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Antiviral Potential of Medicinal Plants beyond HIV

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ABSTRACT

Viral infections remain a major global health challenge, with limitations in conventional antiviral therapies including high costs, drug resistance, adverse side effects, and limited accessibility in resource-constrained regions. Beyond their established role in managing HIV, medicinal plants have emerged as promising sources of antiviral agents with broad-spectrum potential. This paper examines the antiviral properties of selected medicinal plants, including Echinacea, Elderberry, Garlic, Ginger, and Turmeric, highlighting their phytochemicals and mechanisms of action, such as viral entry inhibition, replication blockade, immune modulation, and synergistic activity with existing drugs. Evidence from laboratory studies, clinical evaluations, and ethnomedicinal practices underscores their effectiveness against influenza, herpes simplex virus, hepatitis C, coronaviruses, and other emerging pathogens. While challenges persist in terms of standardization, safety validation, dosage optimization, and regulatory approval, advancements in biotechnology and pharmacological research continue to strengthen the case for integrating phytomedicine into modern healthcare. Harnessing medicinal plants as cost-effective, sustainable, and culturally relevant alternatives offers a vital strategy for expanding the global antiviral arsenal beyond HIV.

Keywords: Medicinal plants, Antiviral phytochemicals, viral inhibition, Phytomedicine, and Traditional medicine.

INTRODUCTION

Medicinal plants have long served as reservoirs of candidate agents for combating a diversity of human pathogens [1]. Widespread continued interest in the application of extracts and derived natural products from medicinal plants currently drives antiviral research during the global pandemic, with herbal products and remedies increasingly under scientific investigation and mechanistic scrutiny [2]. Despite the extensive array of viruses exhibiting susceptibility to medicinal plants, the majority of ever-expanding literature continues to focus almost exclusively on HIV [3]. An overview of available data nevertheless reinforces the value and relevance of a much broader perspective on diverse viral targets and the underlying multifarious means of interference. Compelling justification exists, therefore, for systematic consideration and further concerted development regarding the antiviral potential of medicinal plants beyond HIV [2]. Many plants have been shown to possess antiviral properties [2], with extracts and phytochemicals exhibiting activity against DNA and RNA viruses [1]. In vitro and in vivo studies have demonstrated that various plant-derived compounds can combat numerous pathogenic viruses, and some have been used in traditional medicine to treat viral diseases [4]. The categories of antiviral activity include: inhibiting viral attachment and entry, interfering with viral replication, transcription, and translation, and stimulating the host immune system.

Mechanisms of Antiviral Action

The principal antiviral actions of medicinal plants can be assigned to three major mechanisms: inhibition of viral entry or direct viral inactivation; disruption of viral replication machinery; and modulation of host immune responses. The recognition that viral attachment and entry are key initial steps exploited by numerous phytochemicals to block infection has inspired the search for plants that operate at this stage. Suspicion arose that herbs possessing saponins or lectins may confer antiviral activities by inhibiting the fusion or adsorption of viral particles to the host membrane [1]. In the event that viral fusion is prevented, subsequent treatment with a compound of similar antiviral potency is expected to be ineffective. Consequently, herbs operating through an

alternate mechanism would be preferable when developing an antiviral product based on multiple phyto-constituents [1].

Inhibition of Viral Entry

At least three possible mechanisms are thought to be common to most antiretroviral agents: inhibition of viral attachment/entry; inhibition of viral enzyme activity, or alteration of the viral particle. Antimicrobial substances may also act nonspecifically as immunomodulators; for example, acemannan, a compound isolated from Aloe vera, is normally considered to be an immunostimulant rather than an antiviral agent [1]. The life cycle of a virus involves a series of sequential steps. Virus particles first attach to specific receptor molecules on the host cell surface. They then penetrate through the membrane into the cytoplasm or nucleus and uncoat, releasing the genetic material. This is followed by transcription and translation of viral genes; replication of the viral nucleic acid; assembly of virus particles; and finally, release from the cells. A substance that acts against the first step of virus replication may affect viral attachment/entry into the suitable host cells; for example, it may interfere with the binding of the viral particles to the cellular receptors. This mode of inhibition is typical of antibodies, student vaccines, soluble receptor proteins, nonionic surfactants, and certain carbohydrates. Fucose-containing sulfated polysaccharides and heparinoids, for example, exert their action by blocking cellular receptors [1, 2].

Interference with Viral Replication

Another major mechanism of antiviral action involves interference with viral replication. Different replicated viral components have been proposed as targets for medicinal plants from the pericarp of Garcinia mangostana through inhibition of NS5BRdRp activity of HCV [1]. In the case of HIV-1, the virus could be inhibited at different stages of its replication cycle using cell-free and cell-based enzyme assays for proteinase, reverse transcriptase, and integrase, followed by a single replication cycle infectivity assay. Several studies indicate that the interference with viral replication is a key antiviral mechanism for a range of viruses originating from different viral families [2].

Modulation of Host Immune Response

Host immune response modulation represents a second major mechanism of antiviral action frequently exploited by medicinal plants to accomplish viral clearance. Plant extracts and isolated phytochemicals from a limited number of species employing this mechanism are known to stimulate innate immune responses principally via the enhancement of macrophage and natural killer (NK) cell function and the promotion of dendritic cell maturation [1]. Consistent with this mechanism, Azadirachta indica selectively down-regulates activation and exhaustion markers on CD4+ T cells [5].

Medicinal Plants with Antiviral Properties

The antiviral properties of certain plants have been attributed to their mechanisms of action, which include: inhibition of reproduction by interfering with the virus's ability to replicate within host cells; prevention of viral entry into host cells, thereby blocking the initial stages of infection; and boosting of the host immune system, enhancing the body's natural defenses against viral pathogens [1, 2]. Building on these principles, the following medicinal plants represent some of the most frequently studied herbs cited for their therapeutic potential against viral infections [1, 2].

Echinacea

Echinacea preparations have long been employed as remedies for colds, influenza, and other infections. As purpura-based tinctures and extracts have been shown to modulate immune responses in preventive ways, the question was whether this autoimmune profile would extend to virus infections, where therapeutically beneficial immune modulation was sought [6]. An ethanolic extract of freshly harvested Echinacea purpurea aerial parts, comprising alkylamides, chicoric acid, caftaric acid, and other unknown compounds, exhibited potent antiviral activity that was broadly effective against multiple coronaviruses [6]. The inhibition was not only achieved by pre-treatment of cells but also upon direct contact with the virus itself, suggesting a comprehensive mechanism of action against envelope integrity or functionality within the virions [6]. Testing was performed against endemic and potentially dangerous coronaviruses, including HCoV-229E, MERS-CoV, SARS-CoV, and SARS-CoV-2. Infectivity in all cases was markedly diminished when viruses were incubated with Echinacea extract, and the treatment also prevented a murine coronavirus from infecting a host, further underpinning the broad coronavirus-virucidal properties of the preparation.

Elderberry

Recent literature provides consistent evidence of antiviral activity attributed to elderberry against influenza viruses A and B, offering effective relief from flu symptoms. An in vitro study reports elderberry extract acting on the hemagglutinin envelope glycoprotein to inhibit replication of human pathogenic H1N1 and H5N1 strains, engaging the early steps of viral infection [1]. Another investigation reveals that standardized elderberry treatment boosts production of cytokines, interleukin (IL)-1β, IL-6, IL-8, and tumor necrosis factor (TNF)-α—inflammatory mediators involved in immune defense. An in vivo evaluation assesses the impact of black elderberry

extract on influenza A and B symptoms. Additionally, cyanidin 3-glucoside and cyanidin 3-sambubioside derivatives from elderberry are identified as compounds effective against the human influenza A virus. From Burkina Faso, flavonoids from Sambucus nigra bark are found to inhibit the reverse transcriptase extracted from feline immunodeficiency virus [1, 2]. Research from Sofia University detects elderberry flavonoids and phenolic acids as active agents against Herpes simplex virus type 1 (HSV-1) in vitro. The antiviral activity of extracts from the berries of S. nigra is tested against avian influenza and infectious bronchitis viruses in both embryonated hen eggs and broilers. These extracts consistently slow the progression of viral infection and alleviate disease symptoms. Furthermore, an aqueous extract of elder blossoms, subjected to Gamma irradiation, is examined for antiviral efficacy against equine herpes virus types 1 and 3 [1, 2].

Garlic

Garlic (Allium sativum) is among the most widely used herbal remedies in human history. The primary bioactive constituent, allicin, exhibits antiviral activity both in vitro and in vivo [1]. Sulfur-containing compounds such as allicin, diallyl disulfide, and diallyl trisulfide interact with enzymes critical for microorganism surveillance, contributing to these effects. An aqueous extract of A. sativum demonstrates antiviral activity against coronavirus species. Aqueous extracts incorporated in gold nanoparticles have exhibited antiviral effects against the measles virus by blocking viral entry. HSV-1 and HSV-2 inhibition assays with aqueous extract in gold nanoparticles suggest that the extract disrupts the viral envelope and cell membrane, thereby preventing virus entry [1]. A. sativum extracts reduce replication of human cytomegalovirus (HCMV) and enhance the immune response. Garlic oil effectively reduces cytopathic effects induced by H1N1 influenza A virus infection in vitro. The n-hexane extract of garlic shows positive results in HIV reverse transcriptase inhibition assays. Organosulfur compounds isolated from garlic have demonstrated significant inhibition of a range of human pathogenic viruses [1].

Ginger

Ginger, a common household remedy, has been used for centuries to treat colds and infections [1]. Its antiviral compound, gingerols extracted from the rhizome, was reported to have inhibitory effects against human respiratory syncytial virus (HRSV) in cell lines. The effect on other viruses remains to be determined, although the efficacy against HRSV offers further evidence that ginger may be a useful phytomedicine to combat viral infections [1]. Potential addition of natural products like gingerols to supportive care for patients with SARS-CoV-2 or other viral infections merits additional investigation [1].

Turmeric

Echinacea, Elderberry, Garlic, Ginger, and Turmeric have attracted considerable attention during their investigation in vitro and in vivo against various viral infections, proving bioactive compounds from these plants as beneficial antiviral agents. Various human viruses, such as the influenza virus, herpes simplex virus (HSV), and hepatitis C virus (HCV), are responsible for different viral diseases and infections. Several antiviral drugs available in the market provide treatment to these diseases, but cause adverse health effects and are costlier. To avoid all these factors, medicinal plants and their derivatives provide benefits to all the viruses tested and have an immune-boosting property too [3]. These natural substances have been effective in clinical trials against viral infections. Turmeric (Curcuma longa) has been used widely as a spice, coloring agent, and traditional medicine for centuries. The principal pharmacological bioactive constituents responsible for turmeric's health-beneficial properties are polyphenolic in structure and predominantly represented by the group of curcuminoids, including curcumin, demethoxycurcumin, and bisdemethoxycurcumin [5]. Of these, curcumin is the major curcuminoid present and has been extensively investigated for its pharmacological actions, including anti-inflammatory and antiviral activities. A recent clinical trial involving nano-curcumin in COVID-19 patients demonstrated an accelerated rate of recovery after curcumin therapy, including the prevention of acute respiratory distress syndrome, considered as one of the causes of mortality in SARS-CoV-2 infection [1, 5].

Traditional Uses of Antiviral Plants

Before modern medicine, a variety of plants served as the predominant source of therapeutics [1]. Madagascar's analysis provides a large pharmacological data set on the use of plants for controlling infectious diseases, including viruses, which are particularly prevalent among adults. Several countries have systematically evaluated their flora for antiviral activity, yet little effort has been made to study the marine flora of India's coastline [2]. Many plants and families possess both antiviral and anticancer properties. Plant extracts may enhance the body's innate antiviral defenses and prevent viral replication, with the specific pathway depending on the viral species.

Recent Advances in Research

The recent increase in global viral infections has stimulated intensified research efforts to establish the efficacy of medicinal plants as antivirals, as substantiated by ongoing clinical trials. In vitro studies correlate the antiviral activities of plants with their phytochemical constituents. For example, flavonoids such as quercetin and epicatechin, present in many plants, inhibit viral DNA and RNA synthesis by blocking RNA-polymerase, DNA-

polymerase, and reverse transcriptase. Several medicinal plants, Echinacea, Elderberry, Garlic, Ginger, and Turmeric, are recognized for their antiviral properties; undermining viral attachment and replication, or enhancing immune response [1]. Despite the potency of conventional antiviral drugs, their high cost, frequent side effects, and resistance development have sparked searches for alternatives. Plant-derived antiviral substances are often perceived as safer, less toxic, and more cost-effective. Consequently, recent research is directed toward overcoming the challenges of standardization, identification of active constituents, bioavailability, and ethical concerns (e.g., clinical trials). Current approaches include the utilization of phytopharmaceuticals as pre-therapeutic vaccines, therapy coadjuvants, and components of combination therapies [2].

Clinical Trials

The discovery of new antiviral agents remains a priority in the light of newly emerging viral pathogens and the development of resistance by existing ones [2]. Since the limited antiviral drug pipeline comes with the frequent emergence of drug resistance, broad-spectrum antivirals are urgently needed. Although medicinal plants have been a source of traditional medicine for treating infections and other diseases, only some of them have been evaluated for antiviral potential [2]. The promising preclinical assays of medicinal plants provide a good opportunity to be used clinically. With the emergence and re-emergence of infectious diseases worldwide, plant-derived antivirals offer a source of lead compounds for pharmaceutical innovation [2].

In Vitro Studies

Medicinal plants have frequently been assessed for their tolerance and toxicity in cell culture assays before being investigated for their antiviral potential [7]. Indian tribal communities have traditionally used certain plants, such as Eclipta alba and Euphorbia prostrata, for the treatment of HIV/AIDS [2]. Plant extracts are believed to inhibit viruses by blocking absorption and penetration into host cells, interfering with viral DNA/RNA synthesis, pathogen replication, and gene expression, preventing viral products, or by activating host cellular protective mechanisms. Various plant extracts have demonstrated in vitro activity against different viral species and cell lines, such as HSV-1 and HSV-2 in Hep-2 and Vero cells; influenza virus PR8 in MDCK, Val149, and CV-1 cells; and Coxsackievirus A9 and B3 in Vero and SK-N-SH cells. Most studies have involved persistent viruses such as herpes simplex virus types I and II, hepatitis and influenza viruses, adenovirus, and human immunodeficiency virus [2, 7].

Phytochemical Analysis

Phytochemical analysis aims to identify bioactive compounds responsible for a plant's antiviral activity. Isolation and identification of these compounds can help determine mechanisms of action, develop standardized extracts, and contribute to antiviral drug discovery [1]. The antiviral properties of phytochemicals depend on various factors such as solubility, molecular size, stability, composition, and tumor-promoting effects. Commonly encountered antiviral phytochemicals include alkaloids, flavonoids, phenolics, and terpenoids [1]. For instance, phytochemical analysis of Diplocyclos palmatus revealed saponins, flavonoids, alkaloids, and other bioactive compounds that contribute to significant antiviral activity 8. Another example is the bioassay-guided fractionation of Boerhaavia diffusa, which produced various fractions, all of which reduced viral infectivity. A more polar fraction produced the greater effect by restricting virus entry into the target cells and interfering with glucose metabolism of the virus [2].

Challenges in Antiviral Research

Addressing the challenges associated with antiviral drug discovery is paramount to enhancing therapeutic options. While medicinal plants demonstrate considerable antiviral potential, several constraints impede their progression into clinically viable drugs. The standardization of bioactive molecules represents a critical barrier; without consistent quantification and quality control, reproducibility and efficacy of plant-derived compounds remain uncertain [1, 9]. Moreover, inadequate pharmacokinetic and pharmacodynamic data hinder the comprehensive understanding of absorption, distribution, metabolism, excretion, and toxicity (ADMET) profiles, which are essential for safety and efficacy assessments [1]. The inherent complexity of phytochemical mixtures further complicates the identification and isolation of active constituents. Bioavailability challenges also arise, as many effective compounds exhibit poor solubility in aqueous environments, leading to suboptimal absorption following oral administration. The toxicity and safety profiles of numerous natural products, particularly those with substantial antiviral promise, are yet to be thoroughly investigated, raising concerns about potential adverse effects. Additionally, the lack of patentability associated with natural substances diminishes commercial incentives for pharmaceutical investment, thereby limiting extensive research and clinical development. Ethical considerations also emerge due to the unequal geographic distribution of medicinal plants, raising questions about resource access and benefit-sharing when vested interests potentially exclude indigenous communities from plant resources [1, 9].

Standardization of Extracts

Standardization remains a limiting factor in the development of antiviral medicinal plants, with few extracts properly characterized and little data on pharmacological targets and mechanisms [10]. The bioavailability of many medicinal plants is also poorly studied, and the safety profile of some plants still raises concerns. Limited scientific support for traditional use in clinical practice remains a major obstacle to widespread acceptance, and research must provide stronger links between ethnobotanical use and clinically relevant outcomes to implement viable phytotherapeutic treatments [10].

Bioavailability Issues

Poor water solubility, low cellular permeability, chemical instability, susceptibility to efflux, and first-pass metabolism are the main bioavailability-limiting factors of phytochemical substances of medicinal plants [8]. Many phytochemicals have demonstrated antiviral activities in vitro or in cellular models of viral infection. Unfortunately, active phytochemicals are frequently found to be ineffective in vivo after oral administration because of their low bioavailability, which is responsible for the failure of most phytochemistry-based drug development programmes. Efforts have been devoted to identifying and developing new drug delivery systems to improve the bioavailability of phytochemical substances [8]. Various drug delivery systems, such as polymeric nanoparticles, solid lipid nanoparticles, nanoemulsions, and lipid-based carriers, improve the solubility and stability of phytochemical substances and allow their transport across the cell membrane to the target site. Development of novel drug delivery systems remains for further improvement of the therapeutic benefits of phytochemical substances.

Ethical Considerations

The pursuit of novel molecules with antiviral potential beyond HIV is conducted with awareness of ethical and practical considerations. Medicinal plants exhibiting antiviral activity must be scrutinized for their ability to induce resistance and the determination of doses that minimize such risks [3]. The development of resistance frequently originates from incomplete treatment; consequently, empirical use of medicinal plants as antivirals is discouraged. Additionally, the potential toxicity of these plants is a critical factor in evaluating anti-HIV agents, with the general assumption that, given the mortality associated with certain infections, some level of toxicity may be acceptable [11]. These considerations establish ethical parameters for the administration of antiviral medicinal plants in therapeutic settings.

Comparison with Conventional Antivirals

Conventional antiviral drugs are often effective only against a limited number of viruses and can cause considerable side effects. Established chemotherapeutic agents such as aciclovir, zidovudine, ganciclovir, and lamivudine are used primarily to treat herpes viruses and HIV infections. While there is evidence to support the use of plant-derived drugs for managing many common viral infections, the results are generally less promising compared with other approaches [2]. The widespread occurrence of medicinal plant species and their cost-effectiveness in comparison to pharmaceutical products has increased interest in their antiviral potential [9]. Many plant species, including Echinacea, Elderberry, Garlic, Ginger, and Turmeric, have shown strong activity against a spectrum of viruses, and have effects comparable to those of anti-retroviral drugs [1]. Medicinal plants offer a number of advantages, exhibiting fewer adverse effects than pharmaceuticals, and may rarely be linked to the development of antiviral resistance. However, few clinical trials have been conducted, and the search for broadly useful species remains a requirement.

Efficacy

Efficacy against viruses. Phytochemicals derived from medicinal plants exhibit antiviral activities through several mechanisms: they can inhibit viral entry into host cells, interfere with viral replication, or modulate the immune response to limit cell susceptibility and infection [1]. Medications aimed at reducing viral replication decrease the duration of symptoms but often do not cure the infection: the influenza virus is eliminated by the immune system 5 to 7 days after symptom onset, regardless of medication, and, nevertheless, antiviral compounds lengthen the period in which the virus is detectable and able to be transmitted to other susceptible people [1]. Most plant-derived medications possess fewer side effects.

Side Effects

Medicinal plants have emerged as valuable sources of antiviral agents. An increasing number of plants exhibiting antiviral activity against a broad spectrum of viruses have been identified. The availability of more potent and less toxic phytomedicines, such as anti-HIV drugs from medicinal plants, further encourages scientific research to identify more powerful antiviral agents [2]. Even though the generally accepted view is that herbal drugs are safe, some herbals possess a wide variety of side effects and interactions that should be considered when recommending or using such preparations on a frequent or long-term basis. For example, gastrointestinal complaints, allergic reactions in susceptible persons, skin reactions and photosensitization, neurotoxicity, and carcinogenesis are all

possible side effects [1]. In such cases, an antidote or specific treatment could be necessary. In addition, while chronic administration is normally avoided, particular attention is required when investigating antiretroviral properties of traditional medicine preparations since antiretrovirals (ARVs) need to be taken for life. Psychosomatic reactions and potential ill health may occur instead of the anticipated pharmacological benefits.
Moreover, in the context of HIV/AIDS, the situation is further complicated because drug interactions are a reality even among synthetic drugs. Many plant extracts inhibit cytochrome P450 (CYP3A4) metabolism and P-glycoprotein transport and will thus likely interact with protease inhibitors (PIs) and nonnucleoside reverse transcriptase inhibitors (NNRTIs) [1, 2].

Cost-effectiveness

Pharmaceutical remedies often cause side effects during the treatment of viral infections. Previous studies have shown that viral replication of herpes simplex virus (HSV), influenza virus, feline infectious peritonitis virus (FIPV), human immunodeficiency virus (HIV), and avian influenza A virus H5N1 can be controlled by medicinal plants. Medicinal plants can improve the immune system and potentially control viral infections. A large number of medicinal plants have been screened for in vitro and in vivo antiviral activity, but only a few have shown promising effects [2]. Extracts of medicinal plants can be administered orally or topically according to the clinical symptoms of the patients and the body parts affected by the virus. In many developing countries, medicinal plants are cheap and inexpensive compared to synthetic drugs [2].

Future Directions in Research

Integration of modern biotechnological techniques, traditional or indigenous ethnomedical knowledge, and the application of the concepts of synergy and network pharmacology can enhance the development of safe, accessible, and affordable antiviral medicines from plants [1, 13]. An approach based on combinatorial and networked concepts may also overcome the rapid rate of viral resistance, a major challenge associated with the use of a single antiviral drug. Medicinal plants can play a crucial role in the design of prophylactic or therapeutic antivirals, from the first-line barrier to the immune defensive system [1]. Though medicinal plants have demonstrated antiviral activity against HIV associated with their in vitro inhibition of HIV enzymes, only a small number of antiviral plant-derived products have reached the commercial market, with none yet specifically developed for the treatment of HIV infections. Sufficient data confirm that phytomedicines are valuable sources of compounds essential for the design and development of both anti-HIV and non-HIV antivirals [3].

Innovative Extraction Techniques

Over the last decades, advances in the extraction and formulation of natural compounds have been made. For maximum bioactive performance and therapeutic action, it is necessary to find new technologies to ensure the maximal extraction of effective compounds within medicinal plants. Traditional solvent extraction methods often require large quantities of organic solvents, long exposure, and high temperatures, leading to the formation of artefacts during extraction [2, 3]. Techniques using ionic liquids (ILs) and eutectic solvents (ESs) have been proposed as greener alternatives to replace volatile organic solvents. Monoterpenes, such as limonene and β-pinene, have been considered as solvents in natural product extraction due to their attractive low toxicity and moderately polar aprotic nature. Environmental concerns are forcing the exploitation of more efficient, environmentally friendly, easy-to-use solvents that offer the possibility of direct application in the pharmaceutical or food industries. The use of innovative techniques, such as supercritical fluid extraction, pressurized liquid extraction, microwave-assisted extraction (MAE), or ultrasound-assisted extraction, not only helps increase the extraction yields of natural products but also reduces the limitations, disadvantages, and risks of traditional methodologies throughout the process. Among these, MAE is considered an excellent process intensifier due to the significant reduction in temperature, extraction time, and solvent quantity [1, 3].

Synergistic Effects

Synergy represents the interaction or cooperation of two or more substances to enhance the overall effect. In October 2020, a phase II clinical trial (NCT04574254) commenced to investigate the synergistic combination of Echinaforce® oral spray, an Echinacea purpurea L. herbal preparation, and Angelica sinensis polysaccharide in preventing and treating upper respiratory tract infections (Common Cold)[1, 11]. Despite its vast pharmacopoeia, the largest manufacturers of antiviral herbal products have yet to exploit Echinacea and Elderberry, the top sellers in formulations of their leading ingredients, although bioactivities and sales projections support such strategies, which probably apply to other natural antivirals [1]. Synergistic herbal combinations should be designed to amplify the activity of the main ingredient at the lowest possible dose and maintain the broad spectrum of response to multiple viral targets [11]. To distribute herbal antivirals widely, antibacterial and antifungal components of these mixtures should not affect the oral microflora in the long term.

Personalized Medicine Approaches

Personalized medicine represents a promising strategic approach for developing natural antiviral agents. Broad-spectrum plant agents offer distinct advantages for managing emerging viral infections. A personalized synergy approach becomes important, focusing on techniques such as metabolomics, proteomics, microarray gene expression, and bioinformatics. By targeting specific receptors, enzymes, or viral components, personalized herbal drugs could offer enhanced slowdown of viral proliferation and mitigate drug resistance [12]. Studies demonstrate that selected natural active components specifically acting on influenza A viral receptor neuraminidase can significantly slow viral resistance development. In combination with molecular methods, personalized medicine has the potential to transform natural antivirals into routine therapeutic agents. Progress in personalized medicine transforms the disruption of resistance-associated genes in host cells, and the development of prodrugs can also lead to improved broad-spectrum antiviral therapeutics [2].

Case Studies of Specific Viruses

Medicinal plants with antiviral activities beyond HIV exert their effects via inhibition of viral entry, interference with viral replication, and modulation of immune responses [1, 2]. Competitive inhibition of viral attachment and entry can be achieved by phytochemicals that mimic cellular receptors or block receptor sites on the virion. Agents that interfere with replication act by mechanisms such as degradation of viral nucleic acids, direct inhibition of replicating enzymes, or prevention of viral assembly and release. Immunomodulatory effects result from acceleration of humoral and cellular responses, either by independent stimulation or enhancement of antiviral activity [1]. Under the umbrella of medicinal plants with antiviral potential beyond HIV, roles ascribed to several species are considered below in relation to individual virus types where traditional use or supportive data allow some degree of discrimination [2].

Influenza

Medicinal plants are rich sources of chemical compounds that have been used for the treatment of many infectious diseases. The increasing resistance to current antiviral drugs calls for the screening of medicinal plants for novel antivirals. Evaluation of South African medicinal plant extracts for cytotoxicity and antiviral activity against influenza A virus was carried out in vitro 22. Of the 22 plants screened, seven showed antiviral activity at concentrations ranging from 0.016 to 0.13 mg/mL, with the highest activity seen in Maesa lanceolata and Hypericum roeperianum. Erythrina lysistemon, Erythrina humeana, Markhamia obtusifolia, and Calpurnia aurea also exhibited inhibitory effects. The antiviral activity of most of these plants was reported for the first time. None of the extracts prevented haemagglutination (virus attachment to host cells), suggesting their involvement in later stages of the viral replication cycle to reduce viral nucleoprotein expression [7]. Herbal medicines are promising alternatives to conventional antiviral drugs for the treatment of infectious diseases associated with influenza modulation. According to the World Health Organization (WHO), viral infections are considered a global threat, especially in countries where proper health facilities are unavailable. Medicinal plants provide an alternative source for the treatment of influenza infections [12]. Screening of traditional medicinal plants for anti-influenza virus activity showed that some plants act via a unique mode of action compared to currently available antiviral drugs. The development of herbal medicines based on such plants could provide a third generation of anti-influenza compounds, which would be extremely beneficial in the event of an influenza pandemic.

Herpes Simplex Virus

Herpes simplex virus (HSV) infections constitute a significant public health burden worldwide. HSV-1 seroprevalence approaches 95% in global populations. Reactivation of latent infection can elicit mucosal lesions, as observed in oral and genital herpes, or provoke severe ophthalmitis and life-threatening infections among immunocompromised individuals or neonates [13]. No licensed vaccines have reached the market. The antiviral arsenal primarily comprises DNA-polymerase inhibitors such as acyclovir, valacyclovir, and penciclovir. However, resistance emerges, particularly in immunosuppressed patients: for instance, 5 to 10% of immunocompetent patients exhibit resistance after prolonged acyclovir therapy, while rates surge to 14% or higher among HIV/AIDS patients and transplant recipients [14]. Resistance stems mainly from thymidine-kinase gene mutations comprising deletions, frameshifts, or point mutations that diminish susceptibility without adversely affecting viral fitness. Alternative agents target the viral DNA helicase-primase or DNA-polymerase complex of HSV; yet, persistent side effects constrain their clinical adoption [15]. This scenario engenders an urgent demand for novel, effective, tolerable therapeutics. Natural products cultivated as medicinal herbs characterized by substantial but not fully elucidated viral inhibitory activities provide a promising reservoir for treating resistant HSV infections. Investigations spanning 1996 to 2021 have catalogued a multitude of natural compounds with dampened viral-replication efficacy [14, 15].

Hepatitis C

Hepatitis C remains a major health issue despite the availability of new therapies, with a persistent risk of developing cirrhosis and liver cancer [16]. Several medicinal plants are employed worldwide against hepatitis C virus (HCV) infections, including Cajanus cajan, Cleome viscosa, Croton tiglium, Cissus quadrangularis, Eclipta alba, Glycyrrhiza glabra, Glycyrrhiza uralensis, Nigella sativa, Phyllanthus amarus, Phyllanthus urinaria, and Quercus infectoria [17]. Screening of plant extracts used in traditional medicine for the treatment of jaundice identified the two most active ones: the leaves of Carapa procera and Pericopsis laxiflora. Hydro-ethanolic extraction of leaves collected at the beginning of the rainy season optimised the extraction of anti-HCV tannins, and analyses of their composition provided information on the molecules that could be responsible for the antiviral activity [16, 17].

Global Perspectives on Medicinal Plant Use

The use of medicinal plant extracts and phytochemicals with antiviral properties constitutes an important approach to combat viral infections worldwide. Several hundred plants have been traditionally used for the treatment of viral disorders [17]. The most widespread viruses include herpes simplex virus, respiratory syncytial virus, influenza virus, human immunodeficiency virus, severe acute respiratory syndrome coronavirus, hepatitis C virus, and dengue virus. In addition to herbals with known or putative antiviral properties, supporting remedies such as immune stimulators, rejuvenators, and other therapeutics effective during viral infection are also explored. Approximately 80% of the world's inhabitants rely on traditional medicines that mainly originated from plants [3]. According to the World Health Organization (WHO), about 85% of traditional medicines involve the use of plant extracts. Medicinal plants remain an invaluable health resource and provide mankind with new remedies, rich pharmacophores, and novel drugs [3].

Cultural Significance

Medicinal plant use transcends cultural and ethnic boundaries. Indigenous knowledge of plants and their healing powers, transmitted across generations, forms the basis of several therapeutic interventions. As an example, Azadirachta indica has played a vital role in the traditional medicine of the Indian subcontinent for more than two thousand years. In these and many regions of the world, plants continue to be employed in daily life for both prophylaxis and treatment of a variety of ailments [2]. The medicinal use of herbs and plants against viruses has been observed across numerous ancient civilizations. For example, Chyawanprash Jamun provides beneficial effects when administered against HIV [1]. The ancient Egyptian papyri listed numerous plant species employed to treat cancer, infections, and inflammation, as well as anti-parasitic and antibacterial. The Chinese Compendium of Materia Medica, the oldest and largest pharmacopeia of traditional medicines, provides an index of medicinal plants and their constituents that have been used against infections. The Ayurvedic medicine also lists several plant species for treating viral infections, including plants such as Berberis aristata and Azadirachta indica [1,2, 3].

Regulatory Frameworks

Biodiversity forms the foundation of traditional medicine, a complex mixture where nature provides not only medicinal plants but also waves of viruses and bacteria. These categories are commonly associated with serious infections, including HIV, AIDS, herpes, hepatitis, influenza, dengue, chikungunya, Ebola, and coronavirus. Scientific literature is abundant on the use of medicinal plants against HIV, AIDS, or infections with HIV antigens. Nevertheless, many plants capable of controlling other viral diseases have yet to be scientifically reported. A careful classification of antiviral properties and related mechanisms of medicinal plants is presented. Antiviral properties are grouped according to several mechanisms of action, including inhibition of viral attachment and entry into host cells, inhibition of viral replication, inhibition of viral enzymes, and modulation of the host's immune system [1]. Such classification provides a clearer picture for deeper studies and suggests appropriate properties for the treatment of specific viral diseases. Several medicinal plants are traditionally used worldwide to combat various viral diseases, reshaping societal life and the economy [2]. Herbal remedies such as Echinacea, Elderberry, Garlic, Ginger, and Turmeric are the most commonly used traditional cures for viral infections. Additionally, some seaweed and their extracts have demonstrated potent antiviral effects both in vitro and in vivo. Clinical trials on these natural remedies have confirmed their ability to activate the immune system, thereby strengthening the body's defense against viral infections. Recent studies have identified several phytochemicals in these plants that contribute to their antiviral effects. Several challenges, including a lack of standardization, poor bioavailability, and ethical concerns, have delayed the clinical application of such valuable herbal drugs [7].

Integration of Traditional and Modern Medicine

One inspiring model for better integration is China's convergence of traditional Chinese and Western medicines to combat viral infections, notably COVID-19 [1, 11]. Acceptance of therapeutic modalities, medicinal agents, or practices depends on cultural values, philosophy, individual experience and outcome, and sometimes on regulatory

statutes and economic interests. Given the promising antiviral potential of natural products, especially herbal medicines, further developing appropriate systems for the integration of traditional antiviral and modern medicines holds great promise [11].

Public Health Implications

Expanded and improved knowledge of antiviral medicinal plants beyond HIV will broaden awareness of plant targets as well. Although the vast majority of the currently known antiviral plants were initially investigated as aids to prevent or treat infection with human immunodeficiency virus (HIV) [2], a far greater number of plants have repeatedly demonstrated activity against a diverse panel of pathogenic viruses [1], and numerous others continue to emerge from ongoing screening efforts. The urgent need to bring greater attention to the full antiviral potential of medicinal plants, their candidate formulations, and isolated natural products is therefore clear. Crossing the threshold beyond HIV represents the point at which this potential can finally be recognized and refined to uphold the original promise of antiviral plants to safeguard and improve the health of populations worldwide [1, 2]. Wider consideration would also help to address issues currently responsible for the continued neglect of antiviral plants. Most obviously, people tend to rely primarily on pharmaceutical antivirals during an outbreak or pandemic, overlooking existing plant remedies. Even when such products can be obtained, many users are unaware of the options offered by medicinal plants, which would also benefit from greater public awareness. Expanded discussion throughout the public media, including general news, health bulletins from official bodies, and the circulation of documentaries regarding the use of phytomedicines and their relationship with conventional treatments, would offer a straightforward means to generate such awareness and educate the world's population [1].

Accessibility of Medicinal Plants

The accessibility of medicinal plants is probably one of the reasons for their unsatisfactory investigation, because it is necessary to collect their fruits, flowers, roots, or barks at specific times. The country in which they grow and even the age of the living plant may be important. Another issue is the fact that plants are poorly standardized in comparison with active substances isolated from them, whose antiviral efficiency can be tested quantitatively with reliable results [1]. The biological effects of an extract also depend on the area in which the plant was grown and the time of harvesting. Many plants used as potential antiviral remedies are available in the West and are often grown as common vegetables, including onions, garlic, and ginger. This is especially true concerning treatments in the less-developed countries of the world. In fact, the nutraceutical values of these plants are the main reasons for the large interest in the revealed antiviral properties of their extracts, because they are popular in some countries, such as Turkey, for many illnesses [1, 2]. It is also of great public interest to some people because they are cheaper and easier to use than drugs prescribed by physicians. However, some users may be unaware of the possible adverse effects of these plants or of the fact that they act to inhibit the replication of a limited number of viruses only.

Awareness and Education

A major constraint in the use of medicinal plants in traditional health systems in developing countries is the lack of awareness in the general public. Ayurvedic products are not only free of side effects but also very cheap, unlike expensive and chemically oriented allopathic medicines [1]. The second important point is the lack of sufficient knowledge about the effectiveness of alternative systems of medicine among scientists. Research initiatives are necessary with the objective of collecting comprehensive scientific data on the safety and efficacy of herbs and herbal products. Particular attention also should be given to herbal drugs for the prophylaxis and treatment of viral diseases [4]. Finally, the medicinal values of the plants can become more extensively used only if they are accepted by society as a part of the medical system. The main drawback of the different herbal systems of treatment is the lack of control over them by any central authority, such as a national drug regulatory policy and administration. However, the recent increases in awareness of the safety aspects of synthetic drugs and the introduction of WHO-advocated support for herbal medicine have contributed to establishing medicinal plants as a business [5, 18, 19].

CONCLUSION

Medicinal plants have demonstrated immense potential as sources of antiviral agents, extending far beyond their well-documented activity against HIV. Evidence from in vitro, in vivo, and clinical studies reveals that bioactive phytochemicals can inhibit viral entry, interfere with replication, and modulate host immune responses, offering promising alternatives to conventional antivirals. Plants such as Echinacea, Elderberry, Garlic, Ginger, and Turmeric exemplify this potential, with diverse mechanisms targeting influenza, herpes simplex virus, hepatitis C, coronaviruses, and other emerging pathogens. Despite the challenges of standardization, bioavailability, safety evaluation, and ethical considerations, continued research integrating ethnomedicine, biotechnology, and pharmacology underscores the relevance of medicinal plants in addressing global viral threats. By advancing

innovative extraction methods, synergistic formulations, and personalized medicine approaches, phytomedicine can complement or even surpass conventional therapies, particularly in resource-limited settings. Ultimately, medicinal plants represent a cost-effective, culturally significant, and sustainable avenue for expanding the antiviral armamentarium worldwide.

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