

MEDICINAL HERBS AGAINST EMERGING VIRAL DISEASES: A COMPREHENSIVE REVIEW

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ABSTRACT:

Emerging and re-emerging viral diseases continue to pose significant threats to global public health due to their rapid transmission, high mutation rates, and limited therapeutic options. Recent outbreaks of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), dengue virus, Zika virus, chikungunya virus, Ebola virus, Nipah virus, and monkeypox virus have highlighted the urgent need for safe, effective, and broad-spectrum antiviral agents. Medicinal herbs have gained considerable attention as valuable sources of bioactive compounds with antiviral potential. Traditional medical systems, including Ayurveda, Traditional Chinese Medicine, African traditional medicine, and Unani medicine, have long utilized herbal remedies for the prevention and treatment of infectious diseases. Numerous phytochemicals such as polyphenols, flavonoids, alkaloids, terpenoids, saponins, tannins, and essential oils have demonstrated antiviral activities through diverse mechanisms, including inhibition of viral attachment, entry, replication, protein synthesis, and modulation of host immune responses. This review provides a comprehensive overview of emerging viral diseases, medicinal herbs with reported antiviral activities, major antiviral phytochemical classes, and their mechanisms of action. Furthermore, the review highlights experimental evidence supporting the antiviral efficacy of medicinal plants against COVID-19, dengue, Zika, chikungunya, Ebola, Nipah, and monkeypox infections. Recent advances in phytochemistry, molecular docking, metabolomics, and systems biology are also discussed in the context of antiviral drug discovery. The findings underscore the immense potential of medicinal herbs as promising sources of novel antiviral therapeutics and emphasize the need for further preclinical and clinical investigations to facilitate their translation into evidence-based healthcare applications.

Keywords:

Medicinal herbs, Emerging viral diseases, Antiviral phytochemicals, SARS-CoV-2, Dengue virus, Zika virus, Chikungunya virus, Ebola virus, Nipah virus, Monkeypox virus, Natural products, Antiviral agents, Phytotherapy, Drug discovery

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INTRODUCTION:

Emerging and re-emerging viral diseases continue to represent one of the most significant challenges to global public health in the twenty-first century.¹ The increasing frequency of viral outbreaks, including severe acute respiratory syndrome (SARS), Middle East respiratory syndrome (MERS), coronavirus disease 2019 (COVID-19), Ebola virus disease, Zika virus infection,^{2,3} Chikungunya, Dengue fever, and Nipah virus infection, has highlighted the vulnerability of healthcare systems worldwide. Rapid urbanization, globalization, climate change, ecological disturbances, and increased human-animal interactions have facilitated the emergence and transmission of novel viral pathogens across geographical boundaries. These outbreaks not only result in substantial morbidity and mortality but

also impose severe socioeconomic burdens through healthcare expenditures, productivity losses, and disruptions to global trade and travel.⁴⁻⁸

Despite remarkable advances in modern medicine, the therapeutic management of viral infections remains challenging. Currently available antiviral drugs are effective only against a limited number of viral pathogens and often exhibit restricted therapeutic windows. Furthermore, many antiviral agents are associated with adverse effects, high treatment costs, poor bioavailability, and limited accessibility in low-resource settings. The lengthy and expensive process of antiviral drug discovery further constrains the rapid development of effective therapeutics against newly emerging viral diseases. Consequently, there is an urgent need to identify novel, safe, and broad-spectrum antiviral

agents capable of combating existing and future viral threats.⁹⁻¹¹

Another major challenge in antiviral therapy is the continuous evolution of viruses through genetic mutations and recombination events. RNA viruses, in particular, possess high mutation rates due to the absence of efficient proofreading mechanisms during genome replication. These mutations can alter viral proteins, resulting in increased pathogenicity, enhanced transmissibility, immune evasion, and reduced susceptibility to existing antiviral medications.¹² The emergence of drug-resistant viral strains has been documented in several clinically important viruses, including human immunodeficiency virus (HIV), influenza virus, hepatitis viruses, and severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The development of antiviral resistance significantly compromises treatment efficacy and necessitates the exploration of alternative therapeutic approaches.¹³

Traditional medicine systems have served as valuable healthcare resources for centuries and continue to play a crucial role in disease prevention and treatment across many regions of the world. Medicinal plants constitute the cornerstone of traditional healthcare practices such as Ayurveda, Traditional Chinese Medicine, Unani medicine, and various indigenous healing systems. Numerous medicinal herbs have been traditionally employed for the management of infectious diseases, including viral illnesses. The extensive ethnopharmacological knowledge accumulated over generations provides an important foundation for the discovery of novel antiviral compounds from natural sources. Recent scientific investigations have increasingly validated the therapeutic potential of traditional medicinal plants through pharmacological, phytochemical, and molecular studies.¹⁴⁻¹⁷

Medicinal plants are recognized as rich reservoirs of structurally diverse bioactive compounds, including alkaloids, flavonoids, polyphenols, terpenoids, tannins, saponins, and glycosides. These phytoconstituents exhibit antiviral activities through multiple mechanisms, such as inhibition of viral attachment and entry, suppression of viral replication, interference with viral protein synthesis, modulation of host immune responses, and attenuation of virus-induced inflammation. Several plant-derived compounds have demonstrated promising activity against a broad spectrum of DNA and RNA viruses in in vitro, in vivo, and computational studies. Furthermore, natural products have historically contributed significantly to pharmaceutical development, with many modern drugs originating directly or indirectly from plant sources. The exploration of medicinal herbs therefore represents a promising strategy for the identification of new antiviral drug

candidates with improved safety and therapeutic efficacy.¹⁸⁻²⁰

In recent years, advances in phytochemistry, metabolomics, molecular docking, network pharmacology, and systems biology have enhanced the scientific understanding of plant-derived antiviral agents. These multidisciplinary approaches facilitate the identification of bioactive phytochemicals, elucidation of molecular mechanisms, and evaluation of their therapeutic potential against emerging viral pathogens. Such developments have renewed interest in medicinal herbs as complementary and alternative therapeutic resources for addressing current and future viral health challenges.²¹⁻²²

The present review aims to provide a comprehensive and critical overview of medicinal herbs with demonstrated antiviral potential against emerging and re-emerging viral diseases. The review discusses the global burden of emerging viral infections, limitations of current antiviral therapies, mechanisms of viral resistance, and the role of traditional medicinal systems in antiviral drug discovery. Additionally, it highlights important antiviral phytochemicals, their mechanisms of action, evidence from preclinical and clinical studies, recent advances in omics-based research, and future perspectives for the development of plant-based antiviral therapeutics. By integrating contemporary scientific findings with traditional knowledge, this review seeks to identify promising opportunities and research directions for the development of effective herbal interventions against emerging viral diseases.²³⁻²⁵

Table 1. Major Emerging Viral Diseases and Their Global Health Significance

Viral Disease	Causative Virus	Year of Major Outbreak	Mode of Transmission	Global Significance
COVID-19	SARS-CoV-2	2019	Respiratory droplets and aerosols	Global pandemic with significant mortality and economic impact
SARS	SARS-CoV	2002	Respiratory transmission	First major coronavirus outbreak
MERS	MERS-CoV	2012	Zoonotic and	High case

			respiratory transmission	fatality rate
Dengue Fever	Dengue virus	Recurrent outbreaks	Mosquito-borne	Major tropical public health concern
Chikungunya	Chikungunya virus	2004 onwards	Mosquito-borne	Causes debilitating arthralgia
Zika Virus Disease	Zika virus	2015–2016	Mosquito-borne and vertical transmission	Associated with congenital abnormalities
Ebola Virus Disease	Ebola virus	2014–2016	Direct contact with infected fluids	Severe hemorrhagic fever with high mortality
Nipah Virus Infection	Nipah virus	1998 onwards	Bat-to-human and human-to-human transmission	Emerging zoonotic threat
Mpox (Monkeypox)	Monkeypox virus	2022 global outbreak	Direct contact and respiratory exposure	Re-emerging global viral disease
Influenza	Influenza A and B viruses	Seasonal and pandemic outbreaks	Respiratory transmission	Continuous public health burden

Emerging and Re-emerging Viral Diseases²⁶⁻³⁵

Emerging and re-emerging viral diseases have become a major concern for global public health due to their increasing incidence, widespread geographical distribution, and substantial impact on human health. Emerging viral infections are caused by newly identified pathogens or previously recognized viruses that have recently expanded their host range, transmission capacity, or geographical prevalence. In contrast, re-emerging

viral infections are diseases that were previously controlled but have resurfaced due to changes in environmental conditions, viral evolution, declining immunity, or inadequate public health measures.

The emergence of viral diseases is driven by a complex interaction of ecological, environmental, and socio-economic factors. Rapid urbanization, globalization, international travel, climate change, deforestation, and increased human encroachment into wildlife habitats have significantly enhanced opportunities for zoonotic spillover and viral dissemination. In addition, the high mutation rates of many RNA viruses facilitate genetic adaptation, allowing viruses to evade host immune responses, develop drug resistance, and establish infections in new hosts. These factors collectively contribute to the continuous emergence of viral pathogens with epidemic and pandemic potential. Based on their epidemiological characteristics and modes of transmission, emerging viral diseases can be broadly categorized into respiratory viruses, arboviruses, hemorrhagic fever viruses, zoonotic viruses, and other clinically significant viral pathogens. These viral groups continue to pose serious challenges to healthcare systems worldwide and underscore the urgent need for effective preventive and therapeutic interventions.

Respiratory Viruses

Respiratory viruses represent one of the most significant causes of infectious disease outbreaks globally. These viruses primarily infect the respiratory tract and are transmitted through respiratory droplets, aerosols, and direct contact with contaminated surfaces. Their high transmissibility and ability to rapidly spread among populations make them major public health threats.

SARS-CoV-2

Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), the causative agent of Coronavirus Disease 2019 (COVID-19), belongs to the family Coronaviridae. It is an enveloped, positive-sense single-stranded RNA virus characterized by the presence of spike glycoproteins on its surface. The virus primarily enters host cells through interaction with angiotensin-converting enzyme 2 (ACE2) receptors. COVID-19 manifests with a wide spectrum of clinical symptoms ranging from asymptomatic infection to severe respiratory distress, pneumonia, multi-organ failure, and death. Fever, cough, fatigue, dyspnea, loss of smell and taste, and gastrointestinal disturbances are among the most common symptoms. Current therapeutic approaches include antiviral agents such as remdesivir and nirmatrelvir/ritonavir, immunomodulatory therapies, supportive care, and extensive vaccination programs.

Influenza Viruses

Influenza viruses are enveloped negative-sense RNA viruses belonging to the Orthomyxoviridae

family. Influenza A and Influenza B viruses are primarily responsible for seasonal epidemics and occasional pandemics. The viruses spread mainly through respiratory droplets and aerosol transmission. Clinical manifestations include fever, headache, myalgia, sore throat, cough, fatigue, and respiratory complications. Severe infections may result in viral pneumonia and secondary bacterial infections. Antiviral drugs such as oseltamivir, zanamivir, and baloxavir marboxil are commonly used, while annual vaccination remains the most effective preventive strategy.

Respiratory Syncytial Virus (RSV)

Respiratory Syncytial Virus is an enveloped RNA virus belonging to the family Pneumoviridae. RSV is a leading cause of lower respiratory tract infections in infants, young children, immunocompromised individuals, and older adults. The virus is transmitted through respiratory secretions and close contact with infected individuals. Clinical manifestations include bronchiolitis, wheezing, cough, pneumonia, and respiratory distress. Current management primarily involves supportive care, although recent advances have led to the development of monoclonal antibodies and vaccines for high-risk populations.

Arboviruses

Arboviruses are arthropod-borne viruses transmitted predominantly by mosquitoes and ticks. Their incidence has increased considerably over recent decades due to climate change, urbanization, and the expansion of vector habitats.

Dengue Virus

Dengue virus belongs to the family Flaviviridae and comprises four antigenically distinct serotypes. It is transmitted primarily by *Aedes aegypti* and *Aedes albopictus* mosquitoes. Clinical manifestations range from mild febrile illness to severe dengue hemorrhagic fever and dengue shock syndrome. Currently, no specific antiviral therapy is available, and treatment is largely supportive.

Zika Virus

Zika virus is a mosquito-borne flavivirus transmitted mainly through *Aedes* mosquito species. Although most infections are asymptomatic or mild, severe complications such as congenital Zika syndrome, microcephaly, and neurological disorders have been reported. Management is limited to supportive care and preventive vector-control measures.

Chikungunya Virus

Chikungunya virus is a positive-sense RNA virus belonging to the family Togaviridae. It is transmitted by *Aedes* mosquitoes and is characterized by acute fever, severe polyarthralgia, rash, and prolonged joint pain. Treatment remains symptomatic, focusing on pain management and supportive care.

Hemorrhagic Fever Viruses

Hemorrhagic fever viruses are associated with severe systemic infections characterized by vascular damage, coagulation abnormalities, and high mortality rates.

Ebola Virus

Ebola virus is an enveloped filamentous RNA virus belonging to the Filoviridae family. Human infection occurs through direct contact with infected bodily fluids and contaminated materials. Clinical manifestations include fever, vomiting, diarrhea, hemorrhage, shock, and multi-organ failure. Recent advances have led to the development of monoclonal antibody therapies and effective vaccines.

Marburg Virus

Marburg virus is closely related to Ebola virus and is also classified within the Filoviridae family. The virus causes severe hemorrhagic fever with symptoms including high fever, bleeding, shock, and organ dysfunction. Current treatment is mainly supportive, although several therapeutic candidates are undergoing clinical evaluation.

Zoonotic Viruses

Zoonotic viruses are transmitted from animal reservoirs to humans and represent a major source of emerging infectious diseases worldwide.

Nipah Virus

Nipah virus is a highly pathogenic member of the Paramyxoviridae family. Fruit bats serve as the primary reservoir host. Human infection may occur through contaminated food, infected animals, or direct person-to-person transmission. Clinical manifestations include encephalitis, respiratory distress, seizures, and high mortality rates. No approved antiviral therapy currently exists, and treatment remains supportive.

Hantavirus

Hantaviruses are enveloped RNA viruses transmitted through inhalation of aerosolized rodent excreta. Human infection can result in hantavirus pulmonary syndrome or hemorrhagic fever with renal syndrome. These diseases are associated with severe respiratory and renal complications. Management relies primarily on intensive supportive care.

Other Emerging Viral Diseases

Monkeypox (Mpox) Virus

Monkeypox virus is a large double-stranded DNA virus belonging to the Poxviridae family. Human transmission occurs through direct contact with infected individuals, contaminated materials, or infected animals. Clinical manifestations include fever, lymphadenopathy, and characteristic vesiculopustular skin lesions. Tecovirimat and supportive care are currently used for disease management.

Hepatitis Viruses

Hepatitis viruses comprise a diverse group of hepatotropic viruses including hepatitis A, B, C, D, and E viruses. These viruses differ in their genomic

structures and modes of transmission but collectively contribute to a substantial global burden of liver disease. Clinical outcomes range from acute hepatitis to chronic liver disease, cirrhosis, and hepatocellular carcinoma. Current therapeutic approaches include antiviral drugs, vaccination, and supportive medical management depending on the viral type.

Table 2. Characteristics of Major Emerging and Re-emerging Viral Diseases

Viral Disease	Viral Family	Genome Type	Transmission Route	Major Clinical Manifestations	Available Therapeutic Approaches
COVID-19	Coronaviridae	ssRNA (+)	Respiratory droplets	Fever, pneumonia, ARDS	Antivirals, vaccines
Influenza	Orthomyxoviridae	ssRNA (-)	Respiratory droplets	Fever, cough, pneumonia	Oseltamivir, vaccines
RSV Infection	Pneumoviridae	ssRNA (-)	Respiratory secretions	Bronchiolitis, pneumonia	Supportive care, monoclonal antibodies
Dengue Fever	Flaviviridae	ssRNA (+)	Mosquito-borne	Hemorrhagic fever	Supportive care
Zika Virus Disease	Flaviviridae	ssRNA (+)	Mosquito-borne	Congenital abnormalities	Supportive care
Chikungunya	Togaviridae	ssRNA (+)	Mosquito-borne	Severe arthralgia	Symptomatic treatment
Ebola Virus Disease	Filoviridae	ssRNA (-)	Body fluids	Hemorrhagic fever	Monoclonal antibodies
Marburg Virus Disease	Filoviridae	ssRNA (-)	Bat-associated transmission	Hemorrhagic fever	Supportive care
Nipah	Paramyxo	ssRNA	Bat-	Enceph	Supp

h Virus Infection	xoviridae	NA (-)	to- huma n trans mission	halitis	ortive care
Hanta virus Infection	Hantaviridae	Segmented RNA	Rodent exposure	Pulmonary syndrome	Intensive care
Mpox	Poxviridae	dsDNA	Direct contact	Skin lesions	Tecovirimat
Viral Hepatitis	Various Families	RNA/DNA	Blood, food, sexual transmission	Hepatitis, cirrhosis	Antivirals, vaccines

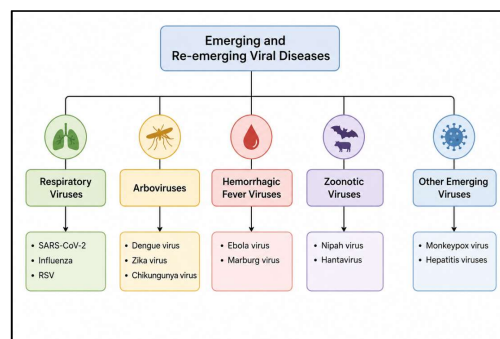


Figure 1. Classification of Emerging and Re-emerging Viral Diseases and Their Global Health Impact

Medicinal Herbs as Sources of Antiviral Agents³⁶⁻⁵²

Medicinal plants have been utilized for centuries as valuable therapeutic resources for the prevention and treatment of various infectious diseases. Long before the advent of modern pharmaceuticals, traditional healthcare systems relied extensively on herbal remedies to manage viral, bacterial, and parasitic infections. The rich diversity of bioactive compounds present in medicinal plants has attracted considerable scientific interest in recent decades, particularly in response to the increasing prevalence of emerging viral diseases and the limitations of conventional antiviral therapies. Numerous plant-derived metabolites have demonstrated antiviral activities against a broad spectrum of human pathogens, highlighting the significant potential of medicinal herbs as sources of novel therapeutic agents.

Historical Perspective of Medicinal Herbs in Viral Disease Management

The use of medicinal plants for treating infectious diseases is deeply rooted in human civilization. Traditional medical systems developed across different regions of the world have accumulated extensive knowledge regarding the therapeutic properties of herbs. These systems continue to provide valuable information for the identification of potential antiviral compounds and have served as an important foundation for contemporary drug discovery research.

Ayurveda

Ayurveda, one of the oldest holistic healthcare systems originating in India more than 5,000 years ago, extensively utilizes medicinal plants for disease prevention and treatment. Ayurvedic literature describes numerous herbal formulations used to strengthen immunity and combat infectious diseases. Herbs such as *Azadirachta indica* (Neem), *Ocimum sanctum* (Tulsi), *Tinospora cordifolia* (Guduchi), *Withania somnifera* (Ashwagandha), and *Curcuma longa* (Turmeric) have traditionally been employed for their immunomodulatory, anti-inflammatory, and antimicrobial properties. Recent pharmacological investigations have validated the antiviral potential of many Ayurvedic herbs against influenza viruses, dengue virus, hepatitis viruses, and SARS-CoV-2. The holistic approach of Ayurveda, which emphasizes host immunity and disease prevention, remains highly relevant in the management of emerging viral infections.

Traditional Chinese Medicine

Traditional Chinese Medicine (TCM) represents one of the most extensively documented herbal medical systems in the world. For thousands of years, TCM practitioners have utilized medicinal plants to manage respiratory infections, febrile illnesses, and epidemic diseases. Common antiviral herbs used in TCM include *Andrographis paniculata*, *Glycyrrhiza glabra* (Licorice), *Lonicera japonica* (Honeysuckle), *Scutellaria baicalensis*, and *Camellia sinensis* (Green tea). During recent outbreaks of SARS, influenza, and COVID-19, several TCM formulations were investigated for their therapeutic benefits and demonstrated promising antiviral, anti-inflammatory, and immune-regulating activities. The integration of traditional knowledge with modern pharmacological research has contributed significantly to the identification of bioactive compounds with antiviral potential.

African Traditional Medicine

African traditional medicine encompasses a diverse range of indigenous healthcare practices that rely heavily on medicinal plants for treating infectious diseases. Various African communities have traditionally employed herbs such as *Artemisia afra*, *Sutherlandia frutescens*, *Vernonia amygdalina*, and *Hypoxis hemerocallidea* for the management of respiratory and febrile illnesses.

Many of these plants contain phytochemicals with demonstrated antiviral, antioxidant, and immunostimulatory properties. The rich biodiversity of the African continent offers a vast but relatively underexplored source of bioactive compounds that may contribute to the development of future antiviral therapeutics.

Unani Medicine

Unani medicine, which originated from ancient Greek medical traditions and later flourished in the Middle East and South Asia, employs a holistic approach to disease management. Herbal preparations play a central role in Unani therapeutics, particularly in the treatment of infectious diseases. Medicinal plants such as *Nigella sativa* (Black seed), *Glycyrrhiza glabra*, *Allium sativum* (Garlic), and *Zingiber officinale* (Ginger) are widely utilized for their anti-inflammatory, antimicrobial, and immune-enhancing properties. Contemporary scientific studies have confirmed the antiviral activities of several Unani medicinal plants against influenza viruses, hepatitis viruses, and coronaviruses, supporting their potential role in antiviral drug development.

Importance of Medicinal Herbs in Modern Drug Discovery

The increasing emergence of viral pathogens and the growing limitations of conventional antiviral therapies have intensified interest in natural products as alternative sources of therapeutic agents. Medicinal plants continue to play a pivotal role in pharmaceutical research owing to their immense chemical diversity and broad spectrum of biological activities.

Natural Products as Drug Leads

Natural products have historically served as an important source of pharmaceutical agents. Many clinically approved drugs have been derived directly from natural sources or developed based on natural product scaffolds. Plant-derived compounds possess unique structural characteristics that often differ significantly from synthetic chemical libraries, thereby providing valuable templates for drug development. The success of natural products in oncology, infectious disease treatment, and immunotherapy has encouraged researchers to investigate medicinal plants for novel antiviral compounds. Advances in computational biology, molecular docking, high-throughput screening, and artificial intelligence have further accelerated the identification of plant-derived molecules with potential antiviral activity.

Phytochemical Diversity and Antiviral Potential

Medicinal plants synthesize a remarkable array of secondary metabolites that contribute to their therapeutic properties. These phytochemicals include alkaloids, flavonoids, polyphenols, terpenoids, tannins, saponins, glycosides, lignans, coumarins, and essential oils. Such compounds

exhibit antiviral activities through multiple mechanisms, including inhibition of viral attachment and entry, suppression of viral replication, interference with viral protein synthesis, modulation of host immune responses, and attenuation of inflammatory pathways.

Unlike conventional antiviral agents that often target a single viral protein, plant-derived phytochemicals frequently exert multitarget effects, reducing the likelihood of resistance development. Additionally, many phytochemicals possess antioxidant and immunomodulatory properties that may enhance host defense mechanisms against viral infections. This chemical diversity provides an extensive reservoir of bioactive molecules for the discovery and development of next-generation antiviral therapeutics. The convergence of traditional medicinal knowledge, modern phytochemical research, and advanced molecular technologies has significantly expanded the scientific understanding of medicinal herbs as antiviral agents. Consequently, medicinal plants continue to represent one of the most promising and sustainable resources for addressing current and future challenges posed by emerging viral diseases.

Table 3. Traditional Medical Systems and Representative Medicinal Herbs with Reported Antiviral Potential

Traditional System	Representative Medicinal Herbs	Major Bioactive Constituents	Reported Antiviral Applications
Ayurveda	<i>Azadirachta indica</i> , <i>Ocimum sanctum</i> , <i>Tinospora cordifolia</i> , <i>Curcuma longa</i>	Limonoids, eugenol, curcuminoids, diterpenoids	Dengue, influenza, SARS-CoV-2
Traditional Chinese Medicine	<i>Andrographis paniculata</i> , <i>Glycyrrhiza glabra</i> , <i>Scutellaria baicalensis</i> , <i>Camellia sinensis</i>	Andrographolide, glycyrrhizin, baicalin, EGCG	SARS-CoV-2, influenza, hepatitis
African Traditional Medicine	<i>Artemisia afra</i> , <i>Sutherlandia frutescens</i> , <i>Vernonia amygdalina</i>	Terpenoids, flavonoids, phenolic compounds	Respiratory viral infections, influenza
Unani	<i>Nigella</i>	Thymoquinone	Influenza

Medicine	<i>sativa</i> , <i>Allium sativum</i> , <i>Zingiber officinale</i> , <i>Glycyrrhiza glabra</i>	ne, allicin, gingerols, glycyrrhizin	, hepatitis, coronavirus infections
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These two sections are among the most important parts of your review because they provide the scientific basis for the antiviral efficacy of medicinal herbs. For a high-impact review, avoid describing every phytochemical individually in excessive detail. Instead, discuss phytochemical classes first, then provide representative examples and summarize them in comprehensive tables.

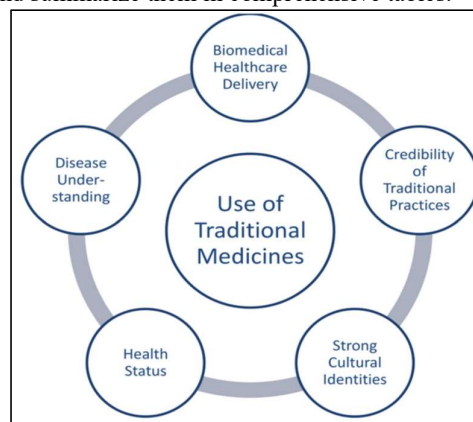


Figure 2. Use of traditional medicines
Phytochemical Classes with Antiviral Activity⁵³⁻⁶⁵

Medicinal plants synthesize a vast array of secondary metabolites that contribute to their therapeutic properties and ecological adaptation. These phytochemicals possess diverse chemical structures and exhibit broad-spectrum antiviral activities against both DNA and RNA viruses. Recent pharmacological and molecular studies have demonstrated that plant-derived bioactive compounds can interfere with multiple stages of the viral life cycle, including viral attachment, entry, replication, assembly, and release. Furthermore, many phytochemicals possess immunomodulatory, antioxidant, and anti-inflammatory properties that enhance host defense mechanisms and mitigate virus-induced tissue damage.

Polyphenols

Polyphenols constitute one of the largest groups of plant secondary metabolites and are characterized by the presence of multiple phenolic hydroxyl groups. These compounds are widely distributed in fruits, vegetables, medicinal herbs, and beverages such as tea. Polyphenols exhibit potent antiviral activity through inhibition of viral entry, suppression of viral replication, modulation of cellular signaling pathways, and enhancement of host immune responses.

Among the most extensively studied polyphenols, quercetin has demonstrated antiviral activity against influenza viruses, dengue virus, hepatitis viruses, and SARS-CoV-2. Catechins, particularly epigallocatechin gallate (EGCG) from green tea, have been shown to interfere with viral attachment and replication. Curcumin, a polyphenolic compound derived from *Curcuma longa*, exhibits broad-spectrum antiviral activity through modulation of inflammatory pathways and inhibition of viral protein expression. Resveratrol, commonly found in grapes and berries, has demonstrated inhibitory effects against respiratory viruses, herpes viruses, and coronaviruses through regulation of cellular antiviral signaling mechanisms.

Flavonoids

Flavonoids represent a diverse subclass of polyphenolic compounds characterized by a C6-C3-C6 carbon skeleton. They are widely recognized for their antiviral, antioxidant, and anti-inflammatory activities. Flavonoids have attracted considerable attention as potential antiviral agents because of their ability to target multiple viral and host cellular pathways simultaneously.

Luteolin has demonstrated inhibitory activity against influenza viruses, dengue virus, and coronaviruses through suppression of viral replication and interference with viral proteases. Apigenin exhibits antiviral activity by regulating viral gene expression and modulating host immune responses. Kaempferol has shown efficacy against influenza virus, hepatitis B virus, and SARS-CoV-2 by inhibiting viral replication and reducing inflammatory responses associated with infection.

Alkaloids

Alkaloids are nitrogen-containing organic compounds that possess significant pharmacological activities. Numerous plant-derived alkaloids have demonstrated broad-spectrum antiviral effects against a variety of clinically important viral pathogens. Their antiviral mechanisms frequently involve inhibition of viral nucleic acid synthesis, disruption of protein translation, and interference with viral replication machinery.

Berberine, an isoquinoline alkaloid found in *Berberis* species, exhibits antiviral activity against influenza viruses, hepatitis viruses, and coronaviruses. Lycorine, isolated from *Amaryllidaceae* plants, has demonstrated potent inhibitory activity against SARS-CoV, SARS-CoV-2, Zika virus, and enteroviruses through suppression of viral replication and protein synthesis.

Terpenoids

Terpenoids constitute one of the most structurally diverse groups of natural products and are synthesized from isoprene units. These compounds are widely distributed in medicinal plants and

exhibit a broad range of biological activities, including antiviral, anti-inflammatory, and immunomodulatory effects.

Glycyrrhizin, a triterpenoid saponin isolated from *Glycyrrhiza glabra*, has demonstrated antiviral activity against SARS-CoV, SARS-CoV-2, hepatitis viruses, and HIV through inhibition of viral entry and replication. Artemisinin and its derivatives, obtained from *Artemisia annua*, have shown promising antiviral activity against several RNA viruses through modulation of host immune responses and inhibition of viral proliferation.

Saponins

Saponins are amphiphilic glycosides characterized by a hydrophobic aglycone linked to hydrophilic sugar moieties. Their surfactant properties enable interactions with viral envelopes and host cell membranes. Saponins have been reported to inhibit viral attachment, disrupt viral membranes, and stimulate both innate and adaptive immune responses. Several saponin-rich medicinal plants have demonstrated activity against influenza viruses, herpes simplex viruses, and coronaviruses.

Tannins

Tannins are high-molecular-weight polyphenolic compounds capable of forming complexes with proteins and other macromolecules. Antiviral tannins exert their effects through direct interactions with viral proteins, inhibition of viral adsorption, and suppression of viral replication. Numerous hydrolyzable and condensed tannins have demonstrated activity against influenza viruses, HIV, herpes simplex virus, and hepatitis viruses.

Essential Oils

Essential oils are volatile aromatic compounds primarily composed of monoterpenes, sesquiterpenes, and their oxygenated derivatives. These compounds possess significant antimicrobial and antiviral properties. Essential oils can inhibit viral infectivity by disrupting viral envelopes, preventing viral attachment, and modulating host immune responses. Essential oils derived from eucalyptus, thyme, oregano, tea tree, and ginger have shown promising antiviral activities against respiratory and enveloped viruses. The remarkable chemical diversity of plant-derived secondary metabolites provides an extensive reservoir of bioactive molecules with potential applications in antiviral drug discovery. Their multitarget mechanisms of action and favorable safety profiles make them attractive candidates for the development of novel therapeutic interventions against emerging viral diseases.

Mechanisms of Antiviral Action of Medicinal Herbs⁶⁶⁻⁷¹

The antiviral efficacy of medicinal herbs is attributed to their ability to interfere with multiple stages of the viral life cycle while simultaneously modulating host defense mechanisms. Unlike

conventional antiviral drugs that often target a single viral protein, phytochemicals generally exhibit multitarget actions that reduce the likelihood of resistance development and enhance therapeutic effectiveness.

Prevention of Viral Attachment

The initial stage of viral infection involves the attachment of viral surface proteins to specific receptors on host cells. Several phytochemicals prevent this interaction by binding either to viral glycoproteins or host cell receptors, thereby blocking viral adsorption and reducing infectivity.

Inhibition of Viral Entry

Following attachment, viruses enter host cells through membrane fusion or endocytosis. Numerous herbal compounds interfere with these processes by altering membrane dynamics, inhibiting receptor-mediated internalization, or preventing fusion of viral and cellular membranes.

Inhibition of Viral Replication

Viral replication represents one of the most important targets for antiviral intervention. Several phytochemicals inhibit viral genome replication by suppressing viral enzymes, interfering with nucleic acid synthesis, or disrupting intracellular signaling pathways essential for viral proliferation.

Protease Inhibition

Many viruses require proteolytic processing of viral polyproteins for maturation and infectivity. Certain flavonoids, polyphenols, and terpenoids inhibit viral proteases, thereby preventing the production of functional viral proteins and reducing viral propagation.

Inhibition of Viral RNA Polymerase

RNA-dependent RNA polymerase plays a critical role in the replication of RNA viruses. Numerous plant-derived compounds have demonstrated the ability to inhibit viral polymerase activity, thereby suppressing viral genome synthesis and replication.

Immunomodulatory Activity

Many medicinal herbs enhance innate and adaptive immune responses through stimulation of macrophages, natural killer cells, dendritic cells, and lymphocytes. Immunomodulatory phytochemicals also promote cytokine production and improve antiviral defense mechanisms.

Anti-inflammatory Activity

Excessive inflammatory responses contribute significantly to viral pathogenesis and tissue damage. Herbal compounds such as curcumin, quercetin, and glycyrrhizin suppress pro-inflammatory cytokines and regulate signaling pathways including NF- κ B, MAPK, and JAK-STAT pathways.

Antioxidant Activity

Oxidative stress is a common feature of viral infections and contributes to cellular damage and disease progression. Antioxidant phytochemicals neutralize reactive oxygen species, protect cellular components from oxidative injury, and enhance

overall cellular resilience during viral infections. Collectively, these mechanisms highlight the multifaceted nature of plant-derived antiviral compounds and their potential as complementary or alternative therapeutic agents for combating emerging viral diseases.

Table 4. Major Antiviral Phytochemicals and Their Mechanisms of Action

Phytochemical Class	Representative Compound	Source Plant	Target Viruses	Major Mechanism of Action
Polyphenol	Quercetin	Onion, Apple, Tea	Influenza, Dengue, SARS-CoV-2	Inhibits viral replication and entry
Polyphenol	EGCG	Green Tea	Influenza, HIV, SARS-CoV-2	Blocks viral attachment
Polyphenol	Curcumin	Turmeric	Influenza, SARS-CoV-2	Anti-inflammatory, replication inhibition
Polyphenol	Resveratrol	Grapes	RSV, Influenza, SARS-CoV-2	Antioxidant and antiviral signaling
Flavonoid	Luteolin	Celery, Chamomile	Dengue, Influenza	Protease inhibition
Flavonoid	Apigenin	Parsley, Chamomile	Influenza, HSV	Replication inhibition
Flavonoid	Kaempferol	Tea, Broccoli	HBV, SARS-CoV-2	Viral enzyme inhibition
Alkaloid	Berberine	Berberis species	Influenza, HBV	Viral replication suppression
Alkaloid	Lycorine	Lycoris radiata	SARS-CoV-2, Zika	Protein synthesis inhibition
Terpenoid	Glycyrrhizin	Licorice	SARS-CoV-	Viral entry

			2, HIV, HBV	inhibiti on
Terpenoi d	Artemisi nin	Artem isia annua	SARS- CoV- 2, Dengu e	Immune modulat ion
Saponin	Glycyrrh izin derivativ es	Licori ce	Influen za, Coron avirus	Membr ane disrupti on
Tannin	Tannic Acid	Vario us medici nal plants	HSV, HIV	Viral adsorpti on inhibiti on
Essential Oil	Eugenol	Ocimu m sanctu m, Clove	Influen za, HSV	Viral envelop e disrupti on

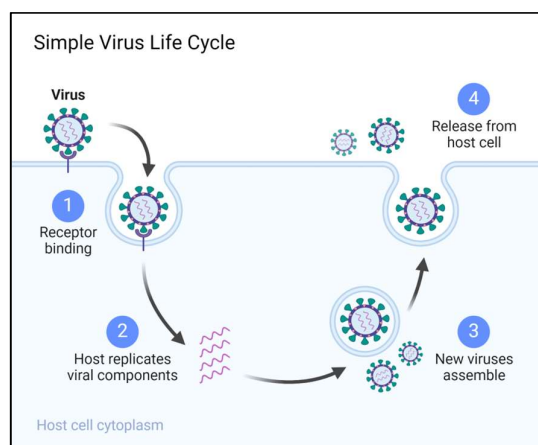


Figure 3. Virus life cycle

Important Medicinal Herbs against Emerging Viral Diseases⁷²⁻⁸¹

Medicinal plants have gained considerable attention as potential sources of antiviral agents due to their rich phytochemical composition and broad-spectrum biological activities. Numerous herbs traditionally used in various medical systems have demonstrated significant antiviral effects against emerging and re-emerging viral pathogens. These antiviral activities are primarily attributed to bioactive constituents capable of targeting multiple stages of the viral life cycle while simultaneously modulating host immune responses. Recent advances in phytochemical analysis, molecular docking, in vitro studies, and animal models have further validated the therapeutic potential of these medicinal herbs against clinically important viral infections.

Andrographis paniculata

Andrographis paniculata, commonly known as the "King of Bitters," is widely used in Ayurvedic and

Traditional Chinese Medicine. The major bioactive constituent, andrographolide, exhibits broad-spectrum antiviral activity against respiratory viruses, including SARS-CoV-2 and influenza viruses. Experimental studies suggest that andrographolide inhibits viral replication, suppresses inflammatory cytokine production, and enhances antiviral immune responses. Molecular docking investigations have demonstrated strong interactions with SARS-CoV-2 main protease and spike proteins, supporting its potential role in COVID-19 management.

Glycyrrhiza glabra

Glycyrrhiza glabra (Licorice) is an important medicinal plant extensively employed in traditional medicine systems. Glycyrrhizin, the principal triterpenoid saponin, possesses antiviral, anti-inflammatory, and immunomodulatory properties. Studies have demonstrated activity against SARS-CoV, SARS-CoV-2, hepatitis viruses, HIV, and influenza viruses. Glycyrrhizin interferes with viral attachment, inhibits viral replication, and modulates host immune responses through regulation of cytokine production.

Curcuma longa

Curcuma longa (Turmeric) contains curcumin as its major bioactive polyphenol. Curcumin exhibits antiviral activity against influenza viruses, hepatitis viruses, dengue virus, and SARS-CoV-2. Its antiviral effects are associated with inhibition of viral replication, suppression of viral protein expression, antioxidant activity, and regulation of inflammatory signaling pathways including NF- κ B and MAPK pathways.

Azadirachta indica

Azadirachta indica (Neem) has been widely used in Ayurvedic medicine for treating infectious diseases. Limonoids, nimbin, azadirachtin, and quercetin contribute to its antiviral activities. Experimental studies have reported inhibitory effects against dengue virus, herpes simplex virus, hepatitis viruses, and influenza viruses. Neem-derived compounds interfere with viral entry, replication, and host-pathogen interactions.

Ocimum sanctum

Ocimum sanctum (Holy Basil or Tulsi) is regarded as an important adaptogenic and immunomodulatory herb. The major active constituents include eugenol, ursolic acid, and rosmarinic acid. Tulsi has demonstrated antiviral activity against influenza viruses, herpes viruses, and respiratory pathogens. Its therapeutic effects are largely attributed to immune enhancement, antioxidant activity, and suppression of inflammatory mediators.

Allium sativum

Allium sativum (Garlic) contains sulfur-containing compounds such as allicin, ajoene, and diallyl sulfides. Garlic extracts have shown antiviral activity against influenza viruses, coronaviruses,

rhinoviruses, and herpes viruses. These compounds inhibit viral replication, stimulate immune responses, and reduce oxidative stress associated with viral infections.

Zingiber officinale

Zingiber officinale (Ginger) contains bioactive compounds including gingerols, shogaols, and zingerone. Several studies have demonstrated antiviral activity against respiratory syncytial virus, influenza virus, and human coronaviruses. Ginger inhibits viral attachment to host cells, modulates immune responses, and exerts significant anti-inflammatory effects.

Camellia sinensis

Camellia sinensis (Green Tea) is rich in catechins, particularly epigallocatechin gallate (EGCG). Green tea polyphenols exhibit antiviral activity against HIV, influenza viruses, hepatitis viruses, and SARS-CoV-2. EGCG interferes with viral attachment, inhibits viral replication, and modulates cellular antiviral pathways.

Artemisia annua

Artemisia annua is best known for producing artemisinin and its derivatives. In addition to their antimalarial activity, these compounds have demonstrated antiviral potential against SARS-CoV-2, hepatitis viruses, and several arboviruses. Artemisinin derivatives inhibit viral replication and modulate inflammatory responses associated with viral infections.

Sambucus nigra

Sambucus nigra (Elderberry) contains anthocyanins, flavonoids, and phenolic acids. Elderberry extracts have demonstrated antiviral activity against influenza viruses and respiratory pathogens. The herb promotes immune stimulation, reduces viral load, and alleviates symptoms associated with respiratory viral infections.

Table 5. Important Medicinal Herbs with Reported Antiviral Activity Against Emerging Viral Diseases

Medicinal Herb	Major Active Constituents	Target Viruses	Major Antiviral Mechanisms
Andrographis paniculata	Andrographolide	SARS-CoV-2, Influenza	Viral replication inhibition
Glycyrrhiza glabra	Glycyrrhizin	SARS-CoV-2, HBV, HCV, HIV	Viral entry and replication inhibition
Curcuma longa	Curcumin	Influenza, Dengue, SARS-CoV-2	Anti-inflammatory and antiviral activity
Azadirachta indica	Limonoids	Dengue	Viral

hta indica	Azadirachtin	HSV, Influenza	inhibition and immune modulation
Ocimum sanctum	Eugenol, Ursolic acid	Influenza, HSV	Immunomodulatory activity
Allium sativum	Allicin, Ajoene	Influenza, Corona virus	Viral replication inhibition
Zingiber officinale	Gingerols, Shogaols	RSV, Influenza	Viral attachment inhibition
Camellia sinensis	EGCG	HIV, Influenza, SARS-CoV-2	Viral replication suppression
Artemisia annua	Artemisinin	SARS-CoV-2, Dengue	Antiviral and immunomodulatory activity
Sambucus nigra	Anthocyanins	Influenza	Immune stimulation and antiviral activity

Medicinal Herbs against Specific Viral Diseases⁸²⁻⁹³

Medicinal Herbs against COVID-19

COVID-19 is caused by SARS-CoV-2, an enveloped positive-sense RNA virus that primarily targets the respiratory system through ACE2 receptor-mediated entry. Although antiviral drugs and vaccines have significantly reduced disease severity, therapeutic challenges remain due to viral mutations and emerging variants. Several medicinal herbs have demonstrated promising anti-SARS-CoV-2 activity. Andrographis paniculata, Glycyrrhiza glabra, Curcuma longa, Camellia sinensis, and Artemisia annua have shown inhibitory effects against viral replication, viral entry, and inflammatory pathways. Experimental evidence from molecular docking, cell culture studies, and animal models supports their therapeutic potential.

Medicinal Herbs Against Dengue

Dengue virus is a mosquito-borne flavivirus that causes dengue fever, dengue hemorrhagic fever, and dengue shock syndrome. The disease is characterized by excessive inflammatory responses, thrombocytopenia, and vascular leakage. Medicinal plants such as Azadirachta indica, Carica papaya, Andrographis paniculata, and Curcuma longa have demonstrated potential therapeutic benefits. These herbs possess antiviral, immunomodulatory, and platelet-supportive activities. Experimental studies have reported reduced viral replication and improvement of clinical parameters in dengue infection.

Medicinal Herbs Against Zika Virus

Zika virus infection is associated with neurological complications and congenital abnormalities. Currently, no specific antiviral treatment is available. Several plant-derived compounds, including quercetin, EGCG, curcumin, and lycorine, have demonstrated inhibitory effects on Zika virus replication in experimental studies. Herbal extracts rich in polyphenols and flavonoids have shown promise as potential antiviral candidates.

Medicinal Herbs Against Chikungunya

Chikungunya virus infection is characterized by severe fever and prolonged joint pain. Current treatment remains largely symptomatic. Medicinal herbs such as *Andrographis paniculata*, *Curcuma longa*, *Artemisia annua*, and *Glycyrrhiza glabra* possess anti-inflammatory and antiviral properties that may alleviate disease symptoms and reduce viral replication. Several in vitro investigations have reported significant antiviral activity against chikungunya virus.

Medicinal Herbs Against Ebola Virus

Ebola virus causes severe hemorrhagic fever with high mortality rates. Despite advances in vaccine development, therapeutic options remain limited. Natural products including flavonoids, terpenoids, and alkaloids derived from medicinal plants have demonstrated inhibitory effects on Ebola viral proteins and replication pathways. Several phytochemicals have shown promising activity in molecular docking and experimental studies.

Medicinal Herbs Against Nipah Virus

Nipah virus is a highly pathogenic zoonotic virus associated with encephalitis and respiratory disease. The absence of approved antiviral therapies necessitates the exploration of alternative therapeutic strategies.

Bioactive compounds such as quercetin, luteolin, glycyrrhizin, and berberine have demonstrated potential inhibitory effects against Nipah virus proteins in computational and experimental studies. Their immunomodulatory properties may further contribute to disease management.

Medicinal Herbs Against Monkeypox Virus

Monkeypox virus is an emerging orthopoxvirus responsible for recent global outbreaks. The disease is characterized by fever, lymphadenopathy, and cutaneous lesions. Several medicinal plants rich in flavonoids, polyphenols, and terpenoids have demonstrated antiviral activity against poxviruses. Compounds such as quercetin, kaempferol, EGCG, and glycyrrhizin are currently being investigated as potential therapeutic candidates against monkeypox virus infection.

Table 6. Medicinal Herbs Investigated Against Specific Emerging Viral Diseases

Viral Disease	Pathogenesis	Current Treatment	Herbal Interventions	Experimental Evidence
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COVID-19	Respiratory and systemic infection	Antivirals, vaccines	Andrographis, Licorice, Turmeric	In vitro, in vivo, docking studies
Dengue	Vascular leakage, thrombocytopenia	Supportive care	Neem, Papaya, Turmeric	Cell culture and animal studies
Zika	Neurotropic infection	Supportive care	Green tea, Curcumin, Quercetin	Experimental antiviral studies
Chikungunya	Joint inflammation	Symptomatic treatment	Andrographis, Licorice	In vitro evidence
Ebola	Hemorrhagic fever	Monoclonal antibodies	Polyphenol-rich herbs	Computational and laboratory studies
Nipah	Encephalitis and respiratory disease	Supportive care	Glycyrrhizin, Berberine, Quercetin	In silico and experimental studies
Monkeypox	Systemic and cutaneous infection	Tecovirimat	Flavonoid-rich medicinal plants	Emerging experimental evidence

CONCLUSION:

Emerging and re-emerging viral diseases continue to challenge global healthcare systems, necessitating the development of innovative therapeutic strategies beyond conventional antiviral drugs. The increasing prevalence of viral outbreaks, coupled with issues such as viral mutations, drug resistance, limited treatment options, and adverse drug reactions, has renewed scientific interest in medicinal plants as alternative and complementary therapeutic resources. Traditional medicinal systems have provided valuable knowledge regarding the use of herbs for managing infectious diseases, and contemporary research has increasingly validated many of these traditional claims through pharmacological and molecular investigations. Medicinal herbs constitute a rich reservoir of structurally diverse bioactive compounds, including polyphenols, flavonoids, alkaloids, terpenoids, saponins, tannins,

and essential oils. These phytochemicals exhibit broad-spectrum antiviral activities by targeting multiple stages of the viral life cycle, including viral attachment, entry, replication, assembly, and release. In addition, their immunomodulatory, antioxidant, and anti-inflammatory properties contribute significantly to host protection against viral infections. Several medicinal plants, including *Andrographis paniculata*, *Glycyrrhiza glabra*, *Curcuma longa*, *Azadirachta indica*, *Ocimum sanctum*, *Allium sativum*, *Zingiber officinale*, *Camellia sinensis*, *Artemisia annua*, and *Sambucus nigra*, have demonstrated promising antiviral activities against major emerging viral pathogens such as SARS-CoV-2, dengue virus, Zika virus, chikungunya virus, Ebola virus, Nipah virus, and monkeypox virus. Recent advances in phytochemistry, metabolomics, molecular docking, network pharmacology, and systems biology have accelerated the identification and characterization of plant-derived antiviral compounds. However, despite encouraging experimental findings, the clinical translation of many herbal antivirals remains limited due to challenges related to standardization, quality control, bioavailability, safety evaluation, and insufficient clinical evidence. Therefore, future research should focus on comprehensive mechanistic studies, large-scale clinical trials, advanced formulation approaches, and integration of multi-omics technologies to fully exploit the therapeutic potential of medicinal herbs. Overall, medicinal plants represent a promising and sustainable source of novel antiviral agents capable of addressing current and future viral health challenges. The integration of traditional medicinal knowledge with modern scientific approaches may facilitate the discovery and development of effective plant-based therapeutics for the prevention and management of emerging viral diseases worldwide.

CONFLICT OF INTEREST:

The author declares that there is no conflict of interest.

REFERENCES:

1. Bachar SC, Mazumder K, Bachar R, Aktar A, Al Mahtab MA, Rahman F, et al. A review of medicinal plants with antiviral activity available in Bangladesh and mechanistic insight into their bioactive metabolites on SARS-CoV-2, HIV and HBV. *Front Pharmacol*. 2021;12:732891.
2. Anand AV, Balamuralikrishnan B, Kaviya M, Bharathi K, Parithathi A, Arun M, et al. Medicinal plants, phytochemicals, and herbs to combat viral pathogens including SARS-CoV-2. *Molecules*. 2021;26(6):1775.
3. Atampugbire G, Akpabey FJ, Asare P, Kyei-Baffour G, Kwarteng A. Medicinal plants as effective antiviral agents and their mechanisms of action. *J Evid Based Integr Med*. 2024;29:1–25.
4. Saleh MSM, Kamisah Y. Potential medicinal plants for the treatment of dengue fever and severe acute respiratory syndrome-coronavirus. *Front Pharmacol*. 2020;11:562149.
5. Lim SYM, Ng YL, Lee SH. Recent insights on anti-dengue virus medicinal plants: Review and assessment of their therapeutic potential. *Explor Res Hypothesis Med*. 2021;6(1):1–15.
6. Hasani SJ, Rahimi M, Ebrahimi S, Hosseini M. Recent advances in the control of dengue fever using medicinal plants and phytochemicals. *Heliyon*. 2025;11:e00319.
7. Sytar O, Brestic M, Hajihashemi S, Skalicky M, Kubes J, Lamilla-Tamayo L, et al. COVID-19 prophylaxis efforts based on natural antiviral plant extracts and their compounds. *Molecules*. 2021;26(23):7279.
8. Ben-Shabat S, Yarmolinsky L, Porat D, Dahan A. Antiviral effect of phytochemicals from medicinal plants: Applications and mechanisms. *Phytother Res*. 2020;34(8):1903–20.
9. Lin LT, Hsu WC, Lin CC. Antiviral natural products and herbal medicines. *J Tradit Complement Med*. 2014;4(1):24–35.
10. Akram M, Tahir IM, Shah SMA, Mahmood Z, Altaf A, Ahmad K, et al. Antiviral potential of medicinal plants: A comprehensive review. *J Pharm Bioallied Sci*. 2018;10(3):109–20.
11. Jassim SAA, Naji MA. Novel antiviral agents: A medicinal plant perspective. *J Appl Microbiol*. 2003;95(3):412–27.
12. Vlietinck AJ, De Bruyne T, Apers S, Pieters LA. Plant-derived leading compounds for chemotherapy of human immunodeficiency virus (HIV) infection. *Planta Med*. 1998;64(2):97–109.
13. Rasve V, Chakraborty AK, Jain SK, Vengurlekar S. Study of phytochemical profiling and in vitro studies on antioxidant properties of ethanolic extract of *Clematis triloba*. *Eur Chem Bull*. 2022;11(12):2658–2677. doi:10.53555/ecb/2022.11.12.2162022.
14. Newman DJ, Cragg GM. Natural products as sources of new drugs over nearly four decades from 1981 to 2019. *J Nat Prod*. 2020;83(3):770–803.
15. Cragg GM, Newman DJ. Natural products: A continuing source of novel drug leads. *Biochim Biophys Acta Gen Subj*. 2013;1830(6):3670–95.
16. Harvey AL, Edrada-Ebel R, Quinn RJ. The re-emergence of natural products for drug discovery in the genomics era. *Nat Rev Drug Discov*. 2015;14(2):111–29.
17. Atanasov AG, Zotchev SB, Dirsch VM, Supuran CT. Natural products in drug

- discovery: Advances and opportunities. *Nat Rev Drug Discov.* 2021;20(3):200–16.
18. Adeosun, W.B.; Loots, D.T., Medicinal Plants against Viral Infections: A Review of Metabolomics Evidence for the Antiviral Properties and Potentials in Plant Sources. *Viruses* 2024, 16, 218. <https://doi.org/10.3390/v16020218>
19. Yang Y, Islam MS, Wang J, Li Y, Chen X. Traditional Chinese medicine in the treatment of patients infected with 2019-new coronavirus (SARS-CoV-2): A review and perspective. *Int J Biol Sci.* 2020;16(10):1708–17.
20. Luo H, Tang QL, Shang YX, Liang SB, Yang M, Robinson N, et al. Can Chinese medicine be used for prevention of coronavirus disease 2019? A review of historical classics, research evidence and current prevention programs. *Chin J Integr Med.* 2020;26(4):243–50.
21. Chojnacka K, Witek-Krowiak A, Skrzypczak D, Mikula K, Młynarz P. Phytochemicals containing antiviral and immunomodulatory properties against emerging viral infections. *Crit Rev Food Sci Nutr.* 2021;61(8):1365–88.
22. Bahadur Gurung A, Ali MA, Lee J, Farah MA, Al-Anazi KM. Unraveling lead antiviral phytochemicals for the inhibition of SARS-CoV-2 main protease using molecular docking studies. *Saudi J Biol Sci.* 2021;28(9):4844–56.
23. Sarkar L, Oko L, Gupta S, Bubak AN, Das B. Azadirachta indica bark extract and its nimbin isomers restrict β -coronaviral infection and replication. *Virology.* 2022;567:19–28.
24. Maurya VK, Kumar S, Prasad AK, Bhatt MLB, Saxena SK. Structure-based drug designing for potential antiviral activity of selected natural products from Ayurveda against SARS-CoV-2 spike glycoprotein and its cellular receptor. *VirusDisease.* 2020;31(2):179–93.
25. Hsu SC, Chung JG. Emodin and its antiviral potential against coronaviruses and other viral pathogens. *Phytother Res.* 2016;30(12):1901–11.
26. Chen G, Hsieh CL, Lin RT, et al. A traditional Chinese medicine formulation (NRICM101) to target COVID-19 through multiple pathways: A bedside-to-bench study. *Biomed Pharmacother.* 2021;133:111037.
27. Hariono M, Hidayat I, Djunarko I, Julianus J, Saqallah FG, Khawory MH, et al. Carica papaya leaf extract inhibits SARS-CoV-2 main proteases: An in vitro and in silico study. *J Herb Med.* 2023;40:100650.
28. Rasve VR, Paithankar VV, Shirsat MK, Dhobale AV. Evaluation of antiulcer activity of *Aconitum heterophyllum* on experimental animals. *World J Pharm Pharm Sci.* 2018;7(2):819-839.
29. Tsugawa H, Cajka T, Kind T, Ma Y, Higgins B, Ikeda K, Kanazawa M, Vanderghenst J, Fiehn O, Arita M. MS-DIAL: Data-independent MS/MS deconvolution for comprehensive metabolome analysis. *Nat Methods.* 2015;12(6):523-526.
30. Guijas C, Montenegro-Burke JR, Domingo-Almenara X, Palermo A, Warth B, Hermann G, Koellensperger G, Huan T, Uritboonthai W, Aisporna AE, et al. METLIN: A technology platform for identifying knowns and unknowns. *Anal Chem.* 2018;90(5):3156-3164.
31. Mahrous EA, Farag MA. Two-dimensional NMR spectroscopic approaches for exploring plant metabolome: A review. *J Adv Res.* 2015;6(1):3-15.
32. Udayakumar M, Chandar DP, Arun N, Mathangi J, Hemavathi K, Seenivasagam R. PMDB: Plant Metabolome Database—A metabolomic approach. *Med Chem Res.* 2012;21(1):47-52.
33. Pieters L, Vlietinck AJ. Bioguided isolation of pharmacologically active plant components: Still a valuable strategy for the finding of new lead compounds? *J Ethnopharmacol.* 2005;100(1-2):57-60.
34. Thissera B, Sayed AM, Hassan MHA, Abdelwahab SF, Amaeze N, Semler VT, Alenezi FN, Yaseen M, Alhadrami HA, Belbahri L, et al. Bioguided isolation of cyclophenin analogues as potential SARS-CoV-2 Mpro inhibitors from *Penicillium citrinum* Tdpf34. *Biomolecules.* 2021;11(9):1366.
35. Altemimi A, Lakhssassi N, Baharlouei A, Watson DG, Lightfoot DA. Phytochemicals: Extraction, isolation, and identification of bioactive compounds from plant extracts. *Plants (Basel).* 2017;6(4):42.
36. Sasidharan S, Chen Y, Saravanan D, Sundram KM, Latha LY. Extraction, isolation and characterization of bioactive compounds from plant extracts. *Afr J Tradit Complement Altern Med.* 2011;8(1):1-10.
37. Zhang M, Yu Q, Guo J, Wu B, Kong X. Review of thin-layer chromatography tandem with surface-enhanced Raman spectroscopy for detection of analytes in mixture samples. *Biosensors (Basel).* 2022;12(11):937.
38. Czaplicki S. Chromatography in bioactivity analysis of compounds. In: *Column Chromatography*. London: InTech; 2013.
39. Medini F, Megdiche W, Mshvildadze V, Pichette A, Legault J, St-Gelais A, Ksouri R. Antiviral-guided fractionation and isolation of phenolic compounds from *Limonium densiflorum* hydroalcoholic extract. *C R Chim.* 2016;19(6):726-732.
40. Royani A, Hanafi M, Dewi N, Lotulung P, Prastya ME, Verma C, Manaf A, Alfantazi A.

- Isolation and identification of bioactive compounds from *Tinospora cordifolia* stem extracts as antibacterial materials in seawater environments. *Arab J Chem.* 2023;16(9):105014.
41. Cecilio AB, De Faria DB, Oliveira PDC, Caldas S, De Oliveira DA, Sobral MEG, Duarte MGR, Moreira CPS, Silva CG, Almeida VL. Screening of Brazilian medicinal plants for antiviral activity against rotavirus. *J Ethnopharmacol.* 2012;141(3):975-981.
42. Visintini Jaime MF, Redko F, Muschietti LV, Campos RH, Martino VS, Cavallaro LV. In vitro antiviral activity of plant extracts from Asteraceae medicinal plants. *Virology.* 2013;10:245.
43. Beuscher N, Bodinet C, Neumann-Haefelin D, Marston A, Hostettmann K. Antiviral activity of African medicinal plants. *J Ethnopharmacol.* 1994;42(2):101-109.
44. Mohamed AK, Shier WT. A simplified plaque reduction assay for antiviral agents from plants: Demonstration of frequent occurrence of antiviral activity in higher plants. *J Nat Prod.* 1990;53(2):340-344.
45. Zhang CJ, Li W, Li HY, Wang YL, Yun T, Song ZP, Song Y, Zhao XW. In vivo and in vitro antiviral activity of five Tibetan medicinal plant extracts against herpes simplex virus type 2 infection. *Pharm Biol.* 2009;47(7):598-607.
46. Huang W, Percie du Sert N, Vollert J, Rice ASC. General principles of preclinical study design. In: *Handbook of Experimental Pharmacology*. Vol. 257. Berlin: Springer; 2020. p. 55-69.
47. Shegokar R. Preclinical testing—Understanding the basics first. In: *Drug Delivery Aspects. Volume 4: Expectations and Realities of Multifunctional Drug Delivery Systems*. Amsterdam: Elsevier; 2020. p. 19-32.
48. England C, Trejo-Martinez J, Perez-Sanchez P, Karki U, Xu J. Plants as biofactories for therapeutic proteins and antiviral compounds to combat COVID-19. *Life (Basel).* 2023;13(3):617.
49. Trivedi P, Abbas A, Lehmann C, Rupasinghe HPV. Antiviral and anti-inflammatory plant-derived bioactive compounds and their potential use in the treatment of COVID-19-related pathologies. *J Xenobiot.* 2022;12(4):289-306.
50. Venturella G, Ferraro V, Cirilione F, Gargano ML. Medicinal mushrooms: Bioactive compounds, use, and clinical trials. *Int J Mol Sci.* 2021;22(2):634.
51. Ward BJ, Makarkov A, Séguin A, Pillet S, Trépanier S, Dhaliwall J, Libman MD, Vesikari T, Landry N. Efficacy, immunogenicity, and safety of a plant-derived quadrivalent virus-like particle influenza vaccine in adults and older adults: Two multicentre, randomised phase 3 trials. *Lancet.* 2020;396(10261):1491-1503.
52. Pandey A, Khan MK, Hamurcu M, Gezgin S. Natural plant products: A less focused aspect for the COVID-19 viral outbreak. *Front Plant Sci.* 2020;11:568890.
53. Kell DB, Oliver SG. The metabolome 18 years on: A concept comes of age. *Metabolomics.* 2016;12(9):148.
54. Khan MTH, Ather A, editors. *Lead molecules from natural products: Discovery and new trends*. 1st ed. Amsterdam: Elsevier; 2006.
55. Bang S, Ha TKQ, Lee C, Li W, Oh WK, Shim SH. Antiviral activities of compounds from aerial parts of *Salvia plebeia* R.Br. *J Ethnopharmacol.* 2016;192:398-405.
56. Gupta S, Schillaci M, Roessner U. Metabolomics as an emerging tool to study plant-microbe interactions. *Emerg Top Life Sci.* 2022;6(2):175-183.
57. Serag A, Salem MA, Gong S, Wu JL, Farag MA. Decoding metabolic reprogramming in plants under pathogen attacks: A comprehensive review of emerging metabolomics technologies to maximize their applications. *Metabolites.* 2023;13(4):424.
58. Sampaio BL, Edrada-Ebel R, Da Costa FB. Effect of the environment on the secondary metabolic profile of *Tithonia diversifolia*: A model for environmental metabolomics of plants. *Sci Rep.* 2016;6:29265.
59. Prinsloo G, Nogemane N. The effects of season and water availability on chemical composition, secondary metabolites and biological activity in plants. *Phytochem Rev.* 2018;17(4):889-902.
60. Adeosun WB, More GK, Steenkamp P, Prinsloo G. Influence of seasonal and geographic variation on the anti-HSV-1 properties and chlorogenic acids content of *Helichrysum aureonitens* Sch. Bip. *Front Mol Biosci.* 2022;9:961859.
61. Manchester M, Anand A. Metabolomics: Strategies to define the role of metabolism in virus infection and pathogenesis. In: *Advances in Virus Research*. Vol. 98. Cambridge (MA): Academic Press; 2017. p. 57-81.
62. Ren Z, Fang M, Muhae-Ud-Din G, Gao H, Yang Y, Liu T, Chen W, Gao L. Metabolomics analysis of grains of wheat infected and noninfected with *Tilletia controversa* Kühn. *Sci Rep.* 2021;11:18876.
63. Nothias-Scaglia LF, Retailleau P, Paolini J, Pannecouque C, Neyts J, Dumontet V, Roussi F, Leyssen P, Costa J, Litaudon M. Jatrophone diterpenes as inhibitors of Chikungunya virus replication: Structure-activity relationship and

- discovery of a potent lead. *J Nat Prod*. 2014;77(6):1505-1512.
64. Ferraz AC, Gomes PWP, Menegatto MBS, Lima RLS, Guimarães PH, Reis JDE, Carvalho ARV, Pamplona SGSR, Muribeca AJB, Magalhães JC, et al. Exploring the antiviral potential of Justicidin B and four glycosylated lignans from *Phyllanthus brasiliensis* against Zika virus: A promising pharmacological approach. *Phytomedicine*. 2024;123:155197.
65. Haggag EG, Elshamy AM, Rabeh MA, Gabr NM, Salem M, Youssif KA, Samir A, Muhsinah AB, Alsayari A, Abdelmohsen UR. Antiviral potential of green synthesized silver nanoparticles of *Lampranthus coccineus* and *Malephora lutea*. *Int J Nanomedicine*. 2019;14:6217-6229.
66. Takeda Y, Okuyama Y, Nakano H, Yaoita Y, Machida K, Ogawa H, Imai K. Antiviral activities of *Hibiscus sabdariffa* L. tea extract against human influenza A virus rely largely on acidic pH but partially on a low-pH-independent mechanism. *Food Environ Virol*. 2020;12(1):9-19.
67. Aati HY, Ismail A, Rateb ME, AboulMagd AM, Hassan HM, Hetta MH. *Garcinia cambogia* phenolics as potent anti-COVID-19 agents: Phytochemical profiling, biological activities, and molecular docking. *Plants (Basel)*. 2022;11(19):2521.
68. Cock IE, Matthews B. Metabolomic profiling of antiviral *Scaevola spinescens* extracts by high-resolution tandem mass spectrometry. *Acta Hort*. 2016;1125:1-18.
69. Nagai T, Shimizu Y, Shirahata T, Sunazuka T, Kiyohara H, Omura S, Yamada H. Oral adjuvant activity for nasal influenza vaccines caused by combination of two trihydroxy fatty acid stereoisomers from the tuber of *Pinellia ternata*. *Int Immunopharmacol*. 2010;10(6):655-661.
70. Mei J, Zhou Y, Yang X, Zhang F, Liu X, Yu B. Active components in *Ephedra sinica* Stapf disrupt the interaction between ACE2 and SARS-CoV-2 receptor-binding domain: Potent COVID-19 therapeutic agents. *J Ethnopharmacol*. 2021;278:114303.
71. Ngoc TM, Phuong NTT, Khoi NM, Park SJ, Kwak HJ, Nhiem NX, Trang BTT, Tai BH, Song JH, Ko HJ, et al. A new naphthoquinone analogue and antiviral constituents from the root of *Rhinacanthus nasutus*. *Nat Prod Res*. 2019;33(3):360-366.
72. Chung CY, Liu CH, Burnouf T, Wang GH, Chang SP, Jassey A, Tai CJ, Huang CJ, Richardson CD, Lin LT. Activity-based and fraction-guided analysis of *Phyllanthus urinaria* identifies loliolide as a potent inhibitor of hepatitis C virus entry. *Antiviral Res*. 2016;130:58-68.
73. Wu SF, Lin CK, Chuang YS, Chang FR, Tseng CK, Wu YC, Lee JC. Anti-hepatitis C virus activity of 3-hydroxy caruillignan C from *Swietenia macrophylla* stems. *J Viral Hepat*. 2012;19(5):364-370.
74. Gómez-Calderón C, Mesa-Castro C, Robledo S, Gómez S, Bolívar-Avila S, Díaz-Castillo F, Martínez-Gutiérrez M. Antiviral effect of compounds derived from the seeds of *Mammea americana* and *Tabernaemontana cymosa* on dengue and chikungunya virus infections. *BMC Complement Altern Med*. 2017;17:57.
75. Abubakar AR, Haque M. Preparation of medicinal plants: Basic extraction and fractionation procedures for experimental purposes. *J Pharm Bioallied Sci*. 2020;12(1):1-10.
76. Savina T, Lisun V, Feduraev P, Skrypnik L. Variation in phenolic compounds, antioxidant and antibacterial activities of extracts from different plant organs of meadowsweet (*Filipendula ulmaria* (L.) Maxim.). *Molecules*. 2023;28(8):3512.
77. Wojdyło A, Nowicka P, Turkiewicz IP, Tkacz K, Hernandez F. Comparison of bioactive compounds and health-promoting properties of fruits and leaves of apple, pear and quince. *Sci Rep*. 2021;11:20253.
78. Herrera-Ruiz M, Román-Ramos R, Zamilpa A, Tortoriello J, Jiménez-Ferrer JE. Flavonoids from *Tilia americana* with anxiolytic activity in the elevated plus-maze test. *J Ethnopharmacol*. 2008;118(2):312-317.
79. Goulas V, Manganaris GA. Towards an efficient protocol for the determination of triterpenic acids in olive fruit: A comparative study of drying and extraction methods. *Phytochem Anal*. 2012;23(5):444-449.
80. Kim KH, Moon E, Kim SY, Choi SU, Lee KR. Lignan constituents of *Tilia amurensis* and their biological evaluation on antitumor and anti-inflammatory activities. *Food Chem Toxicol*. 2012;50(10):3680-3686.
81. Oniszczyk A, Podgórski R, Oniszczyk T, Zukiewicz-Sobczak W, Nowak R, Waksmundzka-Hajnos M. Extraction methods for the determination of phenolic compounds from *Equisetum arvense* L. herb. *Ind Crops Prod*. 2014;61:377-381.
82. Noguerón-Merino MC, Jiménez-Ferrer E, Román-Ramos R, Zamilpa A, Tortoriello J, Herrera-Ruiz M. Interactions of a standardized flavonoid fraction from *Tilia americana* with serotonergic drugs in the elevated plus maze. *J Ethnopharmacol*. 2015;164:319-327.
83. Zhang A, Sun H, Wang X. Emerging role and recent applications of metabolomics

- biomarkers in obesity disease research. *RSC Adv.* 2017;7:14966-14973.
84. Halket JM, Zaikin VG. Derivatization in mass spectrometry—VII. On-line derivatization/degradation. *Eur J Mass Spectrom.* 2006;12(1):1-13.
85. More GK, Vervoort J, Steenkamp PA, Prinsloo G. Metabolomic profile of medicinal plants with anti-Rift Valley fever virus activity. *Heliyon.* 2022;8(2):e08936.
86. Tugizimana F, Piater L, Dubery I. Plant metabolomics: A new frontier in phytochemical analysis. *S Afr J Sci.* 2013;109(5-6):1-11.
87. Markley JL, Dashti H, Wedell JR, Westler WM, Eghbalnia HR. Tools for enhanced NMR-based metabolomics analysis. In: *Methods in Molecular Biology*. Vol. 2037. New York: Humana Press; 2019. p. 413-427.
88. Ludwig C, Günther UL. MetaboLab—Advanced NMR data processing and analysis for metabolomics. *BMC Bioinformatics.* 2011;12:366.
89. Tsugawa H, Tsujimoto Y, Arita M, Bamba T, Fukusaki E. GC/MS-based metabolomics: Development of a data mining system for metabolite identification using soft independent modeling of class analogy (SIMCA). *BMC Bioinformatics.* 2011;12:131.
90. Xia J, Psychogios N, Young N, Wishart DS. MetaboAnalyst: A web server for metabolomic data analysis and interpretation. *Nucleic Acids Res.* 2009;37(Web Server issue):W652-W660.
91. Kılınç H, D'Urso G, Paolillo A, Alankus O, Piacente S, Masullo M. LC-MS and NMR-based plant metabolomics: A comprehensive phytochemical investigation of *Symphytum anatomicum*. *Metabolites.* 2023;13(10):1051.
92. Smith CA, Want EJ, O'Maille G, Abagyan R, Siuzdak G. XCMS: Processing mass spectrometry data for metabolite profiling using nonlinear peak alignment, matching and identification. *Anal Chem.* 2006;78(3):779-787.
93. Du X, Smirnov A, Pluskal T, Jia W, Sumner S. Metabolomics data preprocessing using ADAP and MZmine 2. In: *Methods in Molecular Biology*. Vol. 2104. New York: Humana Press; 2020. p. 25-48.