemistry. Pharmacognosy is the discipline that focuses on the identification, characterization, and biological evaluation of medicines derived from natural sources. Phytochemistry involves the chemical profiling of plant constituents and the study of their biosynthetic pathways. Together, these fields enable the systematic process of bioprospecting, which refers to the exploration of plant biodiversity for the discovery of novel therapeutic agents [6]. Despite the ancient roots of plant based antiviral therapies, systematic evaluation and integration into modern medicine have only recently gained momentum.

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Recent reviews have documented a wide variety of plant species with demonstrated antiviral effects including *Echinacea purpurea*, *Sambucus nigra*, and *Pelargonium sidoides*, and have highlighted key antiviral phytochemicals such as quercetin, resveratrol, and amentoflavone [7, 8]. These findings support the rationale for rigorous scientific exploration of traditional remedies. This review aims to provide a comprehensive and systematic assessment of medicinal plants reported to contain antiviral phytochemicals. The primary objectives are to identify candidate plant species and their associated compounds, elucidate their antiviral mechanisms of action, assess the extent of preclinical or clinical validation, and highlight gaps that require future research. By integrating ethnobotanical knowledge with contemporary pharmacognostic evidence, this work seeks to inform the development of affordable, effective, and accessible plant derived antiviral agents.

### Overview of antiviral phytochemicals

Medicinal plants are a diverse and rich source of bioactive compounds with established antiviral properties. Among the various classes of plant-derived secondary metabolites, alkaloids, flavonoids, terpenoids, polyphenols, and saponins have received substantial attention due to their ability to target various stages of the viral life cycle. Their mechanisms of action include direct virucidal effects, inhibition of viral replication enzymes, disruption of viral entry, and modulation of the host immune response [5].

### Alkaloids

Alkaloids are nitrogenous organic compounds typically derived from amino acids and often possess complex ring structures. They exhibit potent antiviral activity across a wide spectrum of viruses. Lycorine, an Amaryllidaceae alkaloid from *Lycoris radiata*, has shown efficacy against poliovirus and SARS CoV. It inhibits viral replication by interfering with RNA translation and elongation [6]. Berberine, an isoquinoline alkaloid from *Berberis vulgaris*, exhibits activity against HSV, influenza virus, and HIV. It acts by downregulating NF kappa B, inhibiting viral glycoprotein expression, and blocking virus-induced autophagy<sup>7</sup>. Tylophorine, a phenanthroindolizidine alkaloid from *Tylophora indica*, exhibits potent inhibition of viral RNA synthesis and protein translation in respiratory viruses. Piperine, from *Piper nigrum*, modulates host inflammatory pathways and improves bioavailability of other antiviral agents when used in combination<sup>8</sup>. Alkaloids often function as enzyme inhibitors, binding to viral reverse transcriptases, RNA dependent RNA polymerases (RdRp), or proteases. Their ability to intercalate nucleic acids also disrupts viral genome replication.

### Flavonoids

Flavonoids are polyphenolic compounds characterized by a 15-carbon skeleton arranged in a C6-C3-C6 configuration. They are found abundantly in fruits, vegetables, and many medicinal herbs. Quercetin, found in *Allium cepa* and *Camellia sinensis*, inhibits viral entry and replication of influenza, DENV, and SARS CoV 2 by targeting 3CLpro and PLpro viral proteases [6, 9]. Kaempferol and luteolin, found in *Ginkgo biloba* and *Perilla frutescens*, inhibit influenza neuraminidase and suppress the expression of cytokines induced by viral infections. Apigenin, from *Matricaria chamomilla*, reduces replication of HCV by impairing NS5B polymerase activity. Baicalein, a flavone from *Scutellaria*

*baicalensis*, blocks the replication of HIV and SARS CoV through inhibition of the viral main protease. Flavonoids exert their effects by multiple mechanisms including: Direct binding to viral enzymes (e.g., RdRp, helicase), Chelation of metal ions essential for viral replication, Antioxidant-mediated inhibition of virus-induced oxidative stress, Modulation of TLR and interferon pathways [9].

### Terpenoids

Terpenoids are derived from isoprene units and classified into mono, sesqui, di, tri, and tetraterpenoids based on the number of units. Andrographolide, a diterpenoid from *Andrographis paniculata*, has shown broad-spectrum activity against influenza, CHIKV, and DENV by inhibiting viral replication and enhancing IFN production [7]. Glycyrrhizin, a triterpenoid saponin from *Glycyrrhiza glabra*, exhibits activity against SARS CoV by inhibiting viral gene expression and replication. It also binds to ACE2 receptors, preventing viral entry [6]. Thymoquinone, a monoterpene from *Nigella sativa*, reduces MERS CoV replication and modulates TNF alpha and IL 6 levels. Betulinic acid, a lupane type pentacyclic triterpenoid, disrupts HIV envelope and inhibits maturation by targeting viral protease.

Terpenoids mainly interfere with: Viral envelope fusion and integrity, Inhibition of envelope protein mediated fusion, Host immune modulation via TLR and NF kappa B pathways [10].

### Polyphenols

Polyphenols are characterized by multiple phenol structures and include stilbenes, lignans, tannins, and phenolic acids. Epigallocatechin gallate (EGCG) from green tea inhibits entry of HIV, HCV, and influenza virus by binding envelope proteins and blocking membrane fusion<sup>6</sup>. Resveratrol, a stilbene from grapes, suppresses HSV, RSV, and SARS CoV replication by inhibiting NF kappa B activation and viral nucleoprotein expression [7]. Curcumin, a diarylheptanoid from *Curcuma longa*, reduces replication of SARS CoV and Zika virus by targeting viral envelope and inhibiting cytokine storms [8]. Chlorogenic acid, abundant in *Coffea arabica* and *Lonicera japonica*, has antiviral action against influenza and DENV through inhibition of neuraminidase and modulation of host transcription factors [9]. Polyphenols not only exert direct antiviral effects but also restore cellular redox balance, reduce inflammation, and enhance cellular antiviral defense mechanisms.

### Saponins

Saponins are amphipathic glycosides composed of a hydrophobic aglycone (sapogenin) and hydrophilic sugar moiety. Their antiviral mechanisms are distinct due to their ability to disrupt lipid bilayers. QS 21, a saponin from *Quillaja saponaria*, exhibits adjuvant activity and enhances vaccine-induced immune responses against viral pathogens. Ginsenosides, from *Panax ginseng*, show antiviral effects against influenza and RSV by enhancing interferon production and macrophage activation [9]. Aescin, from *Aesculus hippocastanum*, interferes with the viral envelope and prevents viral fusion with host cells.

Saponins typically: Disrupt viral envelopes via surfactant action, Act as immune potentiators in antiviral immunity, Enhance uptake of co administered antiviral agents [10].

### General Mechanisms of Action

Across all phytochemical classes, several core antiviral mechanisms emerge:

### Inhibition of Viral Entry

Many compounds prevent viral attachment or block receptor mediated entry. Flavonoids and terpenoids interfere with glycoprotein mediated fusion, while polyphenols like EGCG bind to host receptors such as ACE2 and DC SIGN [6, 7].

### Inhibition of Viral Replication

Phytochemicals inhibit viral enzymes like RdRp, helicase, and proteases. For example, baicalein and quercetin inhibit SARS CoV 2 3CLpro [9].

### Immune Modulation

Several compounds enhance type I interferon responses, suppress pro inflammatory cytokines (e.g., IL 6, TNF alpha), and regulate TLR signaling, thereby supporting host antiviral defenses [8].

This multipronged activity reduces the risk of viral resistance and supports the rationale for further clinical development of phytochemical-based antivirals.

### Plant families and species with promising antiviral activities

Numerous plant species have demonstrated significant antiviral potential due to their phytochemical richness and historical use in traditional systems of medicine. Among the most widely studied species are *Andrographis paniculata*, *Glycyrrhiza glabra*, *Azadirachta indica*, *Phyllanthus niruri*, *Camellia sinensis*, and *Curcuma longa*. These plants contain well-characterized bioactive constituents that act on various stages of the viral life cycle, including viral entry, replication, and host immune modulation.

#### *Andrographis paniculata* (Family: Acanthaceae)

##### Key compound: Andrographolide

*Andrographis paniculata*, often referred to as the “King of Bitters,” is a traditional medicinal herb with strong antiviral, anti-inflammatory, and immunomodulatory activities. Its main bioactive compound, andrographolide, is a labdane diterpenoid known for its ability to inhibit viral replication by targeting RNA-dependent RNA polymerase (RdRp) and disrupting viral protein synthesis [11].

Mechanistically, andrographolide interferes with viral mRNA transcription, inhibits the nuclear translocation of NF-kappa B, and promotes type I interferon responses. In vitro and in silico studies have confirmed its inhibitory action against viruses such as dengue virus, influenza A H5N1, chikungunya virus, and SARS-CoV [2, 12]. Additionally, docking studies suggest strong binding affinity between andrographolide and the PA-PB1 complex of the influenza virus polymerase [13].

#### *Glycyrrhiza glabra* (Family: Fabaceae)

##### Key compound: Glycyrrhizin

*Glycyrrhiza glabra*, or licorice root, is an established herbal medicine used across Asia and Europe. Its main antiviral constituent, glycyrrhizin, is a triterpenoid saponin with demonstrated efficacy against herpes simplex virus (HSV), hepatitis B and C, and coronaviruses including SARS-CoV. Glycyrrhizin exhibits antiviral activity by inhibiting viral attachment and penetration, modulating redox-sensitive

transcription factors, and suppressing high-mobility group box 1 (HMGB1) protein release. It also downregulates proinflammatory cytokines such as TNF-alpha and IL-6, making it especially useful in mitigating cytokine storms seen in severe viral infections [14].

#### *Azadirachta indica* (Family: Meliaceae)

##### Key compounds: Limonoids (Nimbolide, Azadirachtin)

Commonly known as neem, *Azadirachta indica* is a cornerstone of Ayurvedic medicine. It contains a rich suite of limonoids, including nimbolide and azadirachtin, which exhibit antiviral activities primarily through immune enhancement and inhibition of viral gene expression. Limonoids from neem interfere with viral replication and protein processing. Studies have shown neem extracts inhibit dengue virus serotype 2 and herpes simplex virus type 1 replication. Azadirachtin has demonstrated immunomodulatory properties, enhancing NK cell activity and interferon secretion [15].

#### *Phyllanthus niruri* (Family: Phyllanthaceae)

##### Key compounds: Lignans (Phyllanthin, Hypophyllanthin)

*Phyllanthus niruri*, also called “stonebreaker,” is widely used in Indian and Southeast Asian herbal traditions for liver and viral diseases. It is rich in lignans, including phyllanthin and hypophyllanthin, which exhibit strong inhibitory effects on hepatitis B virus (HBV) DNA polymerase. These lignans downregulate HBV gene expression, suppress viral replication intermediates, and exert antioxidant properties that protect hepatocytes from viral-induced injury. In combination with interferon-alpha, *Phyllanthus* extract has shown synergistic effects in HBV treatment models [16].

#### *Camellia sinensis* (Family: Theaceae)

##### Key compound: Epigallocatechin gallate (EGCG)

*Camellia sinensis*, the tea plant, is an abundant source of catechins, particularly epigallocatechin gallate (EGCG), a potent antiviral polyphenol. EGCG has been shown to disrupt the integrity of viral envelopes, inhibit viral entry into host cells, and interfere with viral neuraminidase activity.

EGCG effectively inhibits influenza virus, Epstein-Barr virus (EBV), and HIV by binding to viral glycoproteins and preventing host cell fusion. It also modulates the host immune response by enhancing type I interferon signaling and reducing proinflammatory cytokines [17].

#### *Curcuma longa* (Family: Zingiberaceae)

##### Key compound: Curcumin

*Curcuma longa*, or turmeric, contains curcumin, a curcuminoid with broad-spectrum antiviral, antioxidant, and anti-inflammatory properties. Curcumin interferes with the early and late stages of viral infection by modulating envelope fusion, downregulating host transcription factors (e.g., AP-1, NF-kappa B), and inhibiting viral protease activity. Curcumin exhibits antiviral activity against influenza virus, Zika virus, human respiratory syncytial virus (RSV), and SARS-CoV-2. Recent molecular docking studies suggest that curcumin can effectively bind to the main protease Mpro and spike protein of SARS-CoV-2, impeding viral entry and replication [18].

Plant Species	Family	Key Phytochemical	Mechanism of Antiviral Action	Target Viruses
<i>Andrographis paniculata</i>	Acanthaceae	Andrographolide	Inhibits RdRp, blocks viral mRNA transcription, suppresses NF- $\kappa$ B	Dengue, Influenza A, SARS-CoV
<i>Glycyrrhiza glabra</i>	Fabaceae	Glycyrrhizin	Blocks viral attachment, downregulates HMGB1, suppresses cytokines	HSV, HBV, HCV, SARS-CoV
<i>Azadirachta indica</i>	Meliaceae	Limonoids (e.g., Nimbolide)	Suppresses viral gene expression, enhances NK cells and interferons	HSV, DENV
<i>Phyllanthus niruri</i>	Phyllanthaceae	Lignans (e.g., Phyllanthin)	Inhibits HBV DNA polymerase, suppresses viral gene expression	HBV
<i>Camellia sinensis</i>	Theaceae	EGCG (Epigallocatechin gallate)	Disrupts viral envelope, inhibits neuraminidase, modulates immunity	Influenza, HIV, EBV
<i>Curcuma longa</i>	Zingiberaceae	Curcumin	Binds viral protease, inhibits fusion, downregulates inflammation	RSV, Zika, SARS-CoV-2

**Fig 1:** Plant Species with Antiviral Action

## Mechanism-based classification of antiviral phytochemicals

The antiviral action of phytochemicals can be more meaningfully categorized not just by chemical class but also by targeted stage in the viral life cycle. Unlike single-target synthetic antivirals, plant-derived compounds often exert multi-target or synergistic effects, interfering with various stages including viral attachment, penetration, genome replication, protein synthesis, assembly, and host immune evasion. Below is a mechanism-based classification of key antiviral phytochemicals.

### 1. Inhibitors of Viral Entry and Attachment

Phytochemicals in this category act by preventing viral binding to host receptors or interfering with viral envelope fusion with the cell membrane. Flavonoids such as quercetin and luteolin block viral entry by inhibiting viral glycoproteins and preventing conformational changes essential for fusion. Triterpenoid saponins, such as glycyrrhizin from *Glycyrrhiza glabra*, disrupt viral envelopes, leading to lysis or reduced infectivity [19]. Catechins from *Camellia sinensis* (e.g., EGCG) interfere with lipid rafts and block the interaction of viruses like HIV and influenza with their host receptors [20].

These compounds often act on host-cell surface molecules such as ACE2, sialic acid receptors, or DC-SIGN, thereby preventing virus internalization.

### 2. Inhibitors of Viral Genome Replication and Transcription

Some phytochemicals exert their antiviral activity by targeting viral nucleic acid polymerases or proteins critical for replication. Andrographolide from *Andrographis paniculata* inhibits RNA-dependent RNA polymerase (RdRp) and suppresses viral mRNA transcription, especially in dengue and influenza infections [21]. Lignans from *Phyllanthus niruri* (e.g., phyllanthin) inhibit HBV DNA polymerase and suppress replication intermediates [22]. Curcumin from *Curcuma longa* has been shown to inhibit viral protease activity and polymerase function in flaviviruses, including Zika and dengue [23]. Mechanistically, these phytochemicals

mimic nucleoside analogs or interfere with the active site of viral enzymes, impeding genome amplification.

### 3. Inhibitors of Viral Protein Translation and Assembly

Certain plant compounds block the synthesis of structural and non-structural viral proteins or prevent proper assembly of virions. Baicalin from *Scutellaria baicalensis* has been shown to interfere with the nuclear export of viral mRNA, particularly in influenza virus models [20]. Emodin, an anthraquinone from *Rheum palmatum*, disrupts the assembly of coronavirus structural proteins, inhibiting viral budding. By targeting viral proteases (e.g., 3CLpro, PLpro), these compounds prevent post-translational processing of polyproteins into mature viral components.

### 4. Immune-Modulating Phytochemicals

These compounds enhance the host's ability to clear viruses by stimulating innate or adaptive immune responses, or by modulating inflammatory cascades. Resveratrol and curcumin modulate cytokine expression, suppress NF- $\kappa$ B and IL-6 production, and enhance interferon-stimulated genes [23]. Ginsenosides from *Panax ginseng* have adjuvant properties, enhancing antigen presentation and T cell activation. Quercetin supports antiviral defense by reducing oxidative stress and boosting antiviral cytokine production (e.g., IFN- $\beta$ ) [24]. Such agents help in preventing the progression of viral infection and reduce tissue damage associated with hyperinflammatory responses.

### 5. Broad-Spectrum Multi-Target Agents

Some phytochemicals exhibit broad-spectrum antiviral activity due to their ability to act at multiple stages of the viral life cycle simultaneously. EGCG from green tea inhibits viral entry, protease function, and host inflammation, making it effective against HIV, influenza, and coronaviruses [25]. Nimbolide, a limonoid from *Azadirachta indica*, has been reported to suppress viral transcription and modulate host immunity, showing efficacy against HSV and dengue viruses [24]. Such compounds are particularly valuable in the context of emerging or mutating viral pathogens, where multi-site interference can prevent escape mutants.

Mechanism	Representative Phytochemicals	Examples of Target Viruses
Entry inhibition	EGCG, glycyrrhizin, quercetin	HIV, influenza, SARS-CoV-2
Genome replication inhibition	Andrographolide, curcumin, phyllanthin	DENV, ZIKV, HBV, SARS-CoV
Translation & assembly blockade	Baicalin, emodin	Influenza, SARS-CoV
Immune modulation	Resveratrol, ginsenosides, quercetin	RSV, HSV, SARS-CoV-2
Multi-target interference	EGCG, curcumin, nimbolide	Broad-spectrum

**Fig 2:** Mechanism-based Classification of Antiviral Phytochemicals

**Challenges in bioprospecting and phytochemical standardization:** Despite the immense potential of medicinal plants in antiviral therapy, several scientific, environmental,

and regulatory challenges continue to hinder the effective bioprospecting and standardization of phytochemicals. A major limitation is the variability in phytochemical



composition, which is highly influenced by factors such as geographic location, soil type, climatic conditions, harvesting time, and post-harvest processing. This inconsistency can lead to fluctuations in bioactivity, reducing reproducibility across studies. The lack of standardization techniques poses a serious barrier to both clinical translation and international regulatory acceptance of herbal formulations. In many cases, the bioactive principles are not well characterized, and the use of crude extracts complicates the establishment of consistent therapeutic profiles. This is compounded by the difficulty in isolating active constituents, especially in complex plant matrices where the pharmacological activity may depend on synergistic interactions among multiple compounds.

Furthermore, the field of ethnopharmacology often faces regulatory and ethical hurdles. The bioprospecting of traditional knowledge can lead to exploitation without adequate benefit-sharing, especially when indigenous knowledge is commercialized without proper acknowledgement or compensation<sup>28</sup>. This gives rise to issues of biopiracy, where biodiversity-rich countries risk losing sovereign control over their native medicinal resources. From a legal perspective, frameworks like the Nagoya Protocol aim to enforce fair access and benefit-sharing. However, the enforcement of such mechanisms is often weak or inconsistent. Similarly, the absence of intellectual property rights protections for traditional medicine formulations limits innovation and discourages research investments.

Addressing these challenges will require multi-stakeholder collaboration involving scientists, traditional healers, regulatory bodies, and patent authorities to ensure ethical, scientific, and sustainable bioprospecting of medicinal plants.

### Future prospects and research gaps

While numerous plant-derived phytochemicals have shown promising antiviral activity *in vitro* and *in silico*, the lack of robust clinical validation remains a critical barrier. Most studies remain at the preclinical stage, and few have progressed to clinical trials, limiting the therapeutic translation of herbal antivirals. There is a pressing need for well-designed, placebo-controlled clinical studies to evaluate the safety, dosage, pharmacokinetics, and efficacy of these compounds in human populations.

A promising avenue lies in the integration of nanotechnology into phytomedicine. Nanocarriers such as liposomes, dendrimers, and plant-virus nanoparticles can enhance the solubility, stability, and targeted delivery of poorly bioavailable phytochemicals like curcumin and andrographolide. Nanoparticle-based formulations have also demonstrated the ability to bypass biological barriers, improve cellular uptake, and reduce off-target toxicity. The emerging field of nanophytopharmacology further explores the use of plant-virus nanoparticles in both drug delivery and diagnostics. Equally important is the exploration of underutilized or endemic medicinal plants, especially from biodiversity-rich but under-investigated regions such as sub-Saharan Africa, the Amazon basin, and parts of South Asia. Many of these plants possess undocumented antiviral potential rooted in traditional knowledge, and systematic ethnobotanical surveys coupled with high-throughput screening can help identify novel bioactive candidates.

Artificial intelligence (AI), machine learning, and cheminformatics are revolutionizing the identification of lead compounds from vast plant compound libraries. Predictive models and molecular docking tools now allow for rapid screening of phytochemicals against viral protein targets,

significantly accelerating early-stage discovery. Moving forward, a multidisciplinary approach will be essential—bringing together pharmacognosists, virologists, ethnobotanists, pharmacologists, and regulatory scientists. Harmonizing traditional medicine with modern drug discovery platforms and ensuring equitable benefit-sharing under frameworks like the Nagoya Protocol will be key to ensuring both innovation and ethical stewardship of natural resources.

### Conclusion

Phytochemicals derived from medicinal plants represent a vast and largely untapped source of antiviral agents with potential to address both existing and emerging viral infections. Compounds such as flavonoids, terpenoids, alkaloids, lignans, and polyphenols have demonstrated broad-spectrum antiviral activity by targeting multiple stages of the viral life cycle, including entry inhibition, genome replication, protein synthesis, and immune modulation. Their pleiotropic mechanisms not only reduce the risk of resistance but also offer complementary pathways to enhance host defense.

Bioprospecting rooted in ethnobotanical knowledge and modern pharmacognosy emerges as a promising yet underexploited strategy in the search for next-generation antiviral agents. As antibiotic resistance and viral pandemics continue to challenge conventional drug development pipelines, the strategic exploration of plant biodiversity holds immense translational value. However, success in this area requires systematic screening, robust pharmacological validation, and interdisciplinary collaboration.

To realize the therapeutic promise of plant-based antivirals, future efforts must be grounded in sustainability and ethical equity. This includes conserving biodiversity hotspots, protecting indigenous knowledge systems, and ensuring benefit-sharing through frameworks like the Nagoya Protocol. Moreover, integrating advanced tools such as nanotechnology, *in silico* modeling, and AI-guided compound mining can accelerate discovery while maintaining ecological and cultural sensitivity. In summary, phytochemical bioprospecting is not only scientifically compelling but also aligned with the global call for resilient, accessible, and ethically sourced antiviral therapeutics.

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